Panorama of interventional oncology procedures in hepatobiliary and pancreatic malignancies

Poster No.: R-0045
Congress: 2019 ASM
Type: Educational Exhibit
Authors: J. Yeh¹, T. Yong¹, S. Leong², D. Burrows¹, H. K. Kok¹; ¹VIC/AU, ²Singapore/SG
Keywords: Biliary Tract / Gallbladder, Liver, CT, Ultrasound, Fluoroscopy, Ablation procedures, Chemoembolisation, Stents, Neoplasia, Cancer
DOI: 10.26044/ranzcr2019/R-0045

This PDF document has been automatically generated from a digital poster submitted online, and is meant for personal use only. Copyright restrictions might apply. Certain materials like for example videos - or multimedia files other than images in general, are not included in this PDF.
Learning objectives

- To provide a comprehensive review of the role of image-guided interventional procedures in the diagnosis and management of hepatobiliary and pancreatic malignancies

- To outline the pearls and pitfalls relevant to the interpretation of pre and post-procedural imaging studies.
Background

The incidence of hepatobiliary and pancreatic (HBP) malignancies (hepatocellular carcinoma, cholangiocarcinoma, pancreatic adenocarcinoma, neuroendocrine tumours and hepatic metastasis) is steadily increasing worldwide, in part due to the improvements in imaging techniques and availability, as well as an aging population(1). Primary HBP malignancies are often diagnosed at an advanced stage when curative surgical options are limited. However, recent years has seen a shift towards earlier diagnoses through timely investigation of incidental imaging findings in conjunction with minimally invasive therapies which can be curative or palliative in select patient groups(2). For patients with hepatic metastases, symptoms such as obstructive jaundice and cholangitis often profoundly impact quality of life which necessitates palliative intervention. Common presentations associated with HBP malignancies include abdominal pain, obstructive jaundice, pruritis and labile blood glucose levels(3). Catastrophic haemorrhage can occur from tumour rupture or secondary to liver failure whilst biliary obstruction may predispose to sepsis.

Concurrently, there has been rapid progress in the field of Interventional Oncology (IO) which now forms one of the four pillars of cancer care in addition to the fields of medical, surgical and radiation oncology(4). Both imaging and minimally invasive procedures have become integral components in not only the diagnosis, but also therapeutic and palliative approaches to management(5).

This article aims to provide a comprehensive review of the spectrum of common IO procedures across four major areas of practice - diagnosis, therapy, palliation and complication management (Table 1 on page 4). Relevant pre and post-treatment imaging examples will highlight imaging pearls and pitfalls of these procedures to the clinician and Radiologist. We will also summarize the contemporary evidence-base supporting the use of current image-guided therapies.
### Table 1: Spectrum of common IO procedures in hepatobiliary and pancreatic malignancies.

© Department of Radiology, Northern Hospital, VIC, Australia
DIAGNOSIS

Most HBP malignancies are initially detected on cross-section imaging studies. In most cases, a primary malignancy such as hepatocellular carcinoma (HCC) or pancreatic adenocarcinoma can be diagnosed with confidence on imaging alone when typical imaging features are demonstrated(6). However, tissue diagnosis is occasionally required when imaging features are equivocal, where liver metastases are present without an obvious primary source or when advanced molecular or mutation testing is necessary to guide subsequent systemic therapy including recruitment to clinical trials(7).

Specific biopsy techniques include percutaneous core biopsy for focal lesions or endobiliary forceps biopsies or cytology brushings for biliary strictures and cholangiocarcinomas (Fig. 1 on page 11).

Percutaneous core biopsies of focal liver lesions are commonly used to identify metastases, most commonly from a lung, colorectal or breast primary. Present guidelines for HCC diagnosis relegate the use of biopsies only for lesions with indeterminate or conflicting imaging features. However, given the increasing knowledge of HCC molecular characteristics and subtypes with prognostic impact, there may be a greater role for biopsies in HCC diagnosis in the future(7).

