CT and MR imaging findings of Cholangiolocellular Carcinoma of the Liver: correlation with histopathologic features and differential diagnosis

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Learning Objectives

- To explain clinical background of cholangiolocellular carcinoma of the liver (CoCC).
- To understand pathologic features of CoCC based on the latest World Health Organization (WHO) classification criteria.
- To describe the findings of CT and MR imaging including gadoxetic acid disodium (EOB)-enhanced MR imaging and histopathologic correlation.
- To identify the characteristic CT and MR imaging features and discuss differential diagnosis among other major primary malignant hepatic tumors such as hepatocellular carcinoma (HCC) and intrahepatic cholangiocarcinoma (ICC).

Background

CoCC was recently categorized as a subtype of combined hepatocellular-cholangiocarcinoma with stem cell features (cholangiolocellular type), according to the latest WHO classification and has been reported to have a better outcome after hepatectomy than other major primary malignant hepatic tumors such as HCC and ICC. Thus, its accurate imaging diagnosis is crucial for determining prognosis and therapeutic planning and radiologists have to be familiar with its characteristic CT and MR imaging features.

Clinical background of Cholangiolocellular carcinoma (CoCC)

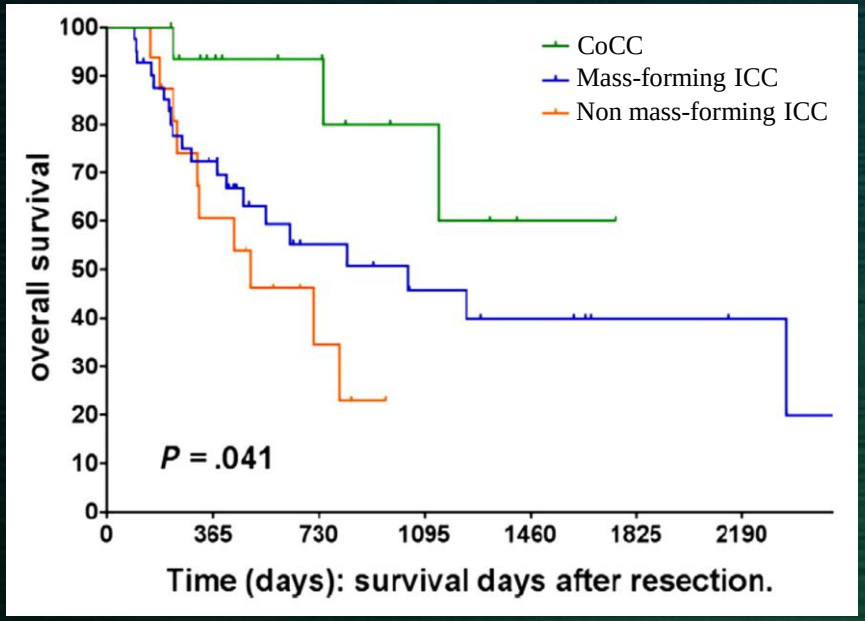
- Cholangiolocellular carcinoma (CoCC) is a rare malignant primary liver tumor and, is considered to originate from the ductules/canals of Hering, where hepatic progenitor cells are located; it was first reported by Steiner and Higginson[1)].
- CoCC is commonly occurred in the middle-aged and older patients (mean, range; 62.2, 41-84)[2)]. but rarely, the young or pediatric case has been reported[3, 4)].
- CoCC can be occurred in the patients with and without chronic liver disease (cirrhosis or chronic hepatitis) (Table 1)[2)].
- The level of tumor marker including AFP, PIVKA-II, or CA19-9 can be elevated in about 60% of CoCC patients (Table 1)[2)].

Table 1

CoCC (n=19)								
Background liver, n (%)				Hepatic viruses , n (%)			Tumor maker, n (%)	
Lver cirrhosis	Chronic hepatitis	Fatty liver	Normal liver	HBV	HCV	Negative	Positive (AFP, CA19-9, etc)	Negative
2 (10.5)	8 (42.1)	2 (10.5)	9 (47.4)	7 (36.8)	3 (15.8)	9 (47.4)	12 (63.2)	7 (36.8)

Clinical background of CoCC

- CoCC is a rare but has been reported to have a better outcome after hepatectomy than other major primary malignant hepatic tumors such as HCC and ICC. The reported 5-year survival rate for patients with CoCC who underwent curative surgery is 75 %, which is considerably higher than that of mass-forming type of ICC (33%, p=0.0005) [5]. The 1-, 3-, and 5-year survival rates in patients with CoCC to be 93%, 79%, and 52%, respectively [6]. Thus, its accurate diagnosis is crucial for determining prognosis and therapeutic planning.



Kaplan-Meier survival curves show the 1-, 3-, and 5-year survival rates in the patients with CoCC to be 93%, 79%, and 52%, respectively, which are significantly higher than those of mass-forming (72%, 46%, and 40%, respectively) and non-mass-forming (61%, 18%, and 0%, respectively; P-.041) ICCs[6].

