EAST MIDLANDS CLINICAL ADVISORY GROUP

FOR HEPATO-PANCREATO-BILIARY CANCER SERVICES

CLINICAL GUIDELINES AND OPERATIONAL POLICY

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Ratified:

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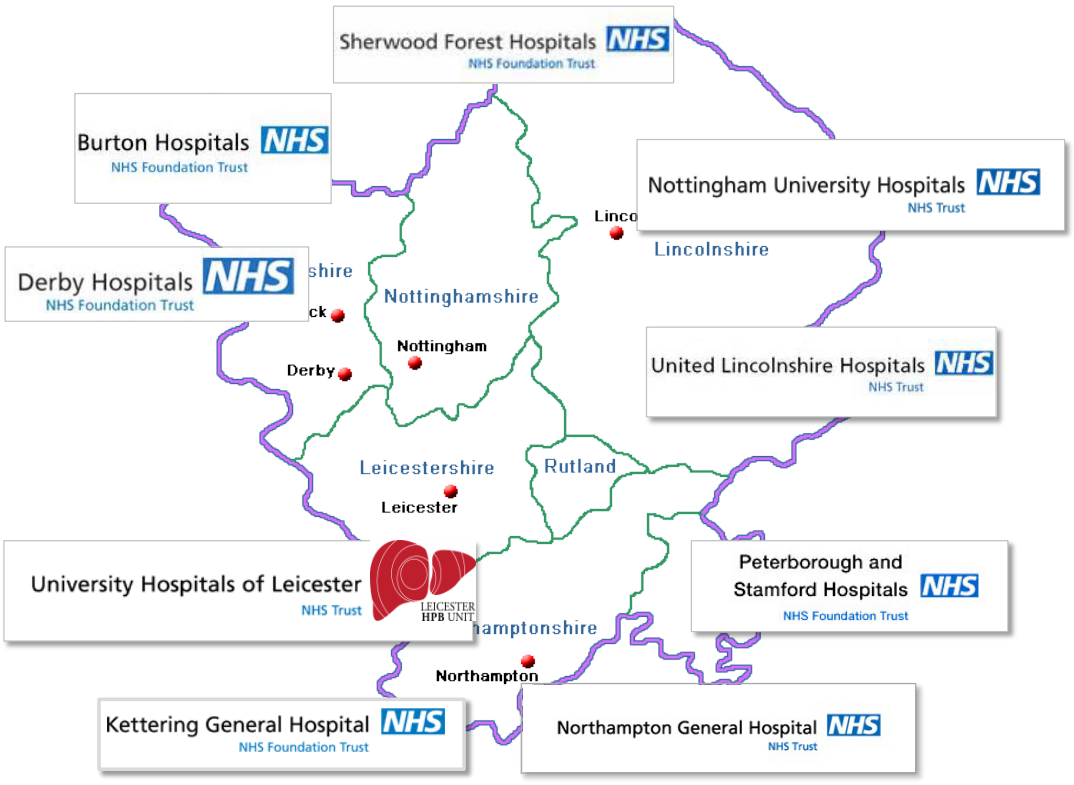

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NETWORK CONFIGURATION (13-1C-101n)

The East Midlands Network superseded the previous NSSG and held its first meeting on the 13th August 2014. The network comprises of two specialist MDTs; Nottingham and Leicester which undertake pancreatic and liver resections for the East Midlands; a combined population of between 4 to 5 million. Both units undertake 80 pancreatic surgical procedures and 150 liver surgical procedures for neoplastic disease or suspected neoplastic disease annually. The chairs of the Nottingham and Leicester sMDTs are Mr Deep Malde (Leicester) and Mr Dhanny Gomez (Nottingham). Each specialist MDT has a population of around 2.5 million. Both sMDTs link with their local diagnostic teams and colorectal MDTs, in addition to the MDTs from surrounding localities in the East Midlands.

There are local diagnostic teams for Upper Gastro Intestinal Cancer, to which GP referrals should initially be made, in each of the localities within the Network. In Lincolnshire these are at Lincoln, Boston and Grantham: in Central Nottinghamshire this is at Kings Mill Hospital; in Nottingham this is at Queens Medical Centre and Nottingham City campuses. In the south of the East Midlands; these are in Northampton, Kettering and the Leicester Hospitals. Peterborough is also included. These local teams may also treat certain patients offering local chemotherapy and palliative care where agreed through the specialist team. These arrangements are summarised in the Table below. The surrounding diagnostic teams and their MDTs provide Level II and III care as appropriate with support from the sMDTs.

Table 1: **Local diagnostic teams for HPB**

Locality	Hospital Site	Lead Clinician
Lincolnshire	Pilgrim Hospital, Boston	Dr M Perry
	Lincoln County Hospital & Grantham	Mr D Andrew
Central Notts	Kings Mill Hospital, Mansfield	Dr N D Wight
Derby	Royal Derby Hospital	Dr A Austin
Burton	Queens Hospital	Dr Altaf Palejwala
Northants	Northampton General	Mr Guy Finch
	Kettering General	Mr Mark Taylor
Peterborough	Peterborough District Hospital	Dr K McAdam

Each locality refers exclusively to its specialist MDT according to service line agreements between trusts. Resection and some aspects of major palliative surgery are provided by the tertiary referral centres (Leicester and Nottingham). The local teams treat certain patients offering local chemotherapy and palliative care where agreed through the specialist team. Interventional procedures such as complicated biliary drainage and biopsies may also be provided by the local area team with sMDT support.

NETWORK GROUP MEMBERSHIP (13-1C-102n)

The lead ECAG chairperson is Mr Giuseppe Garcea (HPB Surgeon Leicester) who was appointed in April 2014 for a tenure of 3 years. Other members are detailed in the table below and meet Network Group guidelines **(Table 1 and 2).**

Table 2: ECAG Positions

ECAG POSITION	DESCRIPTION	EXPRESSION OF INTEREST	PRESENT JOB	EMAIL ADDRESS
ECAG LEAD	ECAG LEAD	Giuseppe Garcea	HPB Surgeon	giuseppe.garcea@uhl-tr.nhs.uk
ECAG DEPUTY	ASSIST ECAG LEAD AT MEETINGS WHERE ECAG LEAD UNABLE TO ATTEND. PROVIDE LOCAL REPRESENTATION FOR LOCALITIES NOT IN CLOSE CONTACT WITH ECAG LEAD	Dhanny Gomez	HPB Surgeon and MDT Chair	dhanny.gomez@nuh.nhs.uk
CLINICAL TRIALS LEAD	REPORT ON PRESENT AND NEW RESEARCH TRIALS	Professor Will Steward	Oncologist	wps1@le.ac.uk
EDCUATION LEAD	CO-ORDINATE EDUCATION COMPONENT FOR FUTURE MEETINGS	Iain Cameron	HPB Surgeon	iain.cameron@nuh.nhs.uk
PATIENT REPRESENTATIVE 1	PATIENT ISSUES, INFORMATION AND FEEDBACK	Ann Micklewright	Patient Rep	Ann.micklewright@nhs.net
PATIENT REPRESENTATIVE 2		*TBC	TBC	TBC
USER ISSUES REPRESENTATIVE	SPECIFIC RESPONSIBLITY FOR USER ISSUES AND INFORMATION DELIVERY	Cris Pollard	CNS	cristina.pollard@uhl-tr.nhs.uk
AUDIT LEAD (EAST MIDLANDS NORTH)	RESPONSIBLE FOR CONDUCT AND CO-ORDINATION OF NETWORK AUDIT	Alex Navarro	HPB Sugeon	alex.navarro@nuh.nhs.uk
AUDIT LEAD (EAST MIDLANDS SOUTH)		Giuseppe Garcea	HPB Surgeon	giuseppe.garcea@uhl-tr.nhs.uk

* *Training to be organised for future patient rep*

Table 2: ECAG Positions for Local Representation

ECAG POSITION	DESCRIPTION	EXPRESSION OF INTEREST	PRESENT JOB	EMAIL ADDRESS
CORE MEMBER BURTON*	Attend at least one ECAG meeting annually. Provide feedback and input on policy decisions and guidelines. Report on areas for concern across the East Midlands	Sarah Johnson	Clinical Nurse Specialist	Sarahjohnson10@nhs.net
CORE MEMBER DERBY*		Dr Andrew Austin	Consultant Hepatologist and Lead Clinician in Gastroenterology	Andrew.austin1@nhs.net
CORE MEMBER NOTTINGHAM*		Mr Iain Cameron	HPB Surgeon	iain.cameron@nuh.nhs.uk
CORE MEMBER LINCOLN*		Dr Pradeep Sanghi & Mr David Andrew	Consultant Gastroenterologist Consultant General Surgery	Pradeep.Sanghi@ulh.nhs.uk & David.andrew@ulh.nhs.uk
CORE MEMBER BOSTON*		Lisa Dichmont	Macmillan Upper GI Nurse	Lisa.Dichmont@ulh.nhs.uk
CORE MEMBER KINGS MILL*		Misrat Shah	Consultant Gastroenterologist	sharat.misrat@sfh-tr.nhs.uk
CORE MEMBER PETERBOROUGH*		Dr Karen Macadam	Oncologist	Karen.mcadam@pbh-tr.nhs.uk
CORE MEMBER KETTERING*		Monica Palmer & Mr Mark Taylor	Cancer Nurse Specialist Consultant GI/Laparoscopic & General Surgeon	monica.palmer@nhs.net mark.taylor@kgh.nhs.uk
CORE MEMBER NORTHAMPTON*		Mr Guy Finch	Upper GI Surgeon	guy.finch@ngh.nhs.uk
HEPATIC SURGEON*		Mr Dhanny Gomez	HPB Surgeon and MDT Chair	dhanny.gomez@nuh.nhs.uk
PANCREATIC SURGEON*		Mr Ashley Dennison	HPB Surgeon	Ashley.dennison@uhl-tr.nhs.uk
RADIOLOGIST*		Dr Rajeev Singh	Consultant Radiologist	Rajeev.singh@nhs.net
ONCOLOGIST*		Professor Will Steward	Oncologist	wps1@le.ac.uk
HISTOPATHOLOGIST*		Dr Philip Kaye	UGI Histopathology Lead	Philip.kaye@nuh.nhs.uk
HEPATOLOGIST/GASTROENTEROLOGIST*		Dr Andrew Austin	Consultant Hepatologist	Andrew.austin1@nhs.net
HPB CANCER NURSE SPECIALIST*		Cris Pollard and Sophie Noble	CNS	cristina.pollard@uhl-tr.nhs.uk sophie.noble@uhl-tr.nhs.uk

The role of the ECAG group is to:

- Provide a clinical opinion on issues related to parity and deliver of cancer care through the East Midlands network.
- Aid and develop patient pathways and clinical guidelines
- Co-ordinate cancer policy and practice guidelines
- Participate in research , audit and service development
- Consult with “cross-cutting” networks groups
- Evaluate the patient experience in their cancer pathway
- Provide support and liaise with commissioning groups

The role of the ECAG chair is to:

- Co-ordinate at least two annual meetings for the ECAG group
- To ensure parity of healthcare across the East Midlands
- To “horizon scan” for new developments and innovations
- To liaise with the HPB Clinical Reference Group

NETWORK GROUP MEETINGS (13-1C-103n)

The last ECAG network meeting was on the 13th August 2014. The next meeting will be in March 2015. It was decided that education (although a direct remit of the ECAG group) should also form a component of the meeting.

WORK PROGRAMME AND ANNUAL REPORT (13-1C-104n)

The network group should produce an annual work programme in discussion with the strategic clinical network (SCN) Clinical Director and Network Manager and agreed with Medical Director NHSE Sub-region. It should include details of any planned service developments and should specify the personnel responsible and the timescales for implementation. The network group will produce an annual report for the SCN and relevant area team.

CLINICAL GUIDELINES (13-1C-105n)

MANAGEMENT OF PATIENTS WITH SUSPECTED PERIAMPULLARY CANCER

Diagnosis

- All patients for whom there is clinical suspicion of pancreatic cancer or evidence of a dilated duct (stricture) should undergo initial evaluation by CT.
- Decisions regarding resectability will be made a sMDT. An initial decision regarding resectability can be made at a diagnostic locality **IF** attended by an HPB surgeon, but these decisions will also be later ratified at the sMDT.
- Pancreas specific MRI could be considered for further information or in contrast-allergic patients.
- PET/CT will not be routinely used in staging or diagnosis, although some patients may benefit.

Pancreatic Cancer Staging

Resectable

- Absence of distant metastases
- Arterial : Clear fat planes around CA, SMA, and HA
- Venous: No SMV/portal vein distortion

Borderline resectable

- Absence of distant metastases
- Arterial: Gastroduodenal artery encasement up to (but not including) the hepatic artery. Tumour abutment of the SMA not to exceed greater than 180 degrees of the circumference of the vessel wall
- Venous: Involvement of the SMV or portal vein with distortion or narrowing of the vein of less than 180 degrees. Sufficient distal and proximal vein length to allow reconstruction.

Unresectable Locally

- Arterial: Aortic invasion or encasement.
- Pancreatic head—More than 180º. SMA encasement, any CA abutment.
- Pancreatic body/tail—SMA or CA encasement greater than 180º.
- Venous: IVC encasement. Unreconstructable SMV/portal vein occlusion

Metastatic

- Evidence of distant metastases (loco-regional lymphadenopathy is excluded).

Positive histology and cytology are essential for confirmation of a diagnosis of PC and are particularly important in patients who are undergoing neo-adjuvant protocols, for those entering clinical trials and for patients with locally advanced or metastatic disease being considered for palliative chemo-(radio-) therapy. Tissue diagnosis should, however, not delay surgery for a suspected resectable cancer, provided the MDT considers the presentation to have sufficient suspicion of cancer5.

Options to obtain a tissue diagnosis are biliary brushings at ERCP, EUS-FNA or percutaneous (CT- or ultrasound-guided) or laparoscopic biopsy of primary or metastatic lesions. There is a risk of tumour seeding with some techniques, so surgical assessment of resectability should be established prior to a biopsy or FNA being performed. All patients should be seen by a dedicated key worker (CNS: Clinical Nurse Specialist) at the first clinical encounter with clinicians when the diagnosis of pancreatic cancer is mentioned. This ensures a contact with a dedicated clinical team member who can follow the patient throughout their entire journey of care and expedite across any bottle-necks should they occur.

Preoperative Biliary Drainage or Definitive Biliary Drainage

The ERCP route is usually favoured above percutaneous drainage for low bile duct strictures. There is no proven benefit of routine PBD prior to surgery, therefore if logistics allow patients should proceed to exploration +/- resection. Routine use of metal biliary stents should be avoided due to the cost involved, although they are proven to have a greater duration of patency.