Most percutaneous biopsies are performed under ultrasound guidance with the use of an outer coaxial needle and an inner core biopsy needle (typically 16-18 gauge) to minimise the number of capsule transgressions, bleeding complications and increase biopsy yield. It is the authors' practice to administer local anaesthesia to the skin, tract and visceral capsule under real-time ultrasound guidance. Percutaneous core biopsies for focal lesions has a reported sensitivity of >90%. Lesions which are inconspicuous on ultrasound can be successfully biopsied with the aid of contrast-enhanced ultrasound with a sensitivity of 92.8% in one series(8).

Biliary strictures can be sampled from a percutaneous transhepatic or endoscopic approach (ERCP cytology brushings or EUS-FNA). The diagnostic yield of percutaneous transhepatic forceps biopsy is comparable to EUS-FNA with a reported sensitivity of 75% and specificity of 100% (9, 10) and can be performed at the time of percutaneous biliary drainage (Fig. 2 on page 11).
Biopsy complications include tumour seeding and haemorrhage. Tumour seeding post-biopsy is low(11). In the setting of HCC, a 2007 meta-analysis found the median incidence to be 2.7%(12) and is lower at 1.1% from metastatic liver lesions(13). Major bleeding following percutaneous biopsy is rare with an incidence of 0.8-1.1%(14, 15). Post-biopsy tract embolisation with gelatin sponge or autologous blood clot has a role in reducing haemorrhage risk.

**THERAPY**

Surgical resection or liver transplantation are the preferred curative treatment options for patients with HPB malignancy. Locoregional IO therapies are primarily reserved for patients deemed non-surgical candidates due to comorbidities or disease status and involve thermal ablation, which is potentially curative for early-stage disease, or embolisation therapies for disease control(16).

**Ablation**

Thermal ablation techniques, utilising either radiofrequency (RFA) or microwave (MWA) energy to produce localized tumour heating and coagulative necrosis, are used to treat early-stage HCC (BCLC Stage A - single to 3 nodules) and liver metastases.

Ablation is performed by placement of an antenna in the epicenter of the lesion under imaging-guidance followed by selection of appropriate energy power and treatment time to achieve a zone of ablation incorporating the tumour (Fig. 3 on page 12, Fig. 4 on page 13). The efficacy between RFA and MWA (overall survival [OS], local recurrence and complication rates) are identical but MWA has largely replaced RFA in the liver due to higher intratumoral temperatures, better thermal convection, faster ablation times and less susceptibility to heat sink effects when tumours are located in proximity to large blood vessels which may result in incomplete ablation(18). The latest generation MWA systems are capable of ablation zones of between 4-5 cm per probe and multiple probes can be used to achieve a larger, overlapping ablation zone for larger tumours.

Current evidence has not conclusively shown superiority of surgical resection over ablation, but resection may have an advantage for larger tumours (3-5 cm) due to the greater risk of incomplete ablation(19). Individual patient and disease characteristics are probably of equal importance in the selection of an appropriate treatment modality.
CT imaging appearances in the early post-treatment period (Fig. 5 on page 14), a spherical area of hypoenhancement corresponding to the ablation zone and in the very early post-treatment period, a hyperenhancing rim due to reactive tissue hyperaemia. Follow-up imaging shows a gradual decrease in size of the ablation zone with scarring. Incomplete treatment or recurrence is detected based on residual or new areas of enhancement on CT or MRI.

**Chemo and radioembolisation**

Transarterial chemoembolisation (TACE) is a locoregional treatment which involves precise intra-arterial delivery of chemotherapy and embolisation of tumour arterial supply to achieve combined cytotoxic and ischaemic effects leading to tumour necrosis. TACE is indicated in the treatment of intermediate stage HCC (BCLC Stage B) or unresectable colorectal liver metastases for disease control. TACE can also be used in the liver transplant setting to downstage a patient into transplant criteria eligibility and extend the patient’s time on the transplant waitlist(20). The best candidates for TACE are patients with solitary or limited multifocal HCC with preserved liver function (Child Pugh A or B) and no evidence of vascular invasion. TACE has been shown to improve survival of patients with HCC compared to best supportive management(21-23) and in patients with colorectal liver metastases after failure of systemic chemotherapy(24).