World Health Organization (WHO) classification criteria of Combined hepatocellular-cholangiocarcinoma

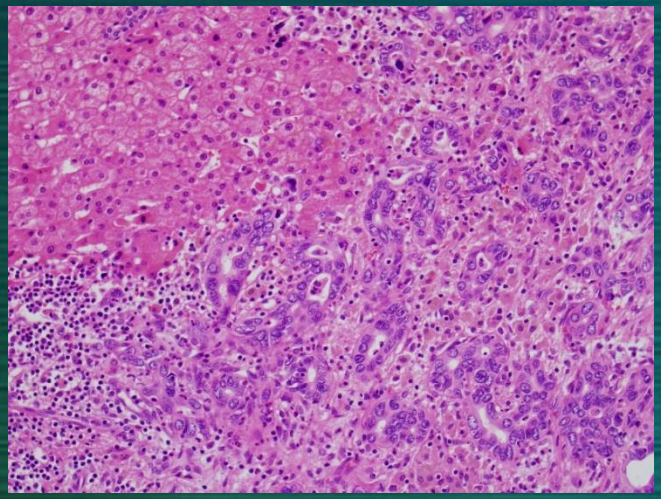
1. Classical type: the mass has typical hepatocellular and cholangiocarcinoma components progenitor/stem cell marker (-)
2. Stem-cell features subtype: progenitor/stem cell marker (+)
   a. typical subtype
   b. intermediate subtype
   c. cholangiolocellular subtype ⇒ CoCC

The characteristic histopathological features of CoCC include

(a) small uniform glands that are arranged in a tubular, cord-like or "antler-like" anastomosing pattern with marked fibrous stroma

(b) continuous tumour cords with normal liver cell cords in a replacing growth pattern

(c) no mucin production



Hematoxylin and eosin-stained section (x10)

CT and MR imaging features of CoCC

Morphological and signal features[2)]

Tumor margin	
lobulated	70%
irregular	30%
Capsule	none
Fat	none
Calcification	none
Capusular retraction	26%
Vessel penetration	32%
IHBD dilatation	10%
Fused-multinodular configuration	65%

T1WI	
low intensity	95%
iso intensity	5%
T2WI	
high intesnity	100%
ring-like	30%
entire	70%
DWI	
high intensity	100%
target	60%
entire	40%

IHBD=intrahepatic duct

CT and MR imaging features of CoCC

Contrast-enhancement features[2)]

Dynamic phases

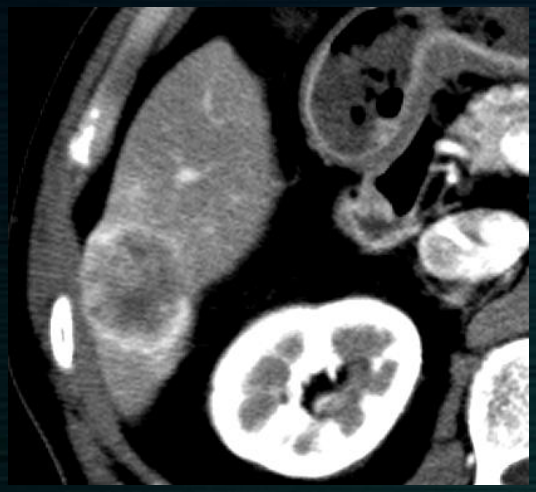
Arterial phase	
ring	80%
global	20%
Portal and late phase	
progressive enhancement	60%
washout	10%
Dot/band-like enhancement	79%

Hepatocyte phase

EOB targt sign	85%
Entirely low	15%

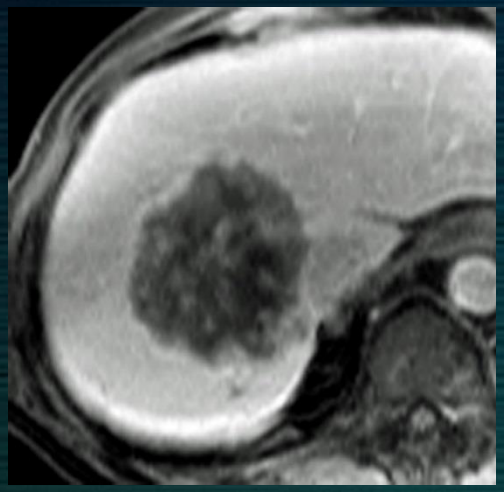
Thickness of ring enhancement CoCC>ICC

Key imaging features of CoCC-histopathological correlations



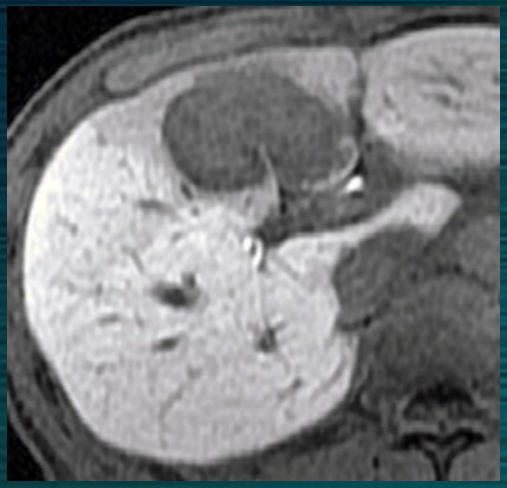
Thicker ring-like enhancement

tumour cell nests in the lesion are specifically arranged in the peripheral part of the tumour[2, 7)]