Nutritional Assessment

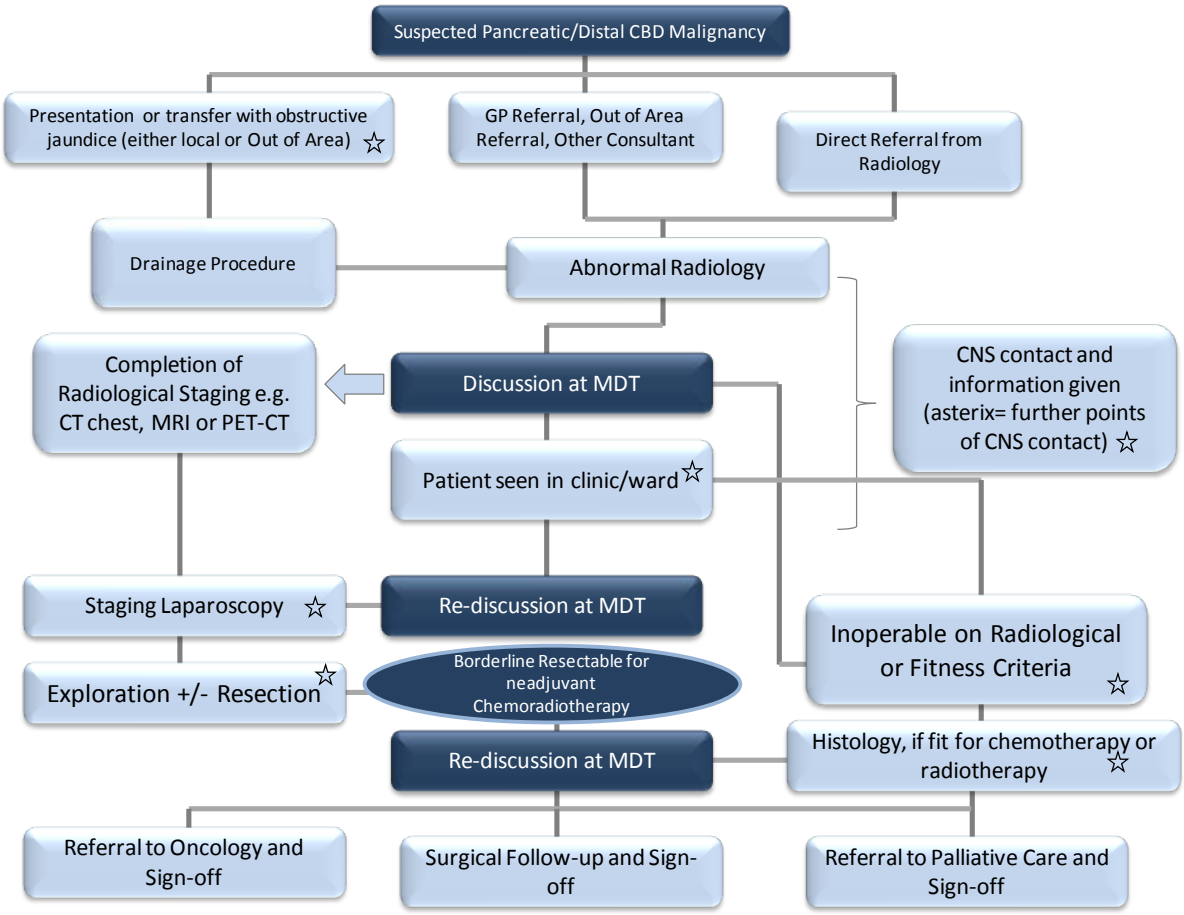
Once the diagnosis has been confirmed all patients should be screened for unintentional weight loss to identify those at nutritional risk and in need of nutrition support pre- treatment.

Weight loss is calculated as a percentage of pre-illness weight: % Weight loss = Usual weight (kg) – Current weight (kg) x 100 Usual weight (kg). 10% weight loss within the last 6 months is classified as clinically significant and a referral to the dietician is recommended. Such weight loss has been associated with negative outcomes post operatively. All patients should also have their BMI calculated. Patients will be routinely be seen by a dietitian prior to resection surgery to ensure optimisation of their nutritional status.

Surgical Resection

Pancreatic resection surgery will be performed in either Leicester or Nottingham by an appropriate HPB surgeon who has undertaken sufficient numbers annually to satisfy Peer Review criteria. Selected patients considered high-risk for surgery either in terms of co-morbidity or in terms of complexity of surgery should be considered for Cardio-pulmonary exercise testing (CPET) for high-risk anaesthetic assessment. Surgical patients are managed on HDU/ITU in immediate post-operative period. There is in place 24 hour HPB consultant cover at both sites for unexpected post-operative complications **(Figure 1).**

Figure 1: **Overview of Periampullary Malignancy Pathway**



EUS is a pivotal resource in assessing equivocal lesions of the pancreas and in obtaining preoperative diagnosis of malignancy (if this is required in high risk patients or those requiring neoadjuvant chemotherapy/chemoradiotherapy).

A standard or a pylorus preserving pancreaticoduodenectomy will be performed with regional lymph node clearance. Tumours in the body or tail are offered a distal pancreatectomy and splenectomy following appropriate immunization. In selected instances, spleen preserving surgery may be carried out. Portal vein resection and reconstruction is occasionally performed in patients with locally advanced tumours of suitable fitness. In cases where the tumour is found to be unresectable a biliary and gastric bypass is usually performed. Intraoperative confirmation of malignancy will always be sought in cases of bypass, but at the surgeon's discretion for resectable tumours. Where applicable, the

pancreatic transection margin will be sent for “frozen” histology to ensure that it is clear from cancer.

Enhanced Recovery

Leicester has an enhanced recovery programme in place for pancreatic resections and Nottingham has plans to implement such a programme for its pancreatic resection patients. This is considered best practice and should in place in all centres.

Discharge, Follow-up and Community Support

Specific follow-up arrangements for local patients will be agreed at MDT meetings. These guidelines include arrangements for patients who are referred to the MDT but are found to be unsuitable for specialist care.

Resected Patients

- Surgical review 2 to 6 weeks following discharge, provided on day of discharge to facilitate patient choice
- Oncology review regarding adjuvant chemotherapy.
- There are no clear guidelines regarding post-operative follow-up. The exact method will vary after discussion with patient and relatives. Follow-up may include 6 monthly CA19.9 and clinical review (Notthingham) or 6 monthly USS with CA19.9. The most intensive follow-up regimen will be CT scan 6 monthly for first two years and then yearly until 5 years
- CA19-9 levels at each clinic visit
- Monitoring of exocrine and endocrine pancreatic insufficiency and treat where required.

Un-resected Patients

Review by Oncology team at cancer centre during in-patient stay or appointment with cancer unit oncologist from two weeks following discharge from hospital (see later for chemotherapy protocols). During oncology clinic visit arrangements made with community palliative care team and/or hospital or community follow-up will be dependent on plans for therapy, patient needs and availability of community support. Before discharge support in the community is always considered. This could be referral to local district nurses; various professionals allied to medicine, or in the majority of cases specialist palliative care teams. The nurses in the hospital, clinic and the consultant nurse in palliative care have responsibility to ensure that appropriate referrals are made and that patients and their carers have information on who, when and how contact will be made prior to their discharge home.

MANAGEMENT OF BILIARY AND GASTRIC OBSTRUCTION IN NON-RESECTABLE DISEASE

Symptoms related to biliary obstruction in unresectable disease may be palliated by insertion of a biliary endoprosthesis. Stenting procedures resulting in adequate biliary drainage improve survival.

- In patients with unresectable disease, metal stents have greater patency rates and are associated with fewer ERCPs, shorter hospital stay and fewer complications, compared with plastic stents. However, their cost precludes their routine use in all patients. In those patients where ERCP is not feasible, percutaneous drainage should be considered.
- Uncovered metal stents should not be deployed for biliary strictures prior to an MDT decision being made on resectability and histological/cytological confirmation of malignancy obtained.

- In the case of cholangitis or decrease in total bilirubin level of <20% from baseline at 7 days post stent insertion, repeat imaging and urgent endoscopic revision should be considered.
- For patients with jaundice and potentially resectable disease who are found to have unresectable tumours at laparotomy, an open biliary-enteric bypass +/- gastrojejunostomy provides durable palliation.
- Patients with locally advanced or metastatic disease and a short life expectancy or poor performance status who develop gastric outflow obstruction may be palliated with an endoscopically placed enteral stent.
- For a fit patient with locally advanced disease, an open or laparoscopic gastrojejunostomy may provide more durable and effective palliation than an enteral stent.

MANAGEMENT OF PATIENTS WITH SUSPECTED INTRAHEPATIC CHOLANGIOCARCINOMA (IHCCA)

Diagnosis and Staging

- IHCCA most frequently arises in non-cirrhotic liver and presents as single or multiple intrahepatic tumours without evidence of other primary extra--hepatic tumours
- A biopsy is the gold standard tool to diagnose IHCCA in appropriate clinical and radiological setting.
- Review of histopathology and immunohistochemistry at the specialist HPB MDT is recommended for all cases.
- TNM staging has prognostic significance in IHCCA

Management

- Initial management for all patients with IHCCA should be guided by the sMDT
- Indication and selection for surgical management (the only potentially curative option) is the primary initial question to be addressed by the sMDT.
- Potentially resectable cases must be discussed at sMDT.
- Unresectable patients should be considered for palliative chemotherapy as indicated by the sMDT or for symptomatic palliative treatment

MANAGEMENT OF PATIENTS WITH SUSPECTED EXTRA-HEPATIC CHOLANGIOCARCINOMA

Diagnosis

- All patients with suspected hilar CCA should have blood tests analysed including simple biochemistry (including liver function tests), FBC, INR and serum CA19.9. CA19-9 is elevated in approximately 75% to 85% of patients with CCA and has a specificity of 50-80%. (in non-jaundiced patients). There is no evidence that measurement of tumour markers is useful for monitoring tumour progression
- IgG4 levels shall be obtained whenever an autoimmune cholangitis is suspected (eg, with evidence of more extensive cholangiopathy, abnormal pancreas or pancreatopathy, and/or evidence of associated distant autoimmune disease). When strongly suspected, ampullary biopsies for tissue IgG4 staining are positive in up to 70% of cases of IgG4 disease.
- Patients deemed potentially suitable for surgical resection should have staging CT of the chest and pelvis to exclude metastatic disease.
- PET scanning is usually not required for diagnosis or staging of CCA but may provide supportive information for some diagnostic difficulties such as the nature of distant lesions.

- Hilar CCA can be difficult to differentiate from benign causes of biliary stricture such as PSC, IgG4 disease an ischaemic bile duct injuries. If there is significant clinical concern about differential diagnoses then patients require thorough evaluation to confirm or exclude these conditions
- Serum (and tissue) IgG4 levels should be measured in all patients with multifocal strictures or evidence of disease in the pancreas or other distant organs
- Consideration for reaching confirmatory tissue diagnosis should be made for each potentially resectable case but this may not be required if alternative diagnoses are unlikely and/or if tissue sampling may compromise future surgical resection fields and risk tumour seeding.
- All patients planned for chemotherapy or other systemic therapy and all patients recruited into clinical treatment trials should have confirmatory tissue diagnosis prior to commencing therapy.
- Molecular testing of tissue samples (including advanced cytological tests such as FISH) are currently not clinically useful and done only as part of research studies.
- Reporting o cytology and histopathology specimen should be carried out by specialist pathologists with reporting by a second pathologist or review at the MDT in cases diagnostic or suspicious for cancer.

Staging

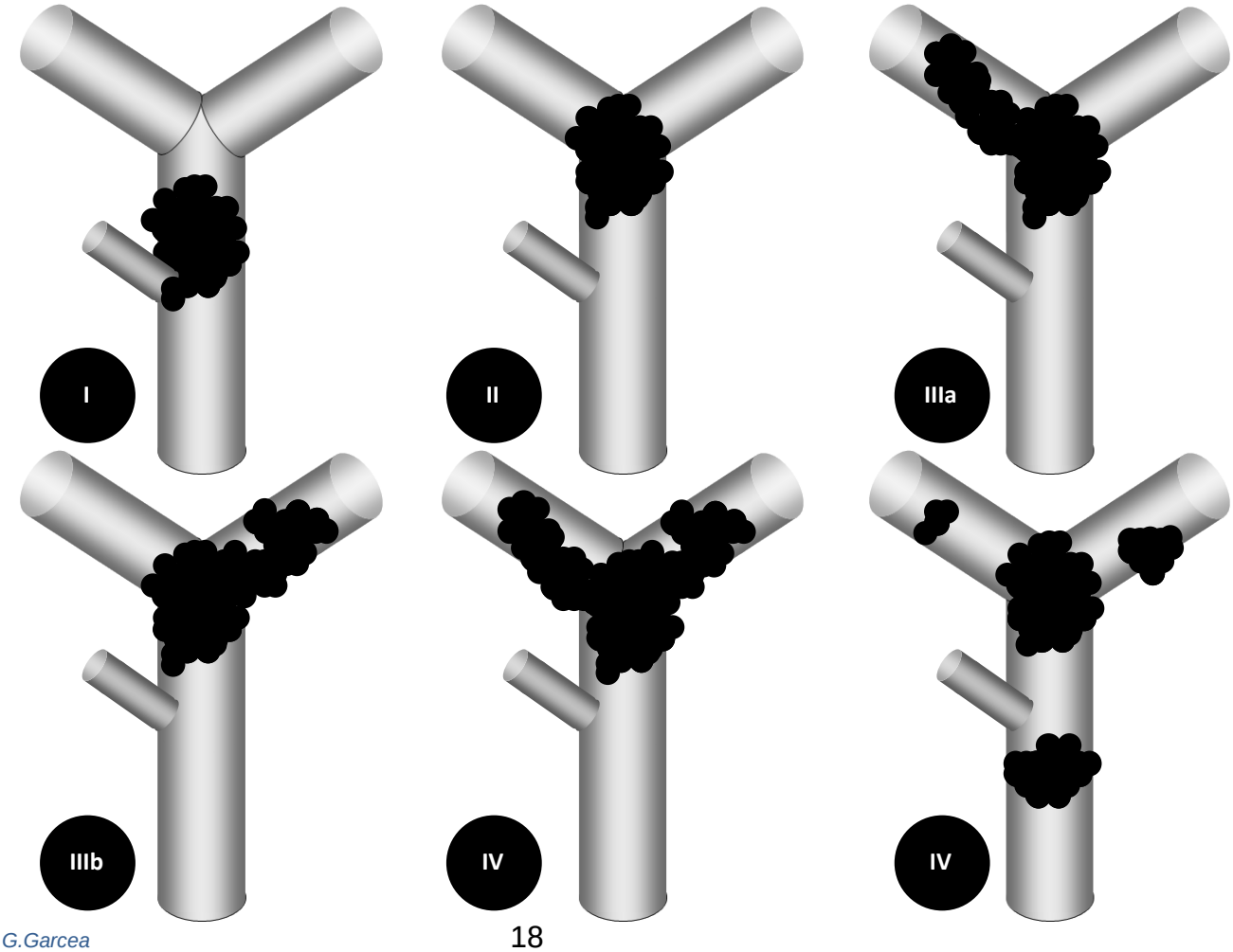
The TNM staging system is not effective or prognostically predictive in hilar CCA. The classification devised by Bismuth and Corlette (types I-IV) is still the most commonly used and clinically useful staging system **Figure 2**:

- MRI/MRCP is the optimal imaging to define local extent of tumour and presence of liver metastases, and accurately guides surgical resectability. It is however inferior to

CT at assessing distant metastases so these modalities should be used in tandem for potentially resectable patients.