TACE can be further divided into conventional TACE (c-TACE) and drug-eluting-bead TACE (DEB-TACE) (Fig. 6 on page 15, Fig. 7 on page 16). c-TACE involves delivery of a liquid mixture of lipiodol with chemotherapy followed by arterial embolisation with gelatin sponge particles. DEB-TACE utilizes 75-300 micron embolic microparticles (e.g. DC Bead, BTG; Tandem, Boston Scientific) which gradually releases chemotherapy into the tumour. Both techniques are similar in efficacy but DEB-TACE is associated with better tolerability and fewer adverse events in comparative randomized-controlled trials(25, 26). TACE is delivered through a microcatheter advanced into the implicated hepatic arterial branches with delivery of the chemotherapy and embolic agent to the tumour. Embolisation works well in this setting as tumours preferentially derive vascular supply via the hepatic artery in comparison to normal liver tissue which is supplied predominantly by the portal vein (70%). Doxorubicin is commonly used as the chemotherapeutic agent for HCC (DEBDOX-TACE) whilst irinotecan is used for colorectal metastases (DEBIRI-TACE).

Transarterial radioembolization (TARE) or selective internal radiation therapy (SIRT) (Fig. 8 on page 17) is a more recent locoregional treatment and is a form of brachytherapy delivered through Yttrium-90 containing resin (SIR-Spheres, Sirtex) or glass (TheraSphere, BTG) microspheres resulting in local emission of beta-radiation. The microspheres are delivered through a microcatheter from the hepatic artery to one liver lobe at a time. Although TARE is less 'targeted' compared to TACE, the technique is
suited for multifocal lesions. As the embolisation effect is minimal due to the small particle size, it is suitable treatment option for patients with portal vein thrombosis or invasion where TACE is contraindicated. Both TACE and TARE have similar clinical outcomes for HCC and colorectal metastases(27-29).

Imaging post-locoregional therapy is based on the detection of residual or new arterial hyperenhancement to indicate residual or recurrent disease or lack of enhancement as an indicator of necrosis rather than lesion size. The modified Response Evaluation Criteria in Solid Tumours (mRECIST) and European Association for the Study of the Liver (EASL) guidelines have been published to specifically guide reporting following locoregional therapy(30, 31). Readers are also directed to an excellent review of post-locoregional therapy imaging by Young et al for further reading(32).

**Portal vein embolisation (PVE)**
In contrast to the aforementioned therapies, PVE has a role in curative-intent hepatectomy(33). Patients who are candidates for major liver resection may require PVE to increase the volume of the future liver remnant (FLR) when the FLR is too small to support essential liver function post-operatively. PVE is indicated when the FLR volume as measured on CT volumetry is between 25-30% of the original liver volume in healthy livers or between 35-40% in the presence of chronic liver disease such as cirrhosis, post-chemotherapy liver injury or cholestasis(34).

Embolization redirects portal vein flow towards the residual segments, promoting liver growth and thus optimising FLR prior to hepatectomy (Fig. 9 on page 17). PVE can be performed via an ipsilateral (to the planned resection side) or contralateral (via the FLR) approach (Fig. 10 on page 18). Following percutaneous transhepatic access into the portal vein, individual portal vein segments are selectively embolised using a mixture of embolic agents to achieve stasis (Fig. 11 on page 19, Fig. 12 on page 20). Commonly used embolic materials include microparticles such as PVA, gelatin sponge, embolisation coils, glue and vascular plugs. Preoperative PVE has a high clinical success rate with a mean FLR hypertrophy rate of 37.9%(34).