Dot-/band-like internal enhancement

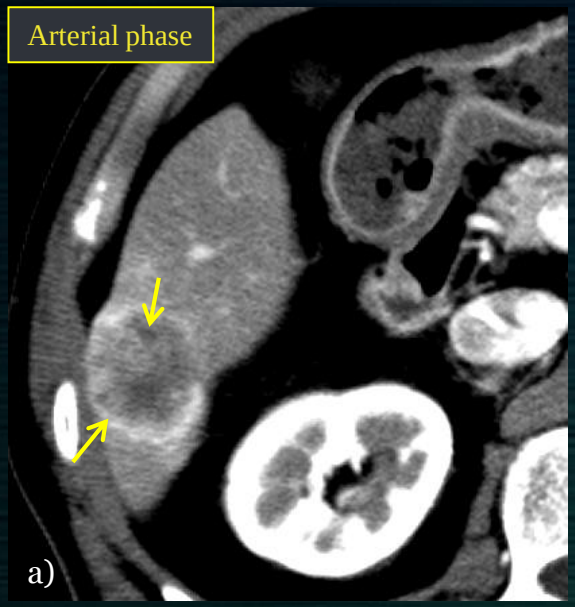
the tumour cell nest with vascular proliferations and retained Glisson's sheath structure [2)]

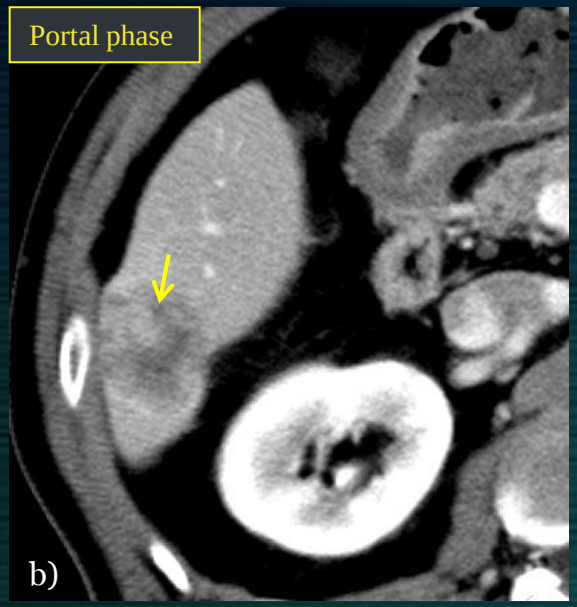


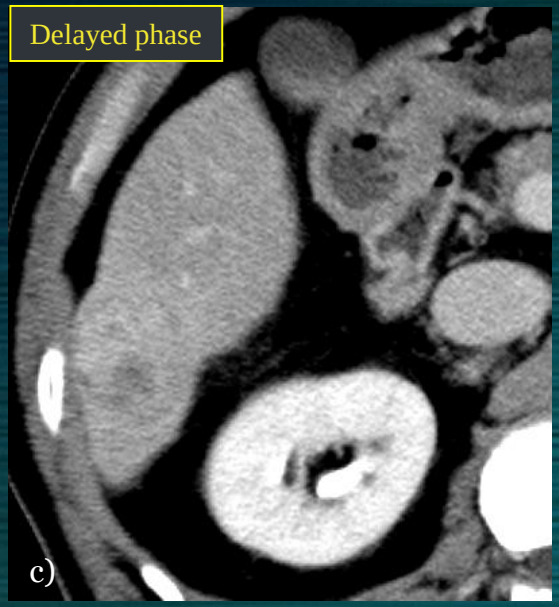
EOB target sign

extracellular accumulation of EOB in hyalinized/edematous stromal fibrosis [8-10)]