- PTBD and/or ERCP allow sampling for cytology (+/- biopsy) and also stent insertion for palliative purposes in unresectable tumours.
- Cholangioscopy may be useful for targeted tissue sampling and macroscopic assessment of extent of tumour margins.
- Laparoscopy should be considered considered to determine the presence of peritoneal or superficial liver metastases where there is suspicion of extrahepatic peritoneal or superficial liver involvement.

Figure 2: **Bismuth Staging of Hilar Cholangiocarcinoma**



PTC / ERCP and biliary drainage

- Urgent biliary intervention is indicated for patients with cholangitis (and occasionally severe pruritis).
- Patients without these indications should be discussed at an sMDT meeting to guide future appropriate biliary intervention
- ERCP is ordinarily the route for sampling and drainage of distal bile duct strictures up to uncomplicated hilar strictures (Bismuth classification <II)
- Patients with proximal hilar strictures beyond the primary bifurcation (Bismuth >II) may require PTD for adequate guided drainage of appropriate liver segments as guided by the sMDT.
- A decision as to whether a patient requires biliary drainage for jaundice is usually guided by the sMDT as some cases (particularly distal CBD strictures) may be treated with pancreato-duodenectomy in the presence of significant but acute jaundice whereas patients undergoing liver resections or with a longer period of jaundice usually require effective relief of jaundice (bilirubin < x3 –x3 ULN) prior to surgery.
- Metal stents should not be deployed for hilar strictures prior to an MDT decision being made on resectability.
- The site (Right vs Left, sectorial or segmental) and extent of PTBD drainage should be directed by the sMDT once a possible surgical indication and plan have been drafted
- Patients due to have palliative treatments such as chemotherapy usually require effective drainage of jaundice (bilirubin < x2-x3 ULN)) before commencing other palliative treatments.
- Some complex hilar strictures with multiple intrahepatic sub-segmental obstructions may not be amenable to effective biliary drainage. Such cases need careful

consideration on appropriateness of intervention before attempting high risk drainage procedures.

- In inoperable patients with distal biliary strictures, metal stents have greater patency rates and are associated with fewer ERCPs, shorter hospital stay and fewer complications, compared to plastic stents.
- Removable fully covered SEMS may be considered for drainage of distal strictures of suspected CCA with or without prior confirmatory tissue diagnosis but should not be deployed across hilar strictures.
- Uncovered SEMS are suitable for palliation of hilar strictures but should only be used in patients with confirmed tissue diagnosis or as directed by the sMDT

Tissue Diagnosis

- Positive histology and cytology are often difficult to obtain, but are essential for confirmation of a diagnosis of CCA and are particularly important in patients who are not proceeding to resection and for those entering clinical trials.
- Tissue diagnosis should however not delay surgery for a suspected resectable cancer.
- It is usual to obtain biliary brushings at ERCP but this is positive in only approximately 40% of CCA cases. Negative cytology does not exclude malignancy.
- Other options to obtain a tissue diagnosis are EUS-FNA/core biopsy, fluorscopically directed intra-biliary or percutaneous biopsies, or laparoscopic biopsy.
- There is a risk of tumour seeding with some techniques, so surgical assessment of resectability should be established prior to a biopsy or FNA being performed.

Cholangioscopy allows direct visualisation of tumour within the major ductal systems and aids directed tissue biopsy with a higher rate of confirmatory tissue diagnosis than is

achieved using standard ERCP techniques. Cholangioscopy should be considered for cases where initial sampling is non diagnostic in order to maximise accuracy of diagnosis. At present this facility is not available within the East Midlands, attempts will be made to secure this investigative modality.

Histology

- Histology should be reviewed at the sMDT prior to determining definitive management
- All surgical resection specimens from both intrahepatic and extrahepatic cholangiocarcinomas need to be reported in a systematic manner. Surgical margins should be adequately sampled, because it has been shown that local recurrence is related to involvement of the margins. Lymph node groups must be specifically identified and it should be noted that peri-pancreatic nodes located along the body and tail of the pancreas are considered sites of distant metastasis.

Surgery

- Radical (R-0) surgery is the only curative treatment of hilar cholangiocarcinoma. Potentially resectable cases should be discussed at sMDT prior to embarking on any kind biliary intervention as some interventions or complications may affect resectability.
- Patients should be assessed for suitability for surgery after staging and anaesthetic review in the surgical centre unless otherwise agreed locally
- Lymph node involvement is present in 30-40% of all patients eligible for surgical treatment and is associated with poor surgical outcome. However N1 hilar CCA may still often be considered suitable for surgical management.
- Potential portal vein and/or hepatic artery involvement impact negatively on outcomes but do not necessarily render patients unresectable.

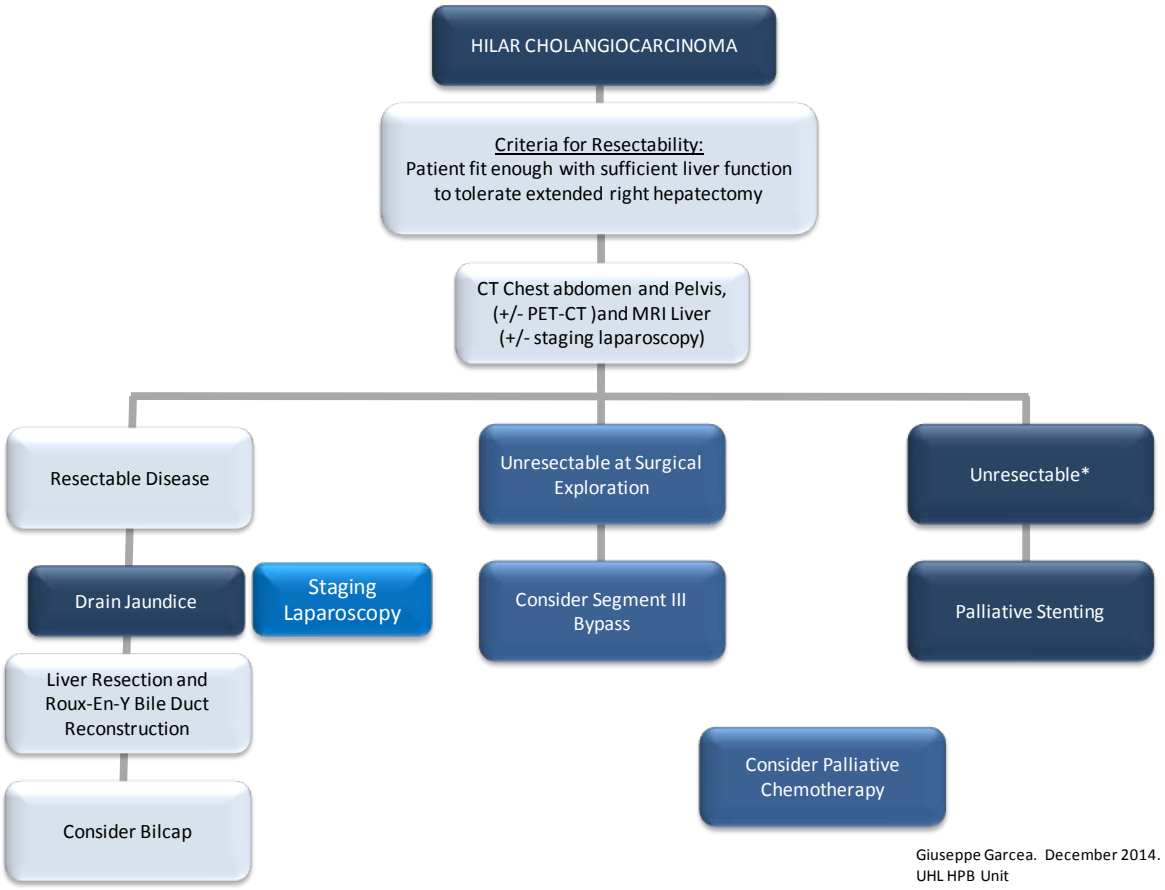
- N2 disease is considered as distant metastasis (M1) and surgery is contraindicated (see diagram in appendix for description of nodal disease).
- A plan for surgical resection will be made via the sMDT and direct review by the HPB surgery clinic at which time important surgical issues such as route for biliary drainage, measurement of liver volumes, vascular involvement and target bilirubin will be decided.
- The routine use of pre-operative biliary drainage (PTBD) is highly recommended, particularly in patients with cholangitis. The use of metal stents is indicated only by the sMDT
- Liver biopsy (non lesional) is indicated if bilirubin levels do not respond to optimal biliary drainage (PTBD) and appropriate antibiotic therapy. Persistent or increasing hyperbilrubinaemia (> x3 ULN) is a high risk for postoperative liver insufficiency and shall be considered a relative contraindication to surgery

Palliative treatments

- Symptoms related to biliary obstruction in unresectable disease may be palliated by insertion of a biliary endoprosthesis, rather than a surgical bypass. Stenting procedures resulting in adequate biliary drainage improve survival
- Non surgical candidates shall be offered effective biliary drainage with internalized stents as indicated at the sMDT, unless patients are suitable only for terminal palliative care
- Unresectable patients should be considered for palliative chemotherapy as fist line treatment for most patients if clinically appropriate
- Following the ABC-02 study, in patients with advanced disease and good performance status, the standard of care for palliative chemotherapy is gemcitabine and cisplatin chemotherapy.

- There is currently no evidence to support post-surgical adjuvant therapy outside a trial setting.
- There is little evidence to support the use of other chemotherapy regimens or radiotherapy, but further studies are ongoing and patient participation should be encouraged, particularly in the setting of recurrent disease (**Figure 3)**

Figure 3: **Overview of Hilar Cholangiocarcinoma Pathway**



MANAGEMENT OF PATIENTS WITH SUSPECTED HEPATOCELLULAR CANCER

Surveillance of High Risk Groups for HCC

The following surveillance strategy is proposed:

- Ultrasound scan of liver every six months in identified high risk groups (listed below).

- Six monthly measurement of alpha-fetoprotein – should be undertaken but will only be used as supporting evidence for image based diagnosis.

Ultrasound scans, wherever possible should be undertaken by a dedicated ultrasonographer (either by a radiologist or radiographer) who is experienced in the imaging of cirrhotic livers. The distinction between neoplastic nodules and regenerative nodules can be extremely difficult. The finding of any new nodule should be regarded as suspicious and further cross sectional imaging should be recommended.

The large volume of cirrhotic patients makes organization of a surveillance program difficult and ideally clinical nurse specialists associated with cancer services are the most appropriate individuals to call patients for surveillance and screen the initial results, identifying concerning ones for review by medical staff. Surveillance programs should undergo continual audit to ensure that appropriate individuals are identified for surveillance and importantly that abnormal results are actioned in a timely fashion. Referrers within the network should work towards the appointment of a specialist nurse to co-ordinate the investigation and treatment of potential/suspected HCC.

High Risk Surveillance Groups

- Patients with Chronic Hepatitis B / Chronic hepatitis B Carriers
- Hepatitis C Cirrhotics
- Alcoholic cirrhotics (Surveillance should be undertaken in all patients who are able/willing to cooperate with surveillance and management. Treatment decision should be influenced only by evidence of active drinking);
- Haemochromatosis
- Primary biliary cirrhosis (evidence stronger for males than females)

- Alpha-1 antitrypsin deficiency
- Non-alcoholic steatohepatitis;
- Autoimmune hepatitis (although evidence is small the relatively small numbers with this condition should probably be surveyed if only to provide more substantive data on the relative risk of hepatoma development in this condition.

Surveillance of Patients Post-antiviral Treatment

This area is still contentious for both hepatitis B and hepatitis C, although studies suggest that the risk of HCC is reduced by interferon or other antiviral drug treatment. On the basis of current evidence and reviews it is suggested that patients with cirrhosis who have been treated with antivirals, whether successful or not (in terms of sero-conversion) should probably continue to be surveyed. Surveillance should also be undertaken on those patients who are on a transplant waiting list.

Where a nodule has been found on surveillance imaging and subsequently been characterized as a regenerative, dysplastic or indeterminate lesion the patient should enter period of enhanced surveillance. The patient should be reimaged preferably with MRI (lower exposure to ionizing radiation) on a 3 monthly basis for at least 6 months to ensure the nodule is stable and the imaging characteristics do not change. If a nodule is stable then the 6 monthly imaging protocol can be reinstituted.

Diagnosis

The diagnostic modalities used to confirm HCC are dynamic contrast enhanced CT and dynamic MRI (enhanced with gadolimium). The new EASL/EORTC guidelines for the diagnosis of HCC recommend that lesions greater than 1 cm with a typical vascular pattern

(arterial enhancement with portal venous washout) on either dynamic contrast enhanced CT or MRI can be treated as HCC.

- Lesions > 1 cm with an atypical vascular pattern on either CT or MRI should undergo imaging with the complementary technique to confirm HCC If HCC is not confirmed i.e vascular enhancement pattern is atypical then the lesion should either undergo biopsy or enhanced surveillance with MRI or CT. This decision should only be made after work up by hepatologist, hepatobiliary radiologist and hepatobiliary surgeon and following discussion at the MDT
- For lesions greater than 2 cm with atypical vascular findings the lesion should be treated as HCC if the AFP is elevated greater than 200 ng/ml
- Lesions <1cm in diameter may be investigated with dynamic imaging but these lesions can be very difficult to separate from regenerative nodules (30% of arterially enhancing nodules <1cm are not HCC).

LESIONS LESS THAN 1 CM SHOULD NOT BE CONSIDERED IN THE CONTEXT OF ASSESSING A PATIENTS SUITABILITY FOR LIVER TRANSPLANTATION

Even if these (<1cm) lesions show a classic “vascular pattern” it is suggested that the appropriate management should be to repeat the MRI or CT at three-monthly intervals and determine whether these nodules are enlarging. Nodules showing evidence of enlargement should then be managed (more actively) as described above. If the nodules are static or regressive then the patient can re-enter a six monthly surveillance programme. NB. In the context of regenerative nodules such as hepatitis B and hepatitis C, alpha-fetoprotein may be raised to a level of above 100iu.