**PALLIATION**
IO has a rapidly expanding role in the palliative management of patients with advanced-stage cancer, often with complex post-surgical anatomy and medical comorbidities; increasing anaesthesia and surgical risk(35, 36). The minimally invasive nature of IO offers suitable alternatives to maximise quality of life and reduce the length of hospitalisation.
**Percutaneous transhepatic cholangiography (PTC), biliary drainage and stenting**

Biliary obstruction with obstructive jaundice is a frequent presentation of advanced HPB malignancy and can arise from tumour or extrinsic nodal compression as well as in-situ tumour growth in the case of cholangiocarcinoma. Most cases of biliary obstruction are now diagnosed on cross-sectional imaging with ultrasound or CT. PTC is a well-established procedure, first conceptualized more than fifty years ago which maps out the biliary anatomy and is now most commonly performed during percutaneous transhepatic biliary drainage (PTBD) to relieve biliary obstruction(37) (**Fig. 13 on page 21**). Although endoscopic (ERCP) management of biliary obstruction has seen an increased role in recent years, PTBD remains indispensable in the treatment of biliary hilar strictures, post-operative anatomy limiting endoscopic access (e.g. following gastrectomy, Whipple resection) or where endoscopic attempts have failed. Potential complications associated with PTBD include malposition or migration of biliary drains, vascular injury during percutaneous access and peri-procedural sepsis(38).

Percutaneous biliary stenting to internalize biliary drainage often follows an initial trial of PTBD as a more permanent solution and increases patient comfort. Self-expanding metal stents are preferred over plastic stents in cases of malignancy due to superior patency, lower likelihood of reintervention and lower risk of migration(39) (**Fig. 14 on page 22**). In addition, hilar strictures which present an anatomical challenge, can be managed with hilar-reconstruction techniques including kissing, Y or trifurcation stents(39) (**Fig. 15 on page 23, Fig. 16 on page 23**). The Achilles heel of biliary stenting is limited long-term primary patency rates which is on average about 1 year as a consequence of tumour ingrowth. Polytetrafluoroethylene-covered stents were once thought to be more effective in resisting tumour ingrowth(39, 40). However, a 2014 randomised controlled trial cast doubt upon the superiority of covered stents(41) and a recent meta-analysis of 14 trials found no significant difference between covered and uncovered metal stents in terms of primary patency and stent dysfunction(42).

**Coeliac plexus neurolysis**

The coeliac plexus, the largest sympathetic plexus, relays nociceptive impulses from the stomach to the proximal transverse colon. Neurolysis of the coeliac plexus with a percutaneous injection of pure ethanol alleviates pain originating from the upper abdominal viscera. This technique has been widely used since its introduction in 1914(43). Image guidance can be provided by fluoroscopy, ultrasound, computer tomography (CT) or magnetic resonance imaging (MRI); CT is now the preferred technique given the superior anatomical detail achievable and greater independence from operator skill(44).
CT guided percutaneous coeliac plexus nerve block is an established therapeutic choice in the treatment of intractable pain in the setting of upper abdominal malignancy. Coeliac plexus neurolysis is an effective technique (Fig. 17 on page 24), found to have lasting analgesic effects in 70-90% of patients with upper abdominal malignancies(45). Neurolysis allows for reduction in the chronic use of high-dose opioid analgesia and the associated adverse effects; improving the quality of life(46, 47). There is a low complication rate associated with this procedure(45, 48).
Fig. 1: Transluminal biliary biopsy forceps (Cook, Bloomington, IN) in the open and closed position. This 5.2 French device can be advanced through a 6 or 7-French introducer sheath to obtain biopsies during percutaneous transhepatic cholangiography (PTC).

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 2: Endoluminal biopsy techniques for intraductal lesions. (A) Coronal fusion 18FDG PET-CT image in a patient with obstructive jaundice showing a large metabolically active mass at the hilum of the liver (arrow). (B) Transluminal biliary biopsy forceps (Cook, Bloomington, IN) demonstrating operation of the forceps. (C) Endobiliary biopsies were taken from the stricture using a transluminal biopsy forceps deployed through a 7-French introducer sheath (arrow), subsequently confirming cholangiocarcinoma. (D) Mid common bile duct obstruction in a different patient with obstructive jaundice. Endobiliary brush cytology taken with a wireguided cytology brush (Boston Scientific, Marlborough, MA) (arrow) confirmed cholangiocarcinoma.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 3:** (A) Microwave ablation antenna and (B) generator system (Emprint, Medtronic, Dublin, Ireland). (C) In vitro microwave ablation of an ox liver showing the spherical ablation zone on the liver surface. (D) Cut section through the treatment zone showing the spherical ablation margin.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 4:** Liver microwave ablation video demonstrating treatment of BCLC Stage A HCC. A microwave ablation antenna has been inserted into the centre of a 2.5 cm HCC lesion under ultrasound guidance followed by delivery of microwave energy leading to formation of echogenic gas bubbles from coagulative necrosis during ablation.