Contrast-enhanced dynamic CT

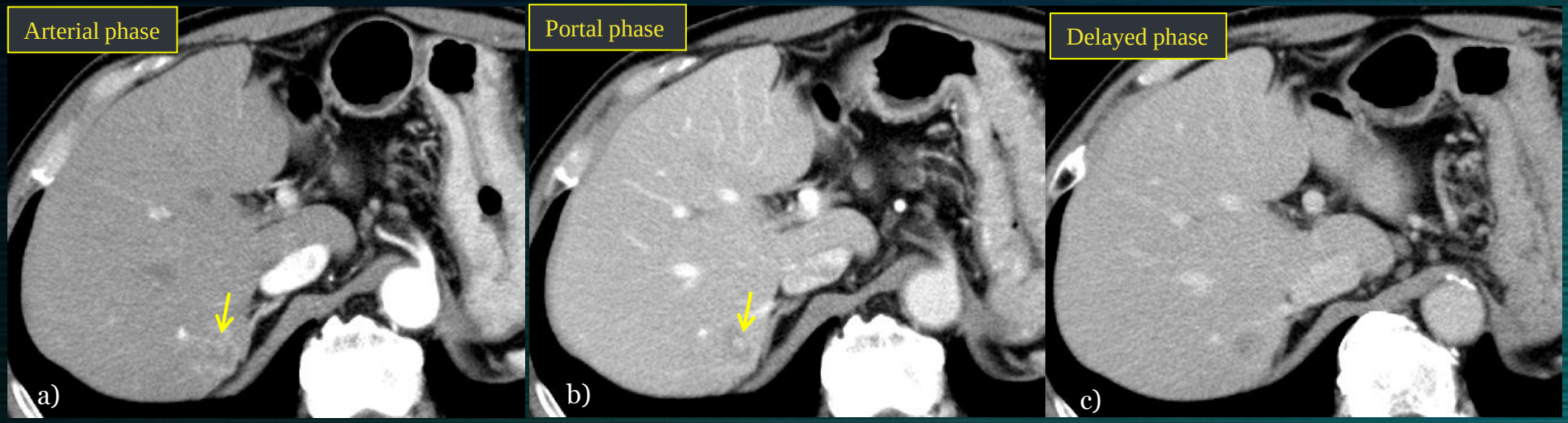






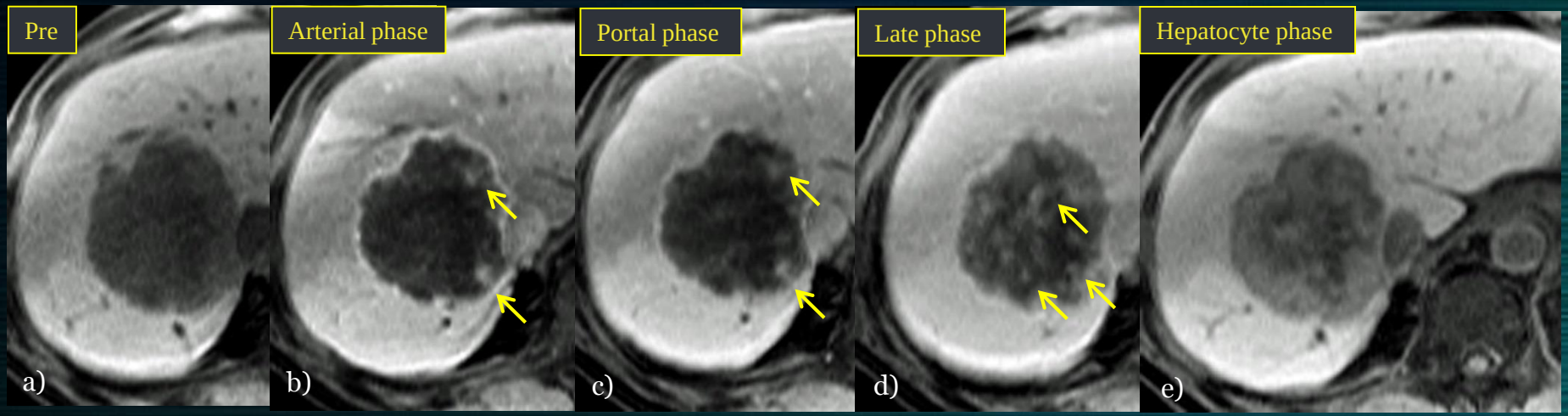
A surgically resected CoCC in a 54-year-old man.
The mass in S6 shows thicker arterial ring enhancement with dot-like internal enhancements (arrows) during arterial and portal phases (a, b). It also shows delayed enhancement due to fibrous stroma and appears almost isointense compared to the surrounding liver parenchyma at delayed phase (c).

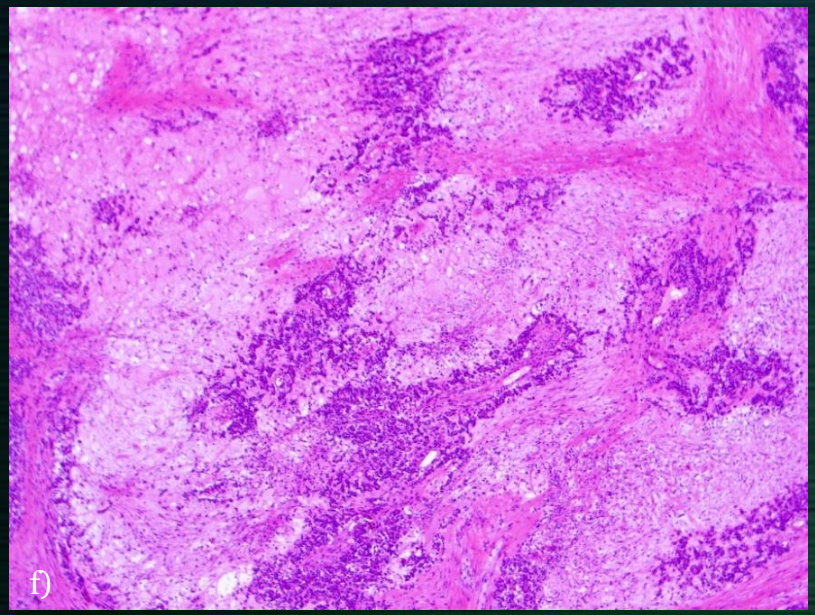
Contrast-enhanced dynamic CT



A surgically resected CoCC in a 62-year-old man.
The mass in S7 shows thicker arterial ring enhancement with dot-like internal enhancement (arrows) during arterial and portal phases (a, b). It becomes almost isointense compared to the surrounding liver parenchyma at delayed phase due to delayed enhancement in the fibrous stroma (c).