Alpha-fetoprotein may be raised in association with regenerative activity but a very high alpha-fetoprotein (>200) is strongly indicative of a hepatocellular carcinoma particularly in

the context of an isolated nodule >2cm diameter. In addition, regardless of the absolute level, a relentlessly rising alpha-fetoprotein on serial measurements is concerning and should prompt a vigorous and thorough radiological investigation with CT or MRI.

Management of Confirmed HCC

The management of the patient with HCC is complex and requires the involvement of the entire multidisciplinary team. There are a number of therapeutic options available to HCC patients (according to the BCLC staging system) and the suitability of a patient for treatment depends on a number of factors including but not limited to

- Size and number of nodules
- Presence of metastases
- Presence or absence of underlying cirrhosis
- Presence of metastases
- Severity of underlying liver disease and presence or absence of complications
- Presence of portal vein thrombosis
- AFP levels
- Performance status of the patient

Figure 3: **Overview BCLC Staging System**

BCLC STAGING SYSTEM[4]

BCLC Stage	PS	Tumor Features	Liver Function	Treatment Options
A1	0	Single <5 cm	No PH	Surgery, RFA
A2	0	Single <5 cm	PH, normal bili	Surgery, RFA, transplant
A3	0	Single <5 cm	PH, abnormal bili	RFA, transplant
A4	0	3 tumors <3 cm	Not applicable	Transplant, TACE
B	0	Large multinodular	CP A-B	TACE
C	1-2	Vascular invasion or metastases	CP A-B	sorafenib
D	3-4	Any	CP C	Supportive care

BCLC: ***Barcelona Clinic Liver Cancer Staging System***
PS: ***Performance Status***
RFA: ***Radiofrequency Ablation (microwave ablation can be alternative)***
PH: ***Portal Hypertension***

Surgical Resection

Surgical resection should be considered in any patient with a single lesion who is non cirrhotic or has Child Pugh Class A cirrhosis depending on the size and or position of the lesion. Patients who are considered for resection should have up to date biochemistry, CT chest and MRI/CT liver imaging available for review at the MDT and should undergo detailed review by a hepatologist to exclude adverse hepatological factors such as uncontrolled Hepatitis B (+/- portal pressure measurement).

Radiofrequency or microwave Ablation can be considered as a possibly curative treatment modality if neither resection nor transplantation is feasible or appropriate with standard risk or as a “bridging” treatment to transplantation.

Liver Transplantation

Liver transplantation should be considered for any patient with cirrhosis and complicating HCC who fulfils the following criteria AND in whom resection with standard risk cannot be safely performed (due to poor liver reserve or remnant or significant portal hypertension):

- Definite HCC 1 nodule 5 cm or less (or >5 and < 7 cm where the lesion has been stable (ie. remains less than 7 cm and no or less than 20% increase in size over 6 months – the 6 month period counts from the first diagnostic scan and adjuvant treatments are allowed)

OR

- 5 nodules – all 3cm or less in size
- Absence of macrovascular tumour involvement (Portal vein thrombus, Arterivenous shunting in the area of the tumour)
- No evidence of metastatic disease
- No evidence of advanced cardiorespiratory disease
- AFP < 1,000 ng/ml

Patients who are actively drinking alcohol should not be referred for liver transplantation immediately – complete abstinence should be advised. All other patients should be considered for liver transplantation and initially referred to the joint clinic for assessment. If thought to be suitable candidates then a member of the liver transplant coordination team will meet the patient in the joint clinic.

Patients thought suitable for work up for transplantation should be managed in accordance to the guidelines of the transplant centre they have been referred to. TACE can be considered as bridging therapy.

Transarterial (Chemo) –embolisation (TACE)

Patients who are not suitable for resection or transplantation may be offered therapy with transarterial embolisation. Alternatively patients who are candidates for other treatment such as transplantation or rarely resection may also be offered transarterial embolisation in an attempt to maintain to prevent tumour growth outside transplant criteria or make surgical resection more favourable. Candidates for TACE are usually indentified via the MDT and suitability for the procedure agreed with the radiologist. There are few absolute contraindications to TACE (except portal vein thrombosis or decompensated liver failure) but the presence of the following characteristics make TACE an unsuitable treatment modality.

- Advanced liver disease (Bilirubin > 50 micromol/L, INR >1.5, History of encephalopathy, ascites, Childs Pugh C or > B7, albumin <28, platelets <60)
- Main portal vein thrombosis
- Renal function > 1.5 x ULN or eGFR <60ml/min
- Performance status > 1
- Patients who are suitable for TACE are assessed in the joint HCC clinic and given appropriate information regarding the risks and benefits of the procedure.

Preoperative work-up of patients includes nil by mouth NBM for 4 hours with clear fluids allowed up to one hour before the procedure. An antiemetic may also be given along with antibiotic prophylaxis (e.g. Co-amoxiclav IV 1.2g followed by two further doses of Co-amoxiclav IV 600mg at 8 hourly intervals as standard prophylaxis and Teicoplanin IV 400mg and Gentamicin IV 120mg in penicillin allergic or MRSA colonised patients.)

Typical preparations include 60mg/m/2 Doxorubicin reconstituted with Iohexol 240mg/ml and 10ml Lipiodol ultra. Final concentrations of Doxorubicin / Lipiodol : 5mg/ml are placed into

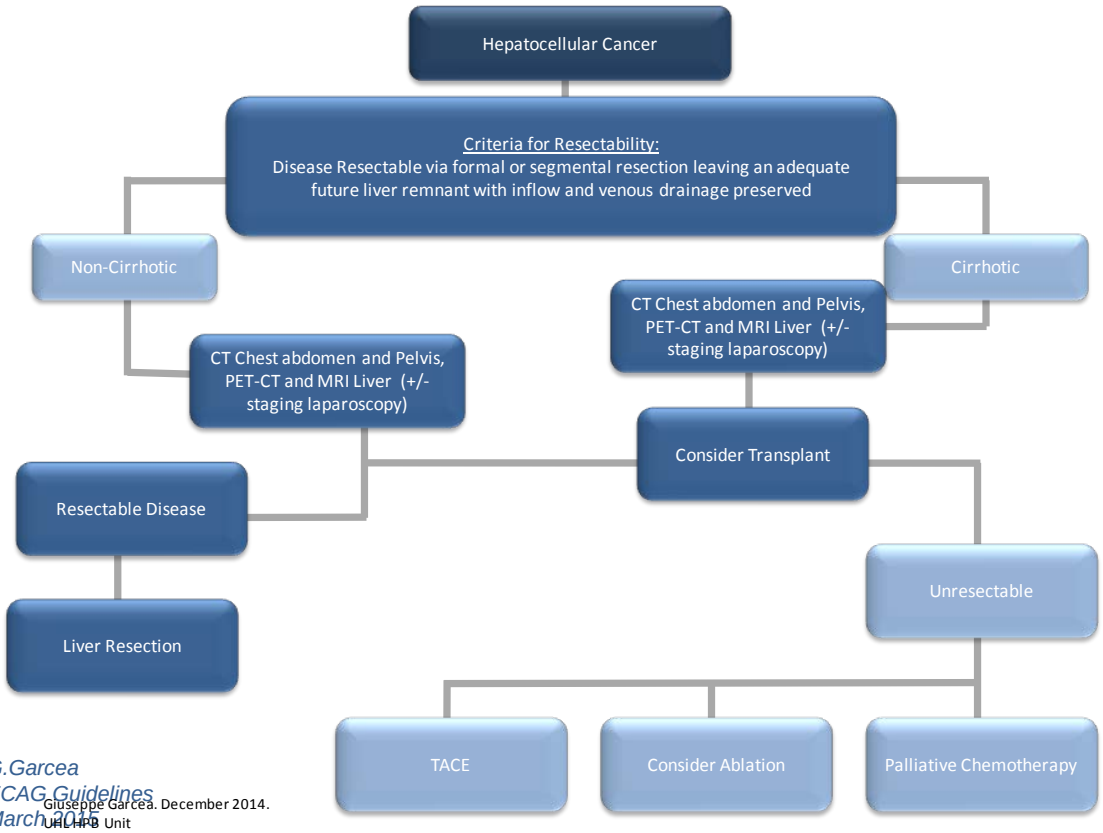
2ml luerlock syringes (to facilitate injection through a microcatheter – larger syringes lack the pressure generation). A dose reduction is required dependent of liver function.

Dose reductions

Bilirubin <18mmol/l	100% dose
Bilirubin 18 – 50 mmol/l	50% dose
Bilirubin >50 mmol/l	No treatment

Following TACE patients undergo repeat cross sectional imaging to determine the need for further embolisation based on residual vascularity. If residual vascularity is noted then a further TAE is performed. In cases of unsuccessful embolisation with persistent vascularity it is useful to review the imaging in the MDT to ensure that the appropriate vessels have been targeted. Patients with stable disease post TACE will have repeat imaging on a 3 monthly basis (**Figure 4).**

Figure 4: **Overview of Treatment of HCC**



MANAGEMENT OF PATIENTS WITH SUSPECTED LIVER METASTASES

Surveillance of Patients Post-Primary Resection

Surveillance of patients following resection of their primary cancer will vary according to the locality and their follow-up protocols. It is expected that any local policy will take into account the UK recommendations that a CT should happen at least once in the first 2 years and that a colonoscopy should be repeated after 5 years.

Diagnosis

Contrast enhanced CT of chest, abdomen and pelvis should be the standard form of staging. Baseline LFTs and CEA should also be part of the initial investigations. At the time of treatment for CLM, the latest axial staging imaging must not be more than 6 weeks old. Further axial imaging in the form of MRI will occasionally be used after review of the initial CT at the HPB MDM. This is mainly indicated where the nature of liver lesions is uncertain or additional information is required prior to planning surgery (i.e. vascular and/or biliary anatomy considerations).

The role of PET scanning is under evaluation worldwide and definitive results are awaited. Current policy is the use of PET where extra-hepatic disease is suspected but cannot be confirmed on CT or MRI. It may be of particular value in patients at high risk of local or peritoneal recurrence e.g. ruptured or advanced stage primary cancer or for high risk groups needing extended or complicated surgical procedures. Other investigative measures such as EUS, image guided biopsy and laparoscopic biopsy can also be used under individual circumstances. Biopsy of liver lesions should always be avoided.

Patients Considered for Resection

All patients who are considered fit to undergo major surgery and in whom all disease sites can be treated with curative intent should be considered for resection.

Inclusions

- No age cut off
- Solitary liver metastases
- Multiple unilobar liver metastases
- Bilobar resectable liver metastases
- Multiple bilobar liver metastases amenable to down-staging
- Synchronous resectable primary and metastatic liver disease
- Liver and localised resectable or abatable lung metastases

Exclusions

- Unfit for major surgery (e.g. IHD, COAD)
- Unresectable primary disease (not amenable to down-staging)
- Pelvic local residual disease
- Peritoneal disease
- Bony or unresectable lung metastases

Any liver resection irrespective of the extent or the mode (laparoscopic or open) should be considered as major surgery. In addition, the majority of these patients would have undergone various periods of systemic chemotherapy. Therefore, appropriate cardiovascular, respiratory and nutritional assessment is mandatory. These patients should undergo consultant anaesthetist led pre-operative assessment.

Surgical Planning

The appropriateness of liver resection should be discussed at the HPB SMDT but the nature and extent of procedure, the risks involved and the likely outcome should be discussed with the patient and family by a consultant HPB surgeon. The CNS Key worker will be present to counsel the patient and their family further. All patients receiving a diagnosis of cancer will be told by an appropriately trained MDT member (i.e. a Consultant) in the presence of a CNS.

The following principles should be observed:

- Complete tumour clearance with clear resection margins; when anatomically feasible the rule of 1cm should be observed.
- Full evaluation of the liver with intra-operative USS
- Planning for resection should (if possible) take into account the extent of the disease at the time of presentation, prior to chemotherapy.
- Relative contraindications for liver resection at the time of surgery are the presence of peritoneal spread and porta-hepatis nodal involvement
- Where the liver resection is following a course of chemotherapy at least 4 weeks should be allowed for liver recovery between the completion of chemotherapy and surgery.

Enhanced Recovery

An enhanced recovery programme in place for liver resections is in place for Nottingham and Leicester to ensure speedy discharge.

Portal Vein Embolisation (PVE)

When, on volumetric studies, the expected remnant functional liver mass after the proposed hepatectomy would be inadequate (<30% of normal liver or 40% with steatotic or post chemotherapy liver), percutaneous right portal vein embolisation could be explored as a means of increasing FLR.

Two-stage Hepatectomy

For patients with bi-lobar disease when complete removal of all tumours is thought not possible with a single procedure a two-stage approach can be adopted by first resecting the most tumour laden lobe. Allowing for a period of 6 weeks for regeneration of the remnant liver, resection is then completed with removal of part of the remaining liver lobe. This approach can be combined with PVE prior to the first stage and/or RFA of the remnant tumours at either stage.

Laparoscopic Liver Resection

In recent years there has been an expansion in the application of laparoscopic techniques in HPB surgery. There is now enough data to support the role for laparoscopic resection in the treatment of patients with CLM. Although almost any type of liver resection can be performed laparoscopically there is a lack of long-term survival data. The advent of the da Vinci^{TM} robot has also raised the possibility of robotically assisted laparoscopic liver resection. Such new treatment modalities should be explored with appropriate training and regular auditing of outcomes to ensure results are maintained.

Microwave Ablation and Radio-Frequency (MVA & RFA)

Resection is the gold standard for treatment of CLM. However, MVA or RFA may be a useful treatment options for patients who:

- Are not candidates for liver resection due to poor performance status.

- Have multi-focal disease that cannot be resected (even after the implementation of the previously discussed pre-operative strategies).
- Have recurrent disease in their liver remnant that will not tolerate further resection
- Are not willing to undergo liver resection, but would accept a less invasive mode of treatment
- Require consideration of MVA / RFA in combination with liver resection when parenchyma sparing is required as means of control of otherwise irresectable disease
- Finally, as a part of a two-stage hepatectomy, as outlined above
- MV/ RFA can be delivered either percutaneously or intra-operatively (laparoscopic or open) based on individual patient needs.
- All patients being considered for RFA of colorectal liver metastases will be discussed at the HPB sMDT.
- Treatment will only be carried out by a surgeon or radiologist experienced with RFA at the specialist centre

Synchronous Liver Metastases with Primary Colon Cancer

There is some data to suggest that it may be safe and effective to resect right sided colonic cancer at the same time as small and isolated liver metastases. Most centres avoid combining a major liver resection (more than 3 liver segments) with left-sided or pelvic colectomies due to increased risk for post-operative liver failure and/or septic complications from anastomotic leaks.