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 5: (A) Pre-ablation contrast enhanced CT in a different patient showing a focal metastasis in segment VIII of the liver (arrow) and (B) post-ablation CT showing a zone of coagulative necrosis larger than the lesion (arrow) consistent with successful treatment.

© Department of Radiology, Singapore General Hospital
**Fig. 6:** Transarterial chemoembolisation (TACE) for HCC. (A) Pre-TACE angiography showing a tumour blush (arrows) corresponding to a hypervascular HCC in segment V. (B) Drug-eluting bead TACE was performed with superselective delivery of (C) doxorubicin-loaded beads (Tandem, Boston Scientific) to the feeding arterial branches. (D) Axial T1 post-contrast MRI liver shows cirrhosis with an arterially hyperenhancing mass in segment V compatible with HCC. (E) Follow-up post-contrast MRI 6 weeks after TACE shows absence of enhancement consistent with treatment response.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 7:** TACE for HCC with cone-beam CT assistance. (A) Selective angiography of the segment VI hepatic artery through a microcatheter shows a faint blush of tumour enhancement. (B) This was confirmed with cone-beam CT performed on the angiography table prior to TACE to facilitate superselective embolisation with drug-eluting beads, sparing the normal liver parenchyma.

© Department of Radiology, Northern Hospital, VIC, Australia

**Fig. 8:** Yttrium-90 transarterial radioembolization (TARE) for HCC. (A) Arterial and (B) portal venous phase contrast-enhanced liver MRI shows a large subcapsular mass in the dome of segment VII (arrows) with arterial hyperenhancement and washout typical for HCC. (C) Follow-up MRI liver 14 months post-TARE shows regression in size of the tumour with no residual enhancement consistent with complete response to treatment.

© Department of Radiology, Singapore General Hospital
Fig. 9: Portal vein embolisation prior to planned extended right hepatectomy (right trisegmentectomy) for metastatic colorectal cancer. (A) Contrast-enhanced CT showing multiple hypoenhancing metastases in the right hepatic lobe involving segment IV. The future liver remnant (FLR) volume of the residual left lobe was insufficient to permit safe resection. (B and C) Follow-up CT liver volumetric study showing hypertrophy of the left hepatic lobe FLR (indicated in green) to 45% from 30% at baseline.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 10:** Fluoroscopic video of portal vein embolisation performed through an ipsilateral approach using a 5-French reverse curve Sim 2 catheter with delivery of PVA microparticles into targeted portal vein branches to stasis.

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 11: Pre-embolisation portal venography following percutaneous right portal vein access outlines the portal vein segmental anatomy.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 12:** Post-embolisation portal venography in the same patient demonstrating pruning of the portal vein branches in the right hepatic lobe with lack of peripheral parenchymal enhancement consistent with technical success.

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 13: Obstructive jaundice due to liver metastatic disease. (A) Contrast-enhanced CT showing a large mass (asterisk) in segment IV compressing the ductal confluence and resulting in biliary obstruction. (B) Bilateral PTC and biliary drains placed across the sites of obstruction (arrows) with decompression of the biliary tree. Multiple side-holes are visible along the length of the biliary drains to permit function as an internal stent when the drain is capped. The proximal limit of the side-holes is indicated by radiopaque markers and the position of the side-holes should be routinely assessed on cross-sectional imaging to detect drain malpositioning.

© Department of Radiology, Northern Hospital, VIC, Australia
**Fig. 14:** Metallic biliary stenting for biliary obstruction secondary to pancreatic cancer. (A) Right-sided PTC shows marked biliary obstruction and extrinsic compression of the CBD from a pancreatic head mass. (B) The stricture was crossed and cholangioplasty was performed with an 8x80mm balloon (arrow) to permit passage of the stent delivery system. (C) A nitinol self-expanding metallic stent was deployed (Zilver, Cook) in satisfactory position across the stricture. The proximal (arrow) and distal radiopaque markers of the stent are visible to aid assessment of position during and after deployment.