EOB-enhanced MRI

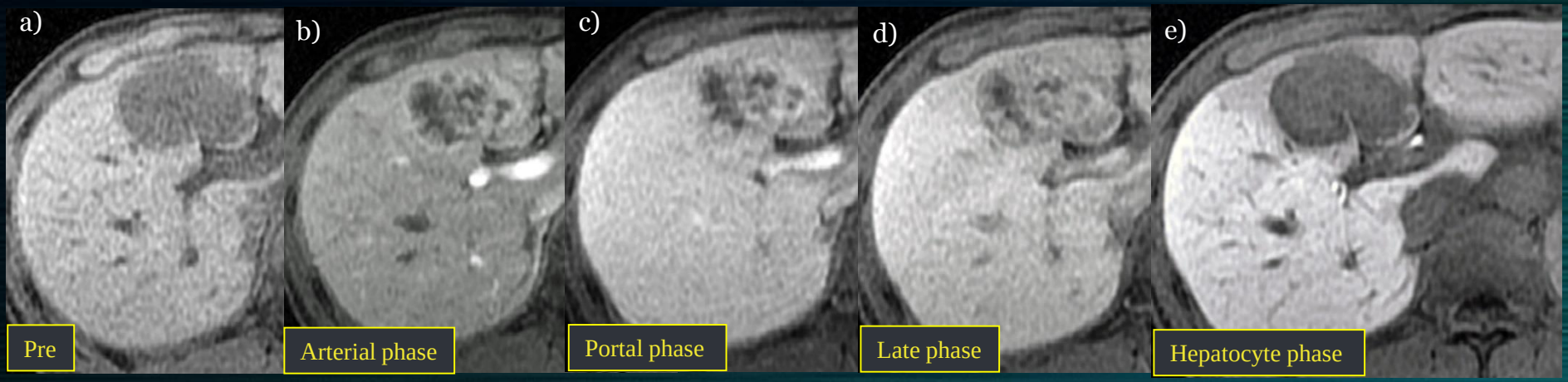


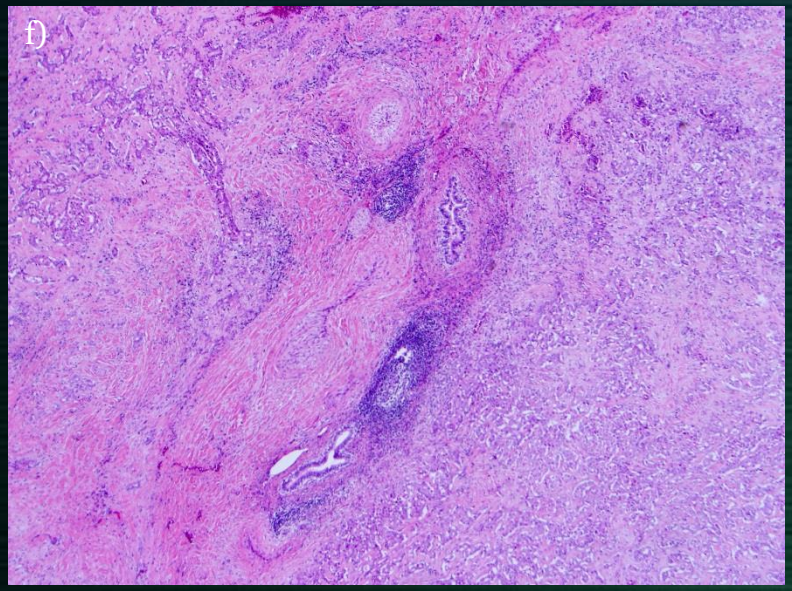


Hematoxylin and eosin-stained section (x4)

A surgically resected CoCC in a 69-year-old man. The mass shows arterial ring enhancement with multiple dot-like internal enhancements (arrows) during arterial and late phases (b-d). Hepatocyte phase MR image (e) demonstrates the mass with a target appearance, which corresponds to fibrous stroma at histopathology. The dot-like internal enhancement during the arterial and late phases, which microscopically corresponds to the tumor cell nest accompanied with vascular proliferations (f).