Recurrent Metastatic Liver Disease

Patients who have undergone a liver resection for their CLM and present with recurrent disease in their liver remnant should be assessed for repeat hepatectomy in the same way as for their first resection. Repeat hepatectomies for CLM in high volume centres follow the same pattern of morbidity and mortality as the primary liver resections. Furthermore, the prognosis for these patients seems to be unaffected by the number of liver resections, but rather by the ability to remove all measurable disease with enough remnant functional liver.

Liver and Pulmonary Metastatic Disease

The simultaneous presence of liver and lung colorectal metastases does not preclude the surgical treatment of both sites. Long term survival in the current literature following resection of pulmonary metastases is almost entirely in patients who have developed pulmonary metastases on follow up after a liver resection for metastatic disease. If, however, by thoracic criteria the pulmonary disease is resectable then the CLM should be assessed for treatment and this should be completed prior to the lung resection(s).

Neo-adjuvant Chemotherapy

Will be addressed in the chemotherapy section (Chemotherapy Treatment Algorithms 13-1C-106n) (**Figure 5).**

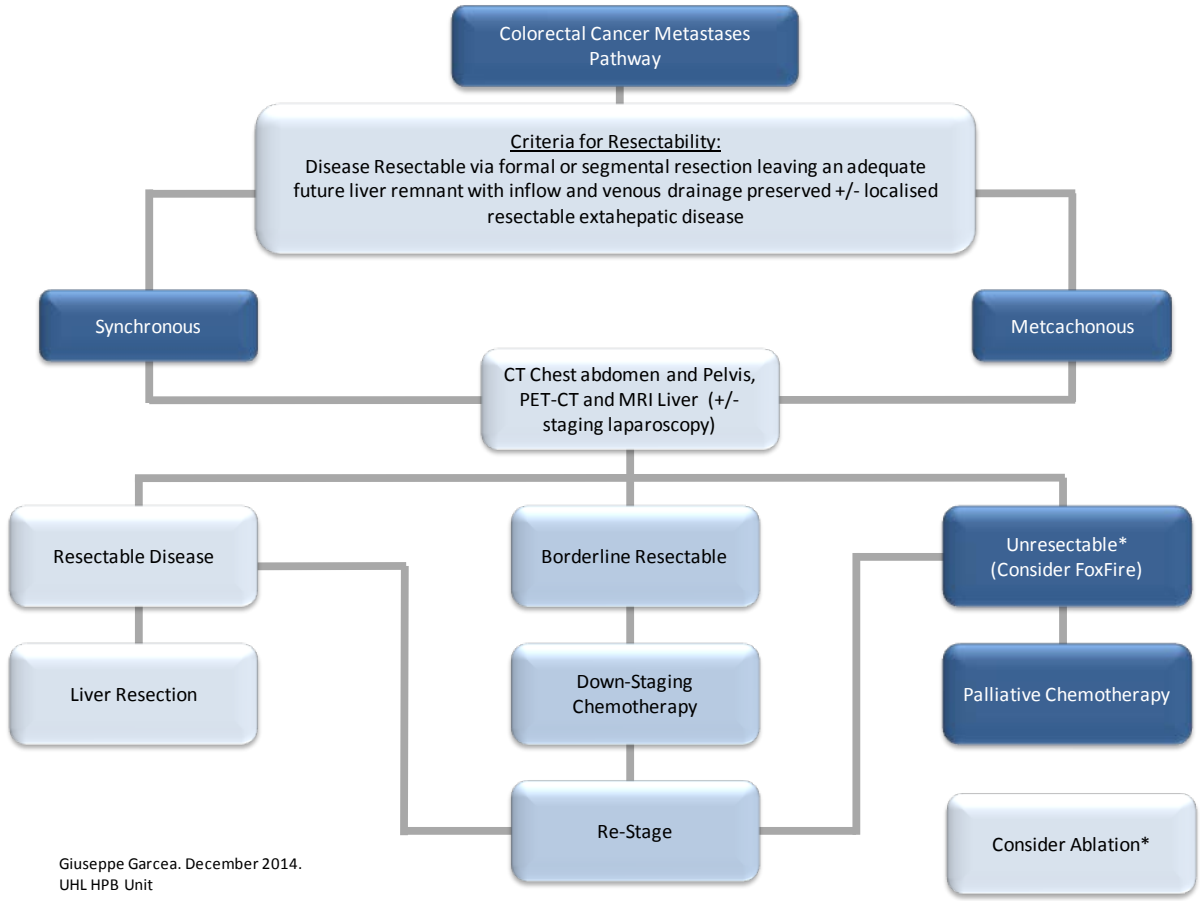
Follow-up Protocol

The follow up protocol will involve 6 monthly CT and tumour markers for the first two years and annually for the subsequent 3 years. With recent evidence that late presentation of CRC (which remain resectable) after 5 years is possible, follow-up may be continued beyond this.

Imaging should consist of a chest, abdomen and pelvis CT with CEA levels (if the liver resection was undertaken for a colorectal liver metastasis).

If the follow up is transferred from the HPB surgical; team to the Oncology team the key worker for the patient will automatically transfer from the HPB CNS to the GI Oncology CNS. If the patient proves unresectable and is not suitable for chemotherapy then the HPB CNS may transfer key worker responsibility to the palliative care CNS in the community.

Figure 5: **Overview of CLM Management Pathway**



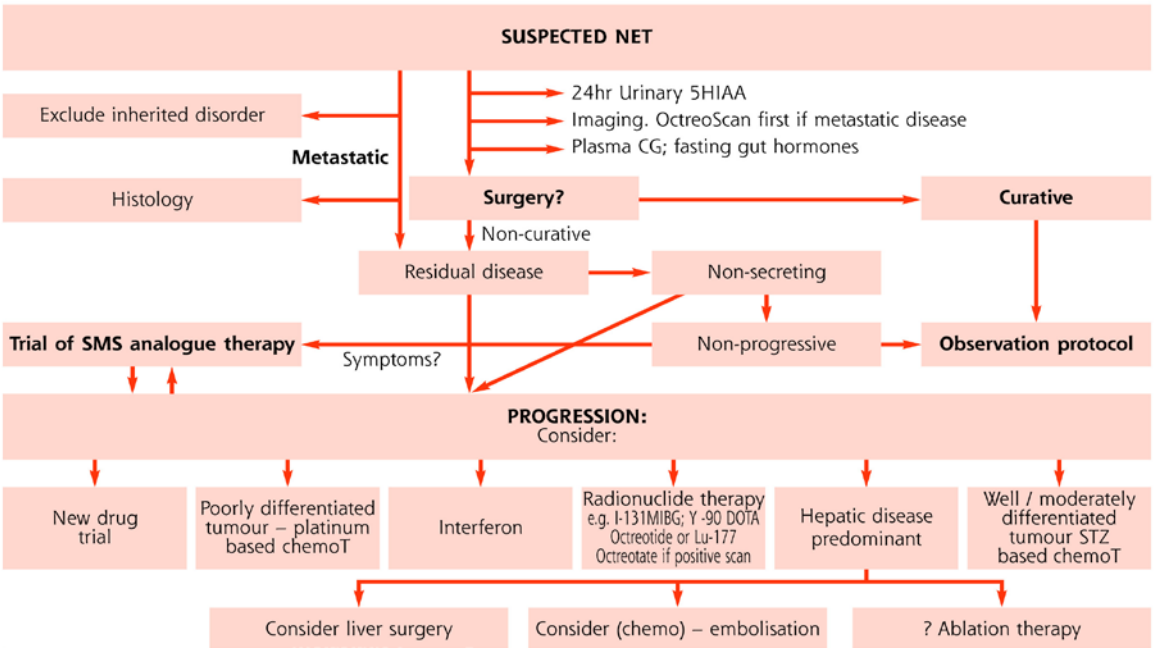
Management of Patients with Suspected Gallbadder Cancer

Management of patients with suspected gallbladder cancer will follow the principles of liver resection for extrahepatic hilar cholangiocarcinomas for the most part. The aim of surgical resection is for R0 margins, the extent of liver parenchyma resection will be determined by vascular involvement by the primary tumour. For incidentally found gallbladder cancers (after routine laparoscopic cholecystectomy), any histological stage of greater than T2 will require follow-up resection consisting of bile duct excision (if cystic duct involved), portal lymphadenectomy and excision of segment V.

Management of Patients with Pancreatic Neuroendocrine Lesions

Most PNETs will be diagnosed during a standard pancreatic cancer pathway (see earlier). Once a PNET is suspected then an octreotide scan is undertaken for staging (+/- diagnostic purposes). Chromagranin A and B levels will also be checked. Potentially functioning PNETs will also require a full hormone screen **(Figure 6).**

Figure 6: **Overview of Diagnosis and Management of Gastropancreatic Neuroendocrine Tumours**



MANAGEMENT OF PATIENTS WITH PANCREATIC CYSTIC LESIONS

All pancreatic cystic lesions will be discussed at the sMDT. The mainstay of characterising their pathology will be cross-sectional imaging either CT or MRCP. Secretin-enhanced MR may be considered to determine connection to the main pancreatic duct. EUS-FNA will be undertaken for indeterminate lesions which cannot be fully characterised on non-invasive imaging. Its use as a surveillance tool is discouraged due to its invasive nature. A non-ionising imaging modality such as MR should be considered for surveillance of branch-type IPMNs **(Figure 7).**

Resection

- All main-duct IPMNs
- BT-IPMNs

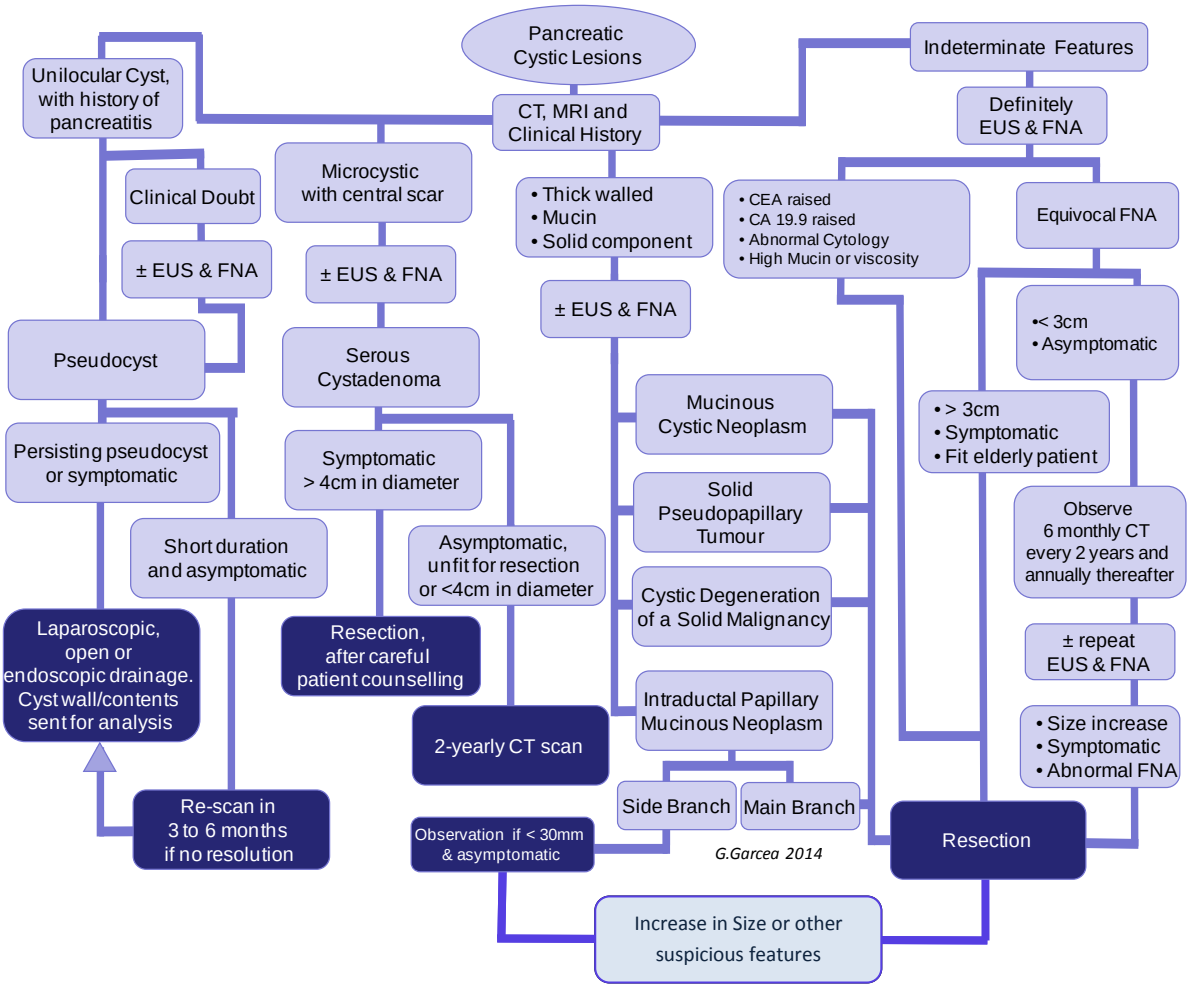
- greater than 3 cm in diameter
- Eccentric wall thickening
- Increasing size
- Intramural nodules

- All mucinous cystic neoplasms
- Any radiological features suggestive of cystic degeneration within an adenocarcinomas, or neuroendocrine lesion
- Cyst fluid CEA of greater than 200. The most appropriate level to be determined by each sMDT according to their biochemistry department.

Post-Resection Follow-up

All post-resection IPMNs require continue follow-up of the pancreatic remnant. A suggested protocol is annual surveillance for 2 years, followed by bi-annual after. At present there is no data to support or suggest any better surveillance protocol. If invasive malignancy is discovered on resection, then the follow-up protocol will follow that of resected adenocarcinomas (see earlier section).

Figure 7: **Overview of Diagnosis and Management of Pancreatic Cystic Lesions**



CHEMOTHERAPY TREATMENT ALGORITHMS (13-1C-106n)

Whilst all resection surgery will be undertaken at either Leicester or Nottingham; chemotherapy and radiotherapy can be administered in Northampton, Lincoln, and the Royal Derby Hospital. This also applies to radiotherapy (dependent on local availability and resources). Patients are free to have their treatment at any centre which they choose.

PATIENTS WITH PANCREATIC CANCER

Adjuvant Chemotherapy

Standard First Line:	Gemcitabine
Clinical Trial:	ESPAC4 (Gemcitabine vs Gemcitabine plus Capcitabine)

Locally Advanced / Borderline Resectable

Standard First Line:	Gemcitabine

Other Options or Second Line

Chemoradiotherapy Regimens:	CRT and concurrent Capecitabine or CRT and Gemcitabine

Following completion of chemo-radiotherapy the patient should have repeat imaging which again should be discussed at the HPB MDT to determine any evidence of resectability. If no evidence of resectability the patient should remain on surveillance and treated upon evidence of disease progression. For those patients with locally advanced disease considered inoperable then referral for Stereotactic Body radiotherapy could be considered.