© Department of Radiology, Northern Hospital, VIC, Australia

**Fig. 15:** Bilateral metallic Y stents for biliary obstruction secondary to widespread liver metastases from colorectal cancer. (A) Bilateral PTC shows obstruction at both the hilum and distal common bile duct. (B) Bilateral 8x60mm self-expanding nitinol stents (Cook) in a kissing Y configuration were deployed into a 10x70mm self-expanding elgiloy Wallstent (Boston Scientific) which was deployed in the common bile duct across the ampulla. (C) Follow-up CT showing satisfactory position of the stents with pneumobilia in the intrahepatic bile ducts consistent with stent patency (arrows). This is a useful sign to look for when assessing stent patency on abdominal CT studies.

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 16: Trifurcation metallic stenting in a patient who presented with biliary sepsis on a background of previous metallic stenting for cholangiocarcinoma. (A) CT demonstrating isolated dilatation of the posterior segments VI and VII due to disease progression. (B) PTC through the obstructed posterior ducts shows contrast hold-up at the junction of the previously deployed bilateral metallic stents. (C) The struts of the existing Y stents were crossed and a new 8x60mm self-expanding nitinol stent was placed to drain the posterior segments (white arrowhead) resulting in a trifurcation stent configuration. Existing stents into the anterior segments V/VIII (black arrow) and II/III (white arrow) are indicated. (D) Final cholangiogram shows satisfactory drainage of all hepatic segments.

© Department of Radiology, Northern Hospital, VIC, Australia
Fig. 17: Coeliac plexus neurolysis for pancreatic cancer with intractable pain. Under CT fluoroscopic guidance, a 22-gauge Chiba needle was advanced through the left hepatic lobe from an anterior approach into the periaortic space at the level of the coeliac artery. Contrast injection through the needle (arrow) confirms extravascular position of the needle tip, layering along the anterolateral aorta. Dehydrated ethanol was injected to perform a neurolytic coeliac plexus block with good clinical improvement.

© Department of Radiology, Northern Hospital, VIC, Australia
Conclusion

Interventional oncology procedures have become an established component for the management of HBP malignancies. An awareness of the versatile spectrum of diagnostic and therapeutic procedures in this setting will assist clinicians and Radiologists in providing the optimal patient outcome.
Personal information

Jennifer Yeh\textsuperscript{1}, MD, BTech
Tuck Yong\textsuperscript{2}, FRACS
Sum Leong\textsuperscript{3}, FFRRCSI, EDIR
David Burrows\textsuperscript{1}, FRANZCR
Hong Kuan Kok\textsuperscript{1}, FFRRCSI, FRCR, FRANZCR, EBIR

\textsuperscript{1}\textit{Department of Radiology, Northern Hospital, Melbourne, AU}

\textsuperscript{2}\textit{Department of Hepatobiliary Surgery, Northern Hospital, Melbourne, AU}

\textsuperscript{3}\textit{Department of Radiology, Singapore General Hospital, SG}
References


8. Cao XL, Zhou, Xiang; Geng, Chengyun; Chang, Qing; Zhu, Li; Feng, Wenqi; Xu, Tianyu; Xin, Yujing. Usefulness of real-time contrast-enhanced ultrasound guided coaxial needle biopsy for focal liver lesions. Abdominal Radiology. 2018;44(1):310-7.


20. She WH, Cheung TT. Bridging and downstaging therapy in patients suffering from hepatocellular carcinoma waiting on the list of liver transplantation. Transl Gastroenterol Hepatol. 2016;1:34-.


35. van den Bosch MP, W; van der Linden, EM; Meijerink, MR; van Delden, OM; Mali, WP; Reekers, JA,: The radiologist as the treating physician for cancer: interventional oncology. Ned Tijdscr Geneeskd. 2009;153(A 532).