EOB-enhanced MRI

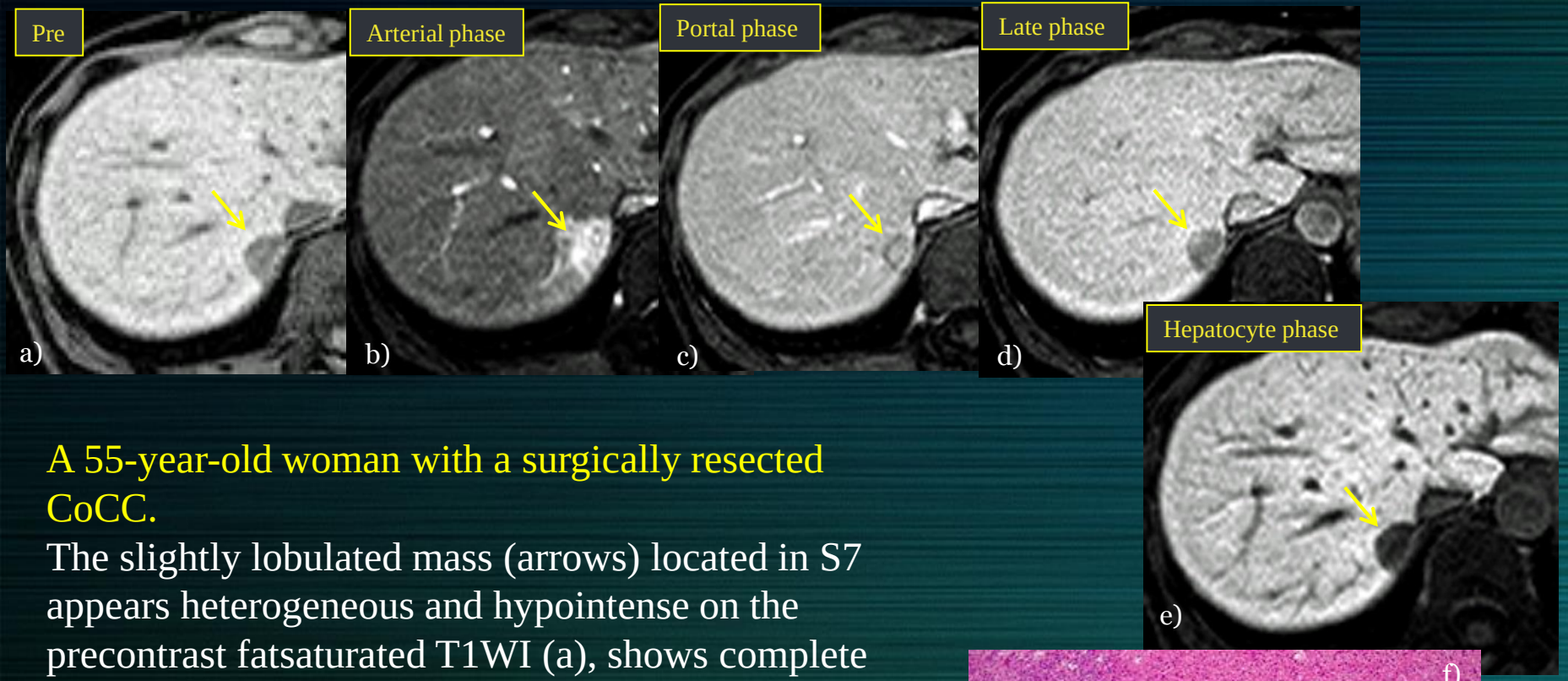




Hematoxylin and eosin (H and E)-stained section (x4)

A surgically resected CoCC in a 50-year-old woman. The lobulated mass located in the medial hepatic segment appears hypointense on the precontrast fatsaturated T1-weighted image (a) and shows relatively thick arterial ring enhancement with delayed progression during the arterial and late phases (b–d). Several dot-/band-like internal enhancements are also seen in the mass during the same phases (b–d). On the hepatocyte phase MR image the mass has a target appearance (EOB target sign) due to central fibrous stroma. The H and E-stained section (f) shows a retained Glisson's sheath structure in the fibrous stroma, which corresponds to the band-like internal enhancement during the arterial and late phases

EOB-enhanced MRI

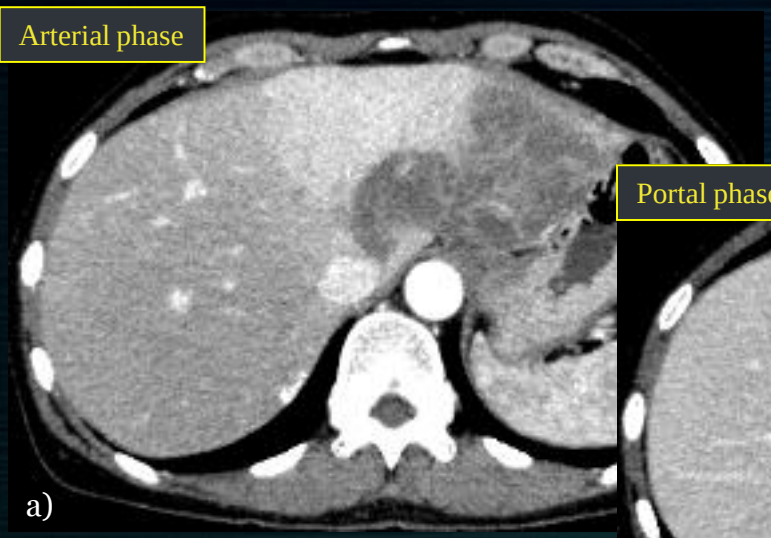


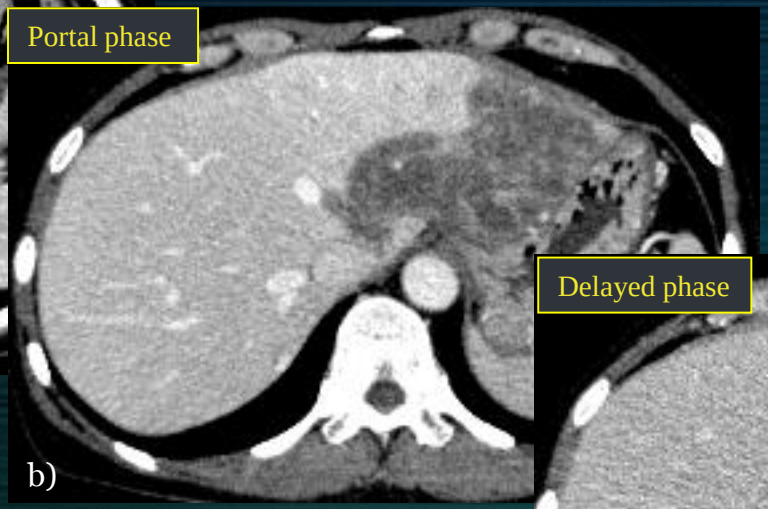
A 55-year-old woman with a surgically resected CoCC.