Clinical Trials (NCRN)

SCALLOP 2 and ESPAC5: both in set-up phase.

- SCALLOP 2: currently involves 5 arms;
  - Arm A: GEMCAP chemotherapy alone,
  - Arm B: induction GEMCAP chemotherapy followed by GEM plus 50.4Gy in 28 fractions,
  - Arm C: induction GEMCAP chemotherapy followed by GEM plus 50.4Gy in 28 fractions plus nelfinavir,

- Arm D: induction GEMCAP chemotherapy followed by GEM plus 59.4Gy in 33 fractions,
- Arm E: induction GEMCAP chemotherapy followed by GEM plus 59.4Gy in 33 fractions plus nelfinavir.

- ESPAC5 is to assess feasibility of randomising to a neo-adjuvant trial. It will compare standard of care (surgery followed by adjuvant chemotherapy) with neoadjuvant GEMCAP chemotherapy vs neo-adjuvant FOLFIRINOX chemotherapy vs neo-adjuvant CRT prior to surgery.

Metastatic Disease

First Line:

Gemcitabine SA (q28): D1, 8, 15 gemcitabine 1,000mg/m2 IV

Or Gemcitabine + Capecitabine (q28x6): D1, 8, 15 gemcitabine 1,000mg/m2 IV, D1-21 Capecitabine 825-830mg/m2 po

Or Capecitabine SA (q21, until disease progression), D1-14 Capecitabine 1000mg/m2 po

FolFirinOx (q14x12)21:

D1 Calcium Folinate (Folinic Acid) 350mg IV

D1 Oxaliplatin 85mg/m2 IV

D1 Irinotecan 180mg/m2 IV

(D1 5-Fluorouracil 400mg/m2 IV) – modified regime drops the bolus

D1 5-Fluorouracil 2400mg/m2 IV over 46 h

Assessment after 4 cycle, treatment indefinite.

Gemcitabine/Nab-Paclitaxel (q28x6)22:

D1, 8, 15 gemcitabine 1,000mg/m2 IV

D1, 8, 15 nab-Paclitaxel 125 mg/m2 IV

Second Line Treatment: *or* FOLFOX after GEM

or GEM after FOLFIRINOX

PATIENTS WITH CHOLANGIOCARCINOMA

All patients should be offered oncology review if clinically appropriate. Present standard of care for chemotherapy is combination of gemcitabine and cisplatin but regimens may change based on patient related factors and future clinical trials

PATIENTS WITH HEPATOCELLULAR CARCINOMA

A licensed indication for Sorafanib is advanced HCC, with a potential improvement in median survival of 2.8 months over best support care. Sorafenib is not recommended (by NICE) for the treatment of advanced hepatocellular carcinoma in patients for whom surgical or loco regional therapies have failed or are not suitable. People currently receiving sorafenib for the treatment of advanced hepatocellular carcinoma should have the option to continue treatment until they and their clinician consider it appropriate to stop.

PATIENTS WITH COLORECTAL LIVER METASTASES

The principles of chemotherapy in patients with CLM are adjuvant treatment following resection of primary in patients with synchronous disease, neoadjuvant chemotherapy for patients with borderline resectable disease or as palliation.

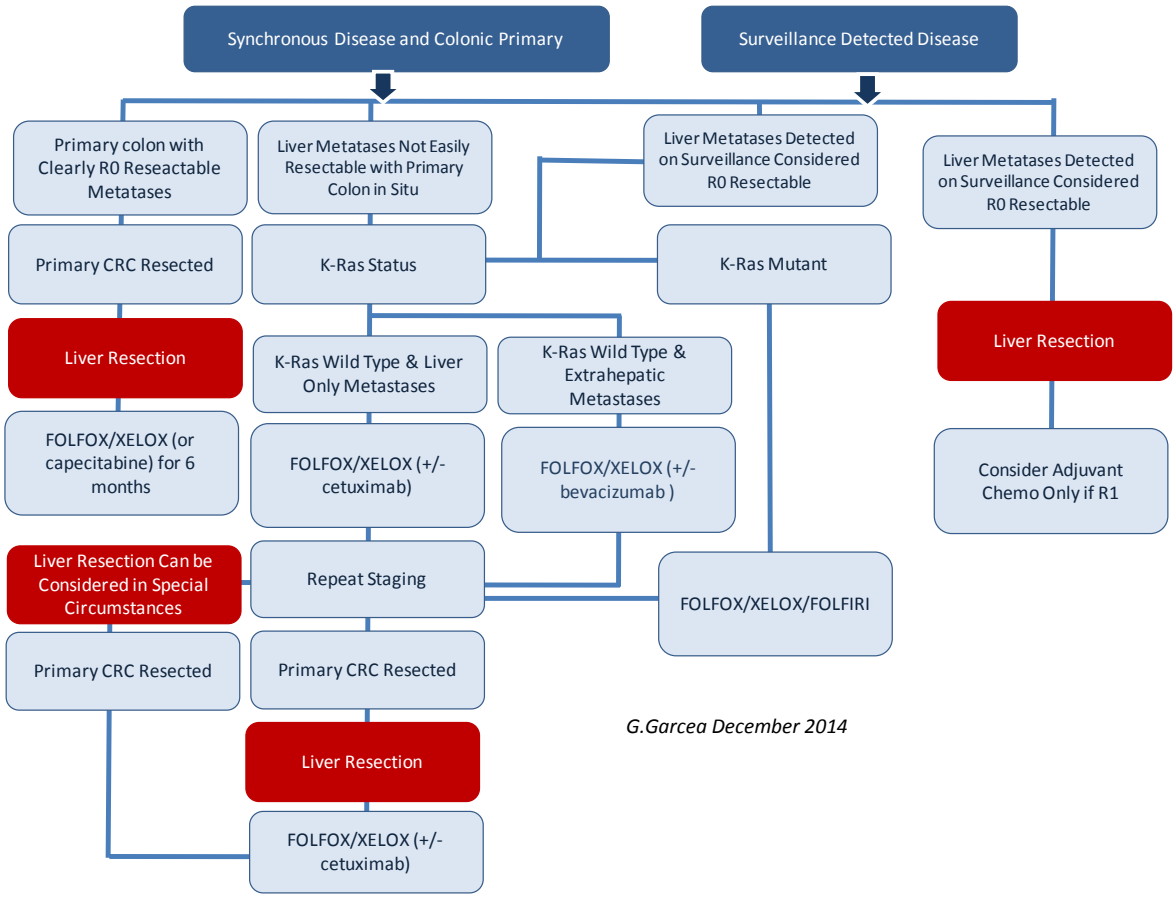
Management of Synchronous Operable Colon cancer with Intact Primary and Clearly RO Resectable Metastases

- Surgery to primary tumour followed by surgery to the liver +/- lung.
- Post-operative adjuvant FOLFOX/XELOX (or capecitabine) for 6 months.

Management of Synchronous Inoperable Liver/lung Metastases with Intact Primary Colon Cancer

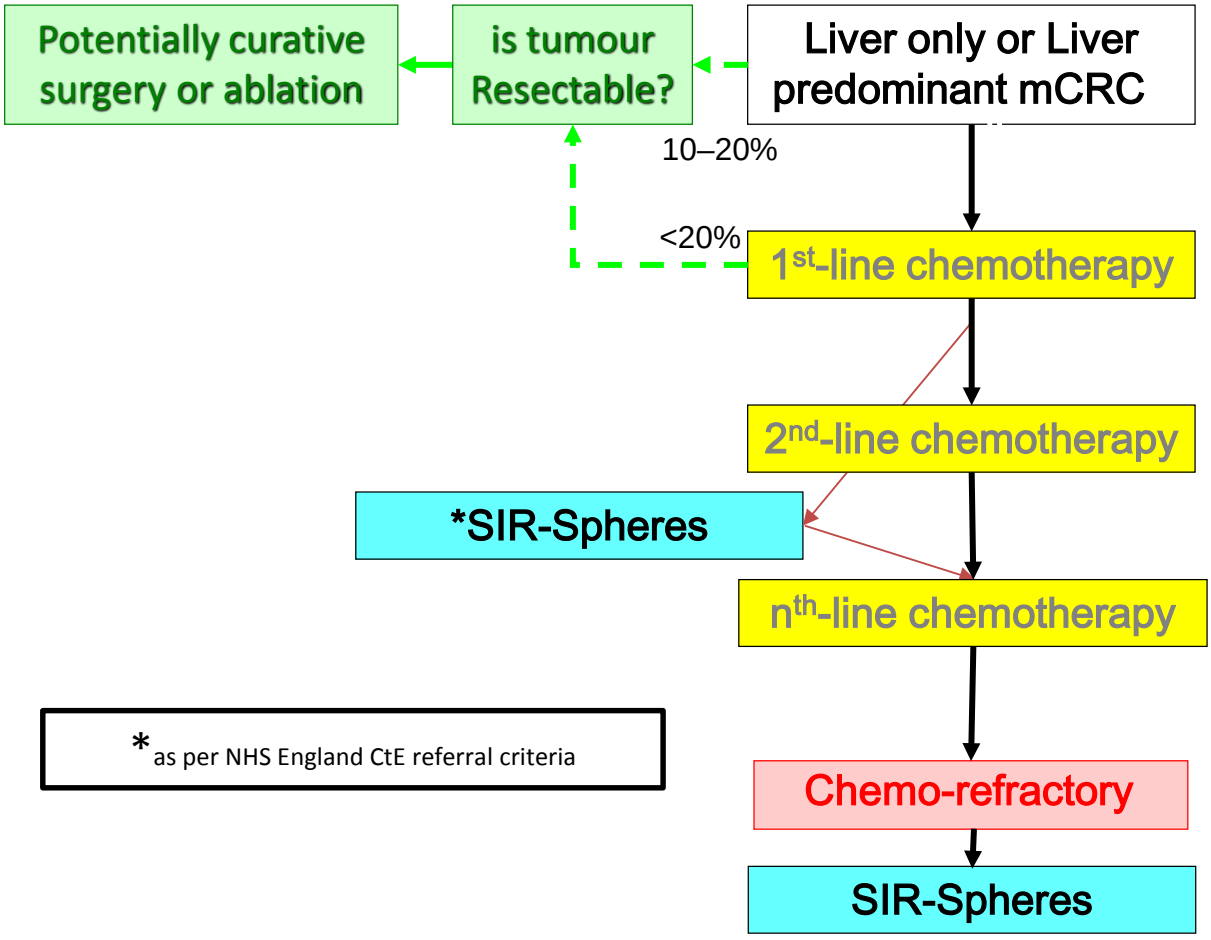
- 3 -6 months pre-operative chemotherapy with FOLFOX/XELOX (+/- cetuximab according to KRAS status) depending on response.
- CT CAP after 3 months to assess response and operability.
- If metastases become operable surgery for primary and metastases should be performed.
- A total of 6 months of chemotherapy should be given peri-operatively.
- If resection is not feasible then escalate/change chemotherapy and reassess regarding operability.

Figure 8: Management of Synchronous Colon Cancer with CLM and Surveillance-Detected CLM



Place of Selective Internal Radiotherapy in mCRC Treatment Pathway

SIRT is available as on the below algorithm.



Management of Synchronous Operable Rectal Cancer with Intact Primary and Clearly RO Resectable Metastases Stratified by Primary Tumour Stage

(a) Low risk (<cT3 and N0)

- Resection of primary and metastases (simultaneous or delayed)
- 6 months postop FOLFOX/XELOX (or capecitabine).
- Post op (chemo) radiotherapy if unexpected T3/T4, N+ or R1/2 followed by adjuvant chemotherapy.

(b) Moderate risk (≥cT3 any N+ but CRM not threatened by primary or nodes)

- SCRT to primary followed by surgery to primary and metastases (synchronous or delayed)
- 6 months postop FOLFOX/XELOX (or capecitabine).

(c) High risk (any T4, threatened/breached CRM or low rectal tumours/borderline moderate to high risk pts)

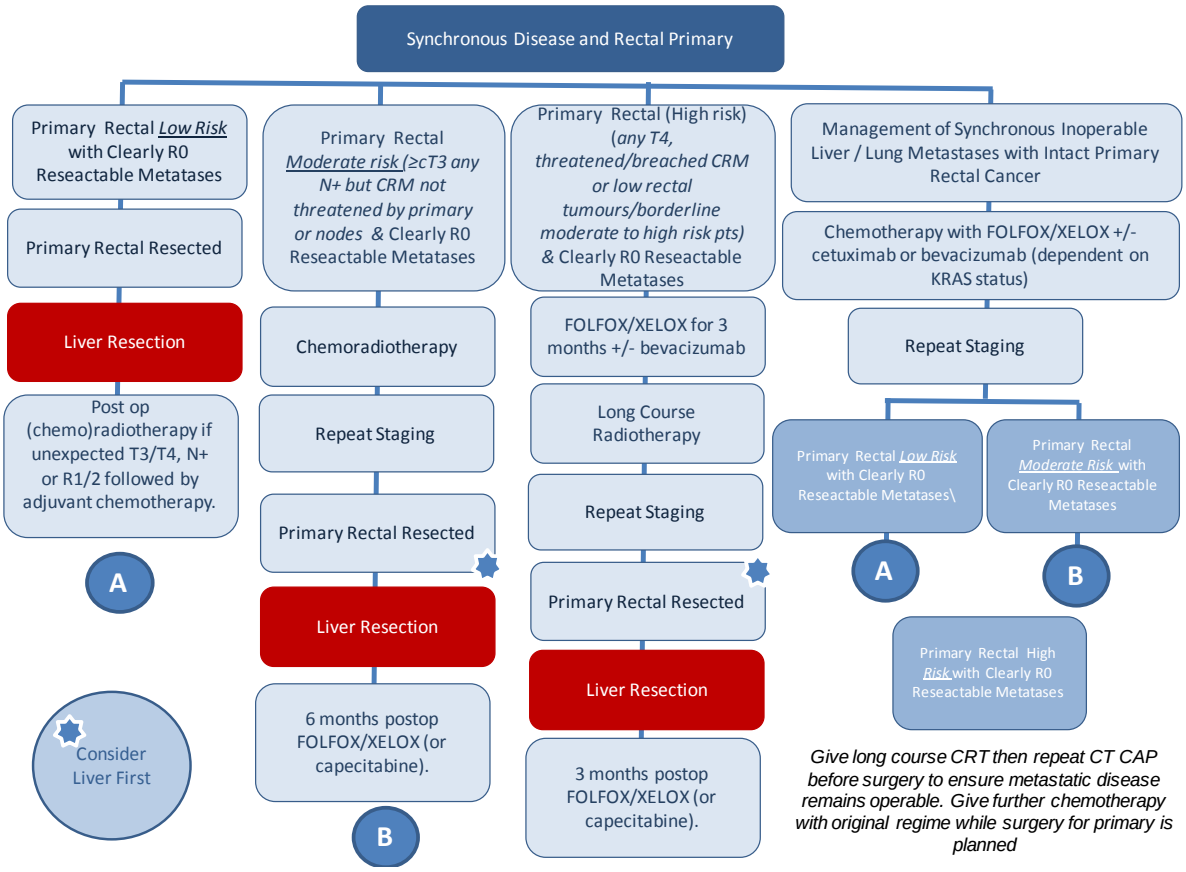
- Upfront chemotherapy with FOLFOX/XELOX for 3 months
- Long course CRT to pelvis (depending on response to chemotherapy).
- Resection of primary and metastases (simultaneous or staged).
- Post op chemo for further 3 months.

Management of Synchronous Inoperable Liver / Lung Metastases with Intact Primary Rectal Cancer

- Upfront chemotherapy with FOLFOX/XELOX +/- cetuximab (dependent on KRAS status).
- CT CAP after 3 months to assess response and operability.
- If metastases become operable, surgery for primary and metastases should be performed immediately for a <T3 N0 (low risk) tumour (simultaneous or delayed). If radiological staging of primary is moderate risk consider SCRT then immediate surgery to primary +/- metastases. If primary tumour remains high risk despite upfront chemotherapy give long course CRT then repeat CT CAP before surgery to ensure metastatic disease remains operable. Give further chemotherapy with original regime while surgery for primary is planned.

- A total of 6 months of chemotherapy should be given peri-operatively.
- If resection is not feasible then escalate/change chemotherapy and reassess regarding operability.

Figure 9: Management of Synchronous Rectal Cancer with CLM



G.Garcea December 2014

There is a lack of definitive data to support a "liver first" resection. A decision to undertake "liver first" should always be made at MDT and following appropriate staging investigations. The option of down-staging systemic chemotherapy should always be considered first.

PATIENT PATHWAYS (13-1C-107n)

REFERRAL GUIDELINES BETWEEN TEAMS

When initial investigations (abdominal ultrasound and CT scan) support a working diagnosis of HPB cancer, responsibility for further diagnostic procedures should shift to the specialist HPB cancer team. A multi-professional approach should be adopted and delays kept to a minimum. Further examinations such as endoscopic retrograde cholangiopancreatography (ERCP) should be carried out by the specialist team except in specific cases after consultation with the specialist team. Patients are referred to the tertiary centre for assessment for definitive treatment by surgery and sometimes chemotherapy. The surgery will be carried out at Queens Medical Centre Campus, Nottingham, Lincolnshire or the University Hospitals of Leicester. Chemotherapy can take place closer to the patient's home i.e. Nottingham Cancer Centre, Lincoln County Hospital, Pilgrim Hospital, Kings Mill Hospital, Northampton General Hospital, Kettering General Hospital or University Hospitals of Leicester with radiotherapy being undertaken at Addenbrookes for Peterborough patients.

Patients with complex diagnoses are often referred to the tertiary centre for additional diagnostic and staging tests. The MDT meetings provide the forum for selection of patients who potentially require curative surgery and who should therefore be seen in the tertiary service. It is important to streamline the diagnostic pathway as much as possible and each unit should ensure that there are no delays between first out-patient appointment and diagnostic test such as CT scanning. Diagnostic tests should be completed by day 21 and the results available to the clinician. The balance of work and referral pathways between the local team and the specialist team are summarised on the next page.

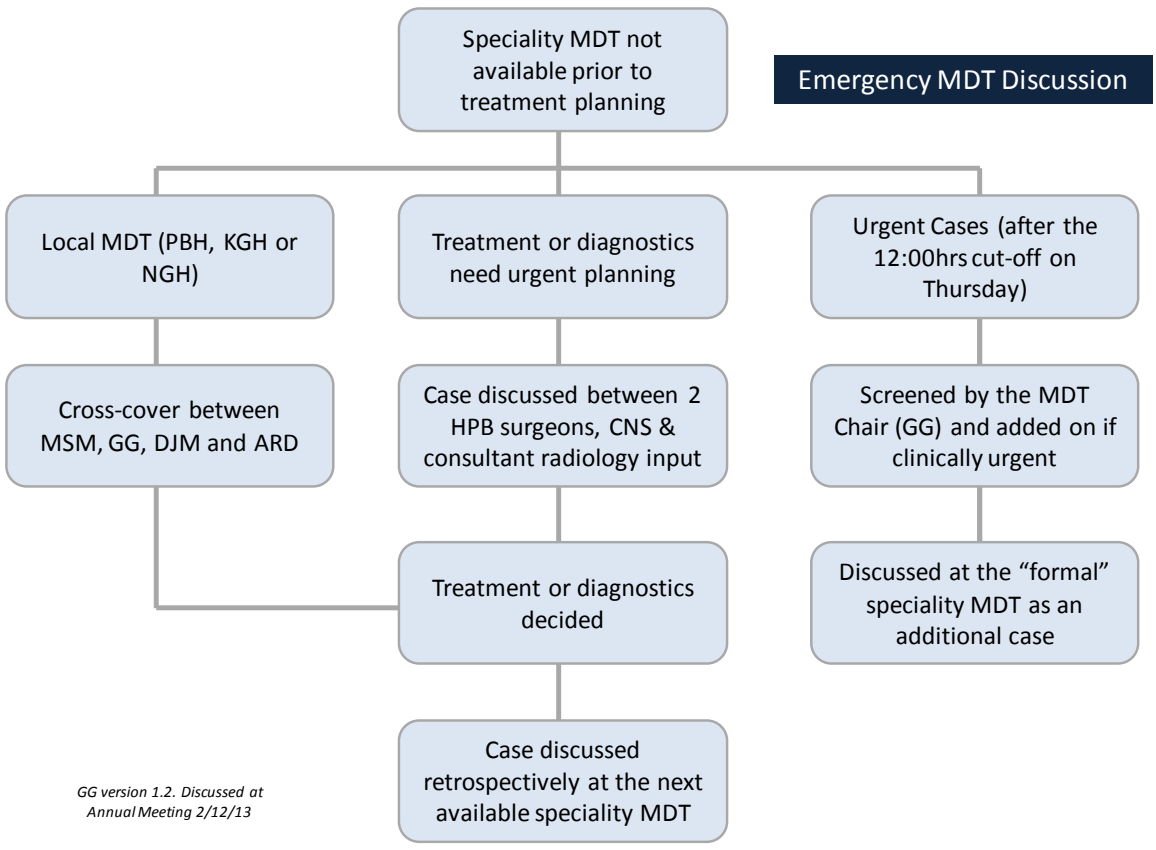
REFERRAL GUIDELINES FOR HEPATOBILIARY SURGICAL CONSULTATION OUTSIDE MULTIDISCIPLINARY MEETINGS

This is an uncommon situation for malignant hepatobiliary disease. For conditions such as cholangitis secondary to a blocked biliary stent contact should be:-

In Nottingham:- Via the on-call hepatobiliary specialist at QMC Nottingham. A specialty rota exists and contact is via QMC switchboard (0115 924 9924). There is a referral proforma for all in-patient emergency transfers to the QMC.

In Leicester:- Direct referral can be made to any of the HPB Surgeons. A specialty rota exists and contact is via Leicester General Switchboard (0300 303 1573). An extraordinary provision for multidisciplinary discussion of patients is in place and the protocol for Leicester is provided as an example. Nottingham has a similar system.

Figure 10: Urgent Treatment Planning for Patients Prior to an Available MDT



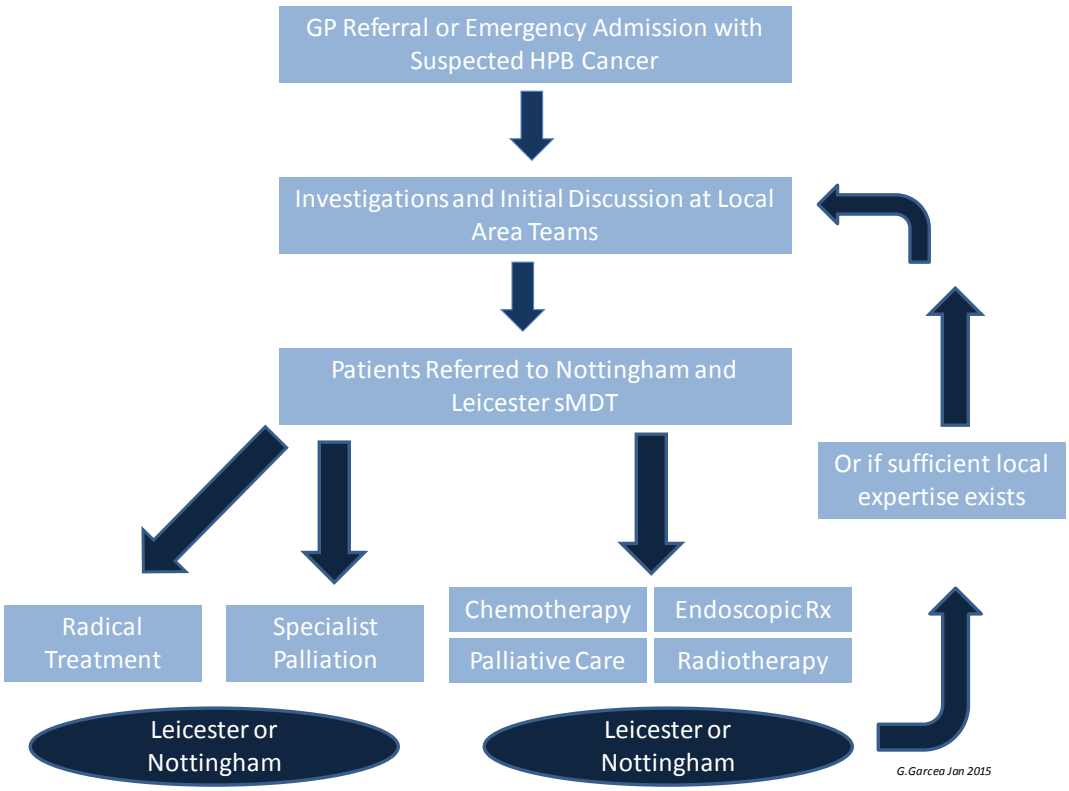
A patient who presents with symptoms suggestive of HPB cancer should be referred to a local diagnostic team specialising in the diagnosis and assessment of HPB cancer.

Specific recommendations: An urgent referral should be made when a patient presents with:

- Jaundice
- an upper abdominal mass
- significant unintentional weight loss
- an ultrasound scan showing liver lesions or a pancreatic mass

This forms part of the 2 week urgent suspected cancer referral process. A report should be made back to the referring primary healthcare professional within 5 days of referral.

Figure 11: Referral and Treatment Pathways in the East Midlands



All members of the ECAG comply with MDT-specific peer-review measures for both specialist HPB, Upper GI and colorectal tumour sites. They all contribute to the ECAG membership and contribute actively to meetings and network research.

IMAGING GUIDELINES

Metastatic Liver Disease Staging objectives

- To determine the presence of liver metastases in patients with a known primary malignancy (see appropriate sections).
- To identify the primary tumour if the liver lesion(s) have the imaging characteristics of metastases.
- To identify the distribution (number and *G.Garcea December 2014* ons and their relationships to the major vascular structures.
- To identify other sites of metastatic disease in patients being considered for resection or ablative therapies.
- To evaluate whether the liver pathology is benign, primary malignant liver disease or metastatic and thereby to decide whether no treatment, radical surgery or chemotherapy is required.
- To avoid biopsy if the lesion(s) are potentially resectable and the patient is a candidate for liver resection.
- To identify the need for percutaneous-targeted biopsy (generally required for systemic chemotherapy in the absence of a known primary or appropriate temporal relationship to a prior primary)

CT

- Oral administration of 1 litre of water or iodinated contrast medium.
- 100-150ml of intravenous iodinated contrast medium injected at 3-4ml/sec.
- MDCT through the liver is commenced at 65-70 seconds post injection.
- Using MDCT, slice thickness will depend on scanner capability. In general, sections are acquired at 1.25-2.5mm and reformatted at 5mm for viewing.
- Additional late arterial phase (approximately 30-35 seconds post injection) may be used for neuroendocrine tumours and hepatocellular carcinomas which are typically hypervascular (as are the benign lesions such as focal nodular hyperplasia and hepatocelluar adenoma).

Some populations of liver metastases from renal cell carcinomas, melanomas, sarcomas and breast cancers are also hypervascular; however, the frequency of liver metastases, only visible on arterial phase that will change the overall stage and affect management, is extremely low; thus additional arterial phase imaging in these patient groups is not routinely recommended.

MRI

- As breathing artefacts are problematic for liver imaging, strategies to overcome this need to be used in all patients. The appropriate strategy will depend on MRI machine specification but could include: breath-holding, navigator assisted, respiratory ordered phase encoding, and respiratory compensation.
- A multichannel surface coil should be used in all cases. The field of view will in general be the whole liver.

- It is to be noted that there is little general consensus with regard to optimal protocols mostly due to compromises that need to be made because of the MRI scanner being used.
- Most imagers would agree that the basic sequences that should be undertaken include T1W and T2W sequences. T1W sequences should be performed using spin- or gradient-echo sequences with the spins “in phase” (such that liver-spleen contrast is maximised). Opposed-phase GRE sequences are also valuable for the assessment of the fatty liver. T2W sequences with moderate and heavy weighting are useful for lesion characterisation and should be undertaken where possible.
- Extracellular small molecular weight contrast medium given intravenously is of value in lesion characterisation and detection (see injection protocol below).
- There is an increasing number of liver-specific contrast agents and these have both characterisation and detection roles. Some studies have demonstrated that liver-specific contrast media have advantages over non-specific small molecular weight chelates in specific circumstances, including prior to liver resection. Liver-specific contrast agents require protocol modification. Agents that increase T1-relaxivity require the use of GRE T1W sequences (with/without fat suppression). Contrast agents reccomedned are Primovist™ or Multihenhance™.

Suggested basic sequences and those for use with extracellular small molecular weight contrast medium given intravenously are given below. Sequences and timings related to liver specific contrast agent vary widely and radiologists using these agents should familiarise themselves on their appropriate usage.

Protocol for imaging of liver metastases			
Sequence	Plane	Slice Thickness	Principle observations
Fast GRE/FSE	Axial/coronal/sagittal	10mm	Overview and planning sequence
GRE T1W (in-and opposed-phase)	Axial	6mm	Demonstrate and eliminate the effects of intrahepatic fat and to characterise lesions
T2W – (fast) spin-echo with moderate and long TE. Alternatives include STIR and HASTE sequences	Axial	6mm	Identify and characterise cysts and haemangiomas
Dynamic contrast study T1W GRE Fat Sat †	Axial (± oblique coronal for vascular relationships		

† Unenhanced, arterial, portal venous phases. Equilibrium phase obtained with a 10 minute delay may be of value in characterising haemangiomas and cholangiocarcinomas. DWI (Diffusion Weighted Images with a high B value) are useful in detecting small lesions but not so helpful in characterisation.