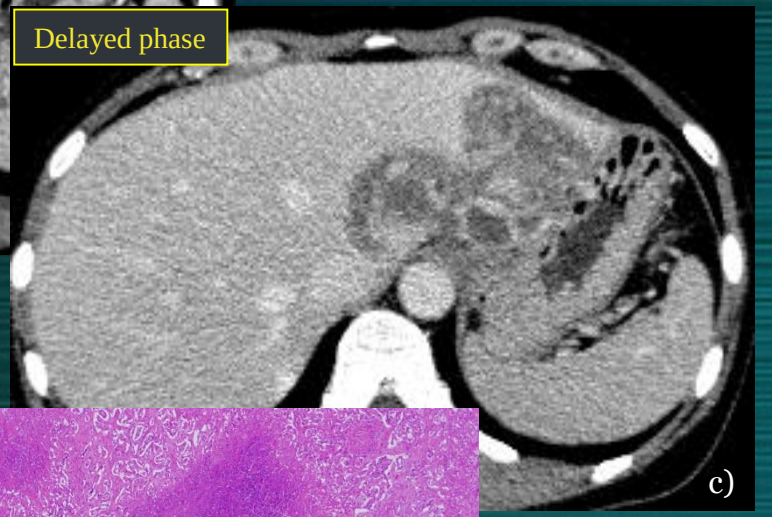
The slightly lobulated mass (arrows) located in S7 appears heterogeneous and hypointense on the precontrast fatsaturated T1WI (a), shows complete arterial enhancement and then becomes gradually hypointense compared to the hepatic parenchyma (pseudo washout) during the portal and late phases (b–d). This mass demonstrates no obvious target appearance on the hepatocyte phase MR image (e). On the H and E-stained section (f), this mass consists mainly of cellular components and only scant central fibrotic stroma.

Hematoxylin and eosin (H and E)-stained section (x4)

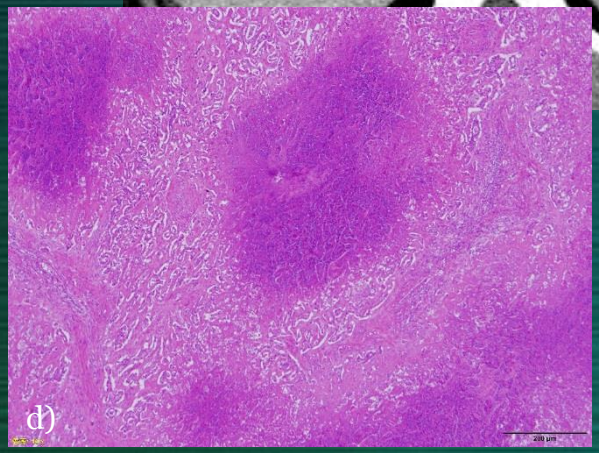
Contrast-enhanced dynamic CT







A surgically resected CoCC in a 51-year-old woman. The mass in the lateral segment appears as fused-multinodular configuration, that is several nodules contact each other. It shows poor enhancement during arterial and portal phases (a, b) and dot and band-like enhancements are prominent at delayed phase (c). On microscopy (d), massive coagulation necrosis was observed and retained Glisson's sheath structures come across in it.

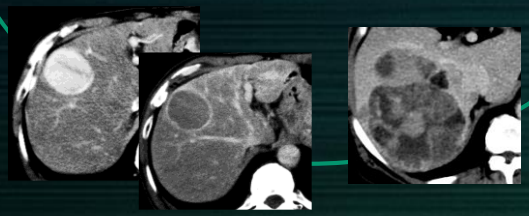


Hematoxylin and eosin-stained section (x4)

Key imaging features in the differential diagnosis of CoCC from HCC, and ICC

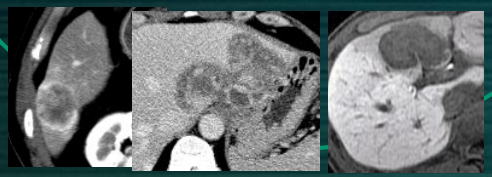
HCC

Capsule
Intralesional fat
Mosaic architecture



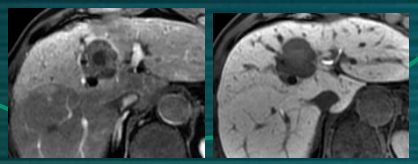
CoCC

Dot/band-like Enhancement
Fused-multinodular configuration



ICC

IHBD dilatation



* Arterial enhancement
Washout

⇒About 20% of CoCC could appear HCC-like enhancement

** Ring-like arterial enhancement
Progressive enhancement
EOB/DWI target sign
Vessel penetration
Capsular retraction
⇒ring-like enhancement of CoCC tends to be thicker than that of ICC