PET-CT

18FDG PET-CT is a useful complementary technique to MRI for hepatic lesion detection (see also comments above). Metastases of the order of 5 mm in diameter can be detected in such tumours as colorectal cancer but it should be remembered that normal liver uptake of 18FDG can be heterogeneous. 18FDG PET-CT is a valuable technique in the post-radiofrequency ablation setting, being an early indicator of complete / incomplete tumour destruction and an effective modality for follow-up. CT and MRI are less sensitive than 18FDG PET-CT in this situation.

Primary Liver Cancer Staging objectives

- To identify the presence and location of the primary tumour and to detect multifocal liver involvement.
- To note the presence of vascular invasion.

- To identify lymph node enlargement.
- To determine the full extent of disease including deposits in the lungs, bones and peritoneum.
- To note whether parenchymal liver disease and portal hypertension are also present.
- To identify features of chronic liver disease.
- To evaluate whether the liver pathology is benign, pre-malignant or primary malignant and consequently to decide whether radical surgery, ablative therapy or palliation is required.
- To avoid biopsy if the lesion(s) are potentially resectable or if alpha-foetoprotein significantly elevated.

CT

CT of the chest, abdomen and pelvis is the investigation of choice.

- Oral administration of 1 litre of water or iodinated contrast medium.
- 100-150 ml of intravenous iodinated contrast medium injected at 3-4 ml/sec.
- MDCT with acquisition through the chest with dual phase acquisition of the liver commenced at 30-35 and 65-70 seconds post-injection the last acquisition continued through the pelvis.
- Using MDCT, slice thickness will depend on scanner capability. In general, sections are acquired at 1.25-2.5 mm and reformatted at 5 mm for viewing.
- If arterial anatomy is required prior to resection, an additional early arterial acquisition at 18-20 seconds with 1 mm collimation can be acquired although this is not routinely advocated.

Values of CTDIvol should normally be below the relevant national reference dose for the region of scan and patient group (see Appendix and section on *Radiation Protection for the Patient in CT* in chapter 2).

MRI

MRI has advantages over CT particularly for the evaluation of focal liver lesions in the cirrhotic liver.

Protocol for imaging of primary liver tumours			
Sequence	Plane	Slice thickness	Principle observations
Fast GRE / FSE	Axial /coronal / sagittal	10 mm	Overview and planning sequence
GRE T1W (in- and opposed-phase)	Axial	6 mm	Demonstrate and eliminate the effects of intrahepatic fat & to characterise lesions
T2W – (fast) spin-echo with moderate and long TE. Alternatives include STIR and HASTE sequences	Axial	6 mm	Identify and characterise cysts and haemangiomas
Dynamic contrast study T1W GRE Fat Sat *	Axial (± oblique coronal for vascular relationships)	2.5 ± 1 mm	To characterise and identify tumours to demonstrate vascular relationships

** Unenhanced, arterial, portal venous phases. Equilibrium phase obtained with a 10 minute delay may be of value in characterising haemangiomas and cholangiocarcinomas*

In patients with liver cirrhosis, contrast agents can be used either singly (usually extracellular small molecular weight contrast medium given intravenously) or in combination (usually SPIO particles) to exploit differences that exist in vascularity, hepatocytes function, or Kuppfer's cell density in order to differentiate between regenerative, dysplastic and neoplastic nodules.

PET-CT

18FDG PET-CT has variable efficacy in hepatobiliary tumours. The sensitivity for detection of hepatomas is in the range of 50-70%. Variable uptake of 18FDG is seen in cholangiocarcinoma although certain histological subtypes such as nodular cholangiocarcinoma can demonstrate sensitivity in the region of 85%. False positive 18FDG uptake is seen in acute cholangitis and inflammatory uptake is also observed following biliary stent insertion. Therefore when ^{18}FDG PET-CT is used for the assessment of cholangiocarcinoma it is generally important to perform the PET-CT study prior to biliary stent insertion.

Further Information

- With dynamic extracellular small molecular weight contrast medium enhancement it is important to have an unenhanced acquisition of the same sequence to identify true arterial enhancement; in liver cirrhosis, dysplastic nodules are often of high signal intensity.
- Sub-centimetre hypervascular lesions only identified on the arterial phase in patients with cirrhosis should be interpreted with caution – not all hypervascular lesions will be small HCCs.
- While the majority of HCCs are hypervascular, a minority are hypovascular.
- Well-differentiated HCCs may take up liver-specific contrast agents, while poorly-differentiated tumours usually do not; evaluation of all sequences with appropriate clinical parameters, including serum alpha-foetoprotein levels, is important in characterising focal liver lesions.
- Enlargement of lymph nodes is common in the presence of cirrhosis and, therefore, caution should be used in interpreting such peri-portal nodes as being involved.

Pancreas Cancer Staging Objectives

- To determine evidence of involvement of the visceral arteries and portal venous system.
- To identify deposits in the liver and peritoneum.
- To detect lymph node enlargement.
- To identify bile duct and duodenal obstruction.
- To evaluate whether the pancreatic pathology is inflammatory or malignant and thereby
- To decide pre-operatively whether radical surgery is required.

CT

- Oral administration of 1 litre of water as a contrast agent to fill the stomach and duodenum.
- 100-150 ml of intravenous iodinated contrast medium injected at 3-4 ml/sec.
- MDCT (dual phase acquisition) commenced at 35-40 seconds (pancreatic phase) and 65-70 seconds (portal venous phase) after onset of injection.
- Using MDCT images should be acquired at 1-1.25 mm slice thickness in the pancreatic phase and 2 mm in the portal venous phase.

Values of CTDIvol should normally be below the relevant national reference dose for the region of scan and patient group (see Appendix and section on *Radiation Protection for the Patient in CT* in chapter 2).

MRI

A negative oral contrast agent is helpful with a phased array surface coil.

Protocol for imaging of pancreatic tumours				
Sequence	Plane	Slice thickness	Field of view	Principle observations
Fast T2W imaging	Axial	10 mm	Liver and Pancreas	Overview and sequence planning
GRE T1W (in- and opposed-phase)	Axial	6 mm	Liver and Pancreas	Demonstrate and eliminate the effects of intrahepatic fat & characterise lesions
T2W Short and Long TE or HASTE	Axial	6 mm liver 4 mm pancreas	Liver and Pancreas	Identify characterize liver lesions Identify neuroendocrine pancreatic tumours
MRCP SSFSE	Coronal	5 cm	Liver and Pancreas	Demonstrate ductal anatomy If necessary supplement with 3-D FSE or 2-4 mm HASTE
T1W with fat saturation	Axial	5 mm	Pancreas	To identify small primary tumours
Dynamic contrast medium enhanced study 2-D / 3-D T1W GRE with or without fat saturation	Axial / oblique coronal * *see Tips*	2.5 ± 1 mm	Liver and Pancreas	To delineate the primary tumour, vascular involvement and identify liver metastases

PET-CT

On 18FDG PET-CT scans, acute pancreatitis and pancreatic carcinoma both show increased 18FDG uptake, and it is therefore not possible to differentiate these conditions,

although there may be some value to PET imaging when distinguishing chronic pancreatitis from carcinoma. 18FDG PETCT is not indicated routinely in pancreatic cancer but has been used to a limited extent to exclude distant metastases in patients being considered for radical treatment.

Tips

- Coronal or sagittal reformatted CT images can be very useful to evaluate vascular involvement. More complex reconstructions such as curved planar reformats are occasionally helpful.
- With the dynamic gadolinium-enhanced MR series, the optimal plane depends upon the location of the tumour. The pancreatic and portal venous phase acquisitions are best acquired using an oblique coronal plane for pancreatic head tumours followed by an axial acquisition. For tumours of the body and tail and for neuroendocrine tumours the initial acquisitions are best obtained axially. This is less critical if 3-D techniques are employed, because an isotropic dataset can be obtained that can be reconstructed in any plane.
- A delayed axial acquisition through the pancreas at 10 minutes is of value in neuroendocrine tumours.
- 3-D T1 with fat saturation is preferable to 2-D sequences for MRCP, because image quality is much improved.

Pathology Guidelines

The pathological diagnosis of HPB cancer may be made from a wide variety of samples including percutaneous biopsy, EUS biopsy or FNA and ERCP cytology and frozen sections.

Examination of surgical resections for HPB cancer is important in order to verify the diagnosis, elucidate prognostic factors, including accurate staging and histological typing. Stage and type may have relevance with respect to further treatment. Surgical histopathology reporting should conform to requirements of the Royal College of Pathologists guidelines –

http://www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/D/datasethistopathologicalreportingcarcinomasmay10.pdf

http://www.rcpath.org/Resources/RCPath/Migrated%20Resources/Documents/G/g085giandptissuepathwayfinal.pdf

PATIENT EXPERIENCE (13-1C-108n)

In the course of their regular meetings, the network group will annually review patient feedback of their associated MDTs and any actions implemented, and will agree an improvement programme with them. Patient experience survey results will be found in the annual report.

CLINICAL OUTCOMES, INDICATORS AND AUDITS (13-1C-109n)

In the course of the regular meetings, the network group will annually review the progress (or discuss the completed results, as relevant), of the associated MDTs' outcome indicators and audits. At least two network audits will be undertaken annually (one every 6 months). Typical performance indicators will be:

- Percentage of patients with cytological/histological diagnosis (target 50%)
- Percentage or patients undergoing resection (target 15%)

- Minimum resections per surgeon (target 15)
- 30-day mortality post-resection (target <5%)
- 90-day mortality post-resection (target <5%)
- Percentage of patients who receive adjuvant treatment after resection (target 50%)
- Percentage of patients receiving chemo- or radiotherapy, if not eligible for surgical resection and if fit (PS: 0 or 1) (target 50%).
- Number of patients participating in clinical trials (target 33%)

DISCUSSION OF CLINICAL TRIALS (13-1C-110n)

The network group will discuss the MDT's report on clinical trials, annually with each of its associated MDTs and agree an improvement programme with them.

TEENAGE AND YOUNG ADULT (TYA) PATHWAYS

All patients suspected with cancer between the ages of 13-18 living within the East Midlands (East Midlands region as part of the East Midlands Cancer Network boundaries) to be referred to the East Midlands Children's and Young Persons' Integrated Cancer Service *(Principal Treatment Centre at Nottingham University Hospitals, Queen's Medical Centre Campus (Nottingham Children's Hospital) and University Hospitals of Leicester, Leicester Royal Infirmary site)*. This service is accessed by contacting the Paediatric Oncology Consultant on-call at Queens Medical Centre in Nottingham when a patient is judged likely to have cancer. The contact number for this service is 0115 849 3302.

- ✓ The paediatric pathway requires the centralisation of diagnostic investigations, surgery and the most intensive chemotherapy to QMC but most patients from Leicestershire, Rutland and Northamptonshire will receive most or all of their treatment in Leicester. There is also a shared care arrangement with the paediatric team at Northampton General Hospital.

- ✓ The Paediatric team would welcome a discussion about patients in this age group in case a specific patient needs an individualised pathway.

- ✓ Patients aged **18 years (but <19y)** also need to be treated in an age-appropriate cancer facility but depending on education/employment/diagnosis/trial availability etc it may be appropriate for them to be treated by the Paediatric or the Adult site-specific pathway (in age-appropriate facilities). A discussion between the Paediatric team and the Site-specific consultant about patients in this age group helps to ensure that patient's needs are best served. This decision will be made on a patient-by-patient basis but the location of care should be in an age appropriate environment. *

All patients aged 19-24 years will be offered the choice:

- to be referred to a young adult age-appropriate cancer facility
- access local adult cancer services

*Should patients (Hepatobiliary) require surgery; this will take place as per current pathway's Leicester General Hospital or Queen's Medical Centre (dependent upon where the patient resides at time of diagnosis). Patients will be offered choice for all follow up/chemotherapy care.

The East Midlands will have young adult (19 – 24y) age-appropriate cancer facilities at the following sites:

- Leicester Royal Infirmary, University Hospitals of Leicester (13-24 years)
- Nottingham City Hospital, Nottingham University Hospitals (19-24 years)
- *(Nottingham Children's Hospital, Queen's Medical Centre Campus – Nottingham University Hospitals (13-18 years)*

Choice regarding place of care will also be offered as appropriate at relapse, palliative and end of life care and for long term follow up. The young adult age-appropriate inpatient, day care and outpatient facility is under development and until this is in place the additional age-appropriate support that these patients will be able to access in Leicester and Nottingham will be limited to an on-site teenage and Young Adult Activity Coordinator/Development Officer, Social Worker and TYA Clinical Nurse Specialist. As soon as the facilities are completed all Site - Specific MDT's will be informed**.** All patients diagnosed with cancer between the ages of 13-24, living within the East Midlands (East Midlands region as part of the East Midlands Cancer Network boundaries) to be discussed at the TYA MDT and relevant Site Specific MDT.

TYA MDT will discuss the treatment plan forwarded from the (Site Specific MDT/Paediatric Cancer MDT) and discuss the patients psychosocial care needs. Please refer to the East Midlands TYA Multidisciplinary Operational Policy for the referral process *(referral information outlined in brief below)*

- Referrals to the TYA MDT will need to made via the referral form, this referral form

can be obtained from your trust Cancer Centre, East Midlands Cancer Network website www.eastmidlandscancernetwork.nhs.uk or the Principal Treatment Centre.

- The following referral routes have been identified:
  - Site Specific MDTs (MDT Coordinator or Medical Team treating the patient) 19-24 years
  - Surgeon at Biopsy stage of the pathway
  - Children's and Young Persons' Integrated Cancer Service 13-18 years
  - In exceptional circumstances trusts/departments/GPs

All patients should be referred back to the TYA MDT on completion of treatment, at relapse, and when commencing palliative and end of life care. Responsibility for making the referral will lie with local MDT Coordinators, Consultants, Cancer Centres and Clinical Nurse Specialists. All referral forms accompanied with relevant information relating to the patient will either be faxed to the Principal Treatment Centre or electronically using the nhs.net email address or via post. Contact details can be found by telephoning UHL 0116 2586721 and NUH 0115 9691169 ext 54550 and asking for assistance relating to the TYA MDT. Hepatobiliary MDTs North and South will refer directly to the TYA MDT and forward details of contact person(s) to the TYA MDT. Referrers and clinical teams will be encouraged to log into discuss their patient. All patients aged 15-24 years will need to be registered with the TYAC Registration Process; this will be completed via the TYA MDT. The Teenage and Young Adult Pathways for patient with HPB cancer were ratified by:-

Donna Hakes, Director of Clinical Effectiveness

Midlands and Eastern SCG

Chair, EMCN TYACNCG

August 14th 2012