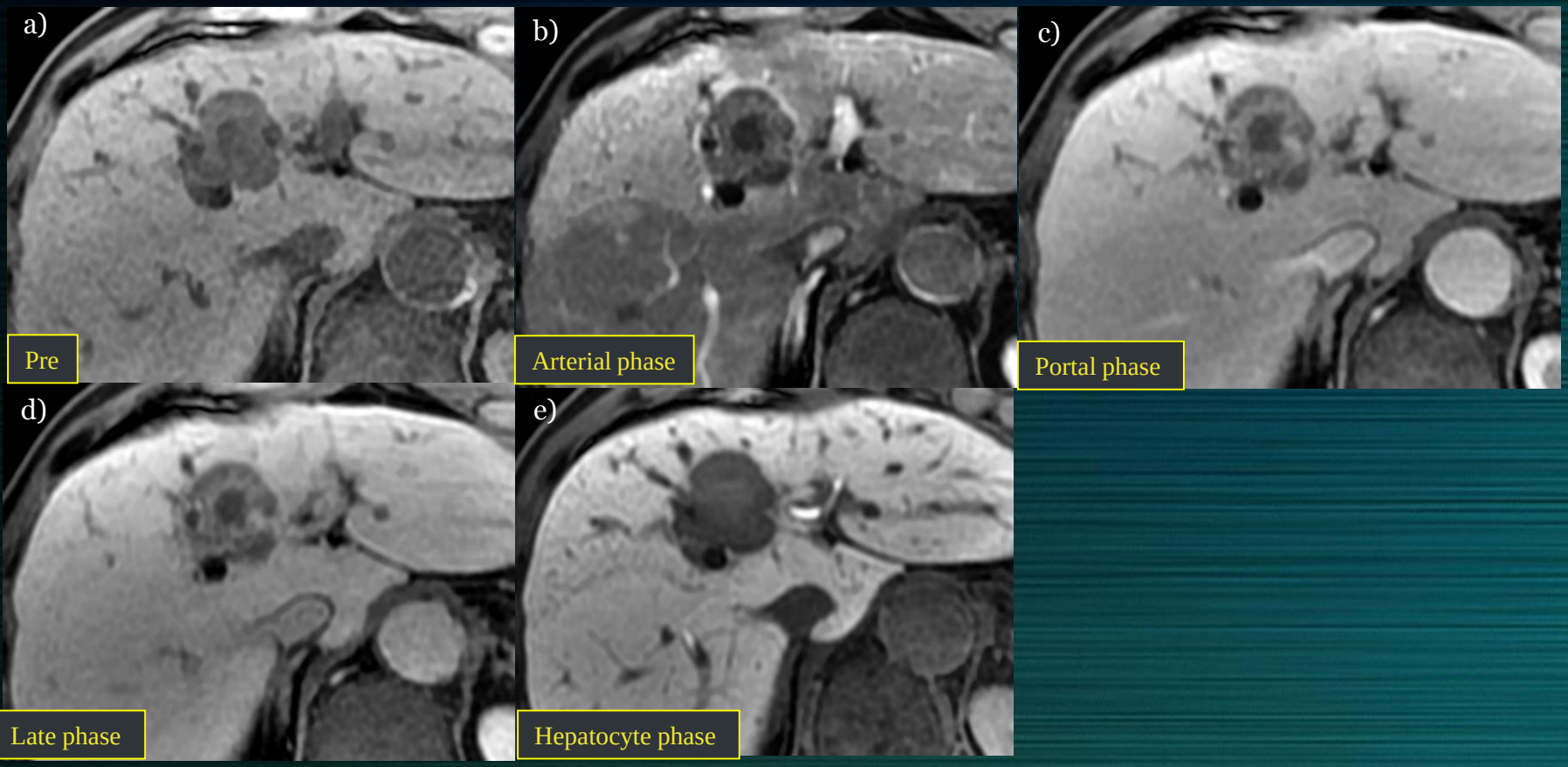
* overlapping imaging features between CoCC and HCC
** overlapping imaging features between CoCC and ICC

Characteristic CT and MR imaging features that can be helpful for discriminating CoCC from ICC and HCC

CoCC vs ICC	CoCC vs HCC
Strong findings	**Strong findings**
Thicker arterial ring enhancement	Tumor margin (lobulated)
Dot/band-like enhancement	Capsular retraction
Fused-multinodular configuration	DWI (target)
	Ring arterial enhancement
Weak findings	Progressive portal and late phase enhancement
Hepatocyte enhancement (target)	Dot/band-like enhancement
IHBD dilataion*	Hepatocyte enhancement (target)
	Vessel penetration
	Weak findings
	Capsule†
	Intratumoral fat†

Strong findings are defined to be characteristic for CoCC.
Weak findings are more common in CoCC, ICC* or HCC†, but their frequency are not so high or can appear in both.

EOB-enhanced MRI



A 64-year-old man with a surgically resected moderately differentiated ICC.
The lobulated mass located in S4 appears hypointense on the pre-contrast fat-saturated T1-weighted image (a) and shows arterial ring enhancement with target-like internal enhancement, which has slightly progressed during the portal and late phases (b–d). Peripheral intrahepatic dilatation (arrows) and vessel penetration into the mass (arrowheads) are also seen during the arterial and late phases (b–d). The hepatocyte phase MR image (e) shows the mass to have a target appearance (EOB target sign)

Conclusions

CT and MR imaging features of CoCC are similar with those of ICC. However, the finding of thicker arterial ring enhancement with the dot/band-like internal enhancement and fused-multinodular configuration could be helpful to differentiate CoCC from ICC.

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