

Accuracy of Contrast Enhanced CT Portal Venous Phase Alone Compared with Multiphase for Follow Up Liver Metastases of Various Primary Malignancies

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Abstract

OBJECTIVES: This study was designed to evaluate the accuracy of portovenous phase-computed tomography (CT) scanning compared with the conventional multiphase scanning in post-treatment imaging of metastatic liver lesions.

MATERIALS AND METHODS: Medical records and imaging of patients with metastatic liver disease were obtained by searching an ICD-10 coding. Imaging was first retrospectively reviewed only in portovenous phase (PVP). After a 7 days interval, imaging was reviewed again in all phases [Multiphase; non-contrasted (NECT), portovenous phase (PVP), hepatic arterial phase (HAP) and delayed phase (DP)]. Imaging of each patient was interpreted by consensus of two advanced diagnostic body imaging radiologists. All data were recorded and analyzed by the researcher.

RESULTS: A total of 274 patients were diagnosed with secondary malignant neoplasm of the liver and intrahepatic bile duct by ICD-10 coding during the study period. After reviewing the medical records, 127 patients were excluded. Among the 147 patients included, the lesions were further categorized as isolated-lesion group (80 patients, 245 lesions) and overall-lesion group (67 patients). Most patients had colorectal primary site (84 patients, 57.14%). For the isolated-lesion group, PVP showed the highest performance to detect metastatic lesion and the highest conspicuity (90.2%, 221 lesions) followed by HAP (26.5%, 65 lesions). Similar findings were noted in the overall-lesion group, PVP had the highest detection rate of 85.1% (57 patients) followed by HAP (10 patients, 14.9%) while NECT and DP showed no superiority over the other phases in lesion detection. About one-third of breast cancer patients had better visualized lesions in HAP than PVP.

CONCLUSION: In most malignancies, PVP was the best phase of CT scan both in terms of detection rate and conspicuity, particularly in colorectal primary. However, HAP should be added in some specific kinds of malignancies to increase the lesion detection rate, especially in breast cancer (about one-third of patients). NECT and DP had no superiority over other phases in term of lesion detection rate in follow-up CT scan of metastatic liver disease. However, there were some limitations in this study due to a small number of patients of some primary sites.

Keywords: CT scan, liver metastases, radiation dose

Liver is a common metastatic site for cancer, especially from large bowel, breast, lung, pancreas and stomach.¹ Metastatic liver disease from other malignancies are 18-40 folds more frequently found than primary hepatic tumor.² An accurate detection of metastatic disease, both at the time of diagnosis and during the course of treatment, remains crucial to patient management, providing the opportunity for surgical treatment to prolong survival time of patients.³

Standard multiphase contrast-enhanced CT of the liver includes non-contrasted imaging, portovenous- phase imaging, arterial-phase imaging and delayed-phase imaging. It is a reliable method for detection liver metastatic disease with 92% sensitivity⁴, widely available, familiar to

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radiologists and has been the mainstay of hepatic imaging when performed properly.⁵

However, performing CT scan in multiphase increases not only the patient's radiation dose, it is also time consuming for interpretation and takes up valuable storage space in the picture archiving and communication system (PACS). Recently, concerns around radiation doses from CT scans have increased due to a fear of radiation-induced cancer.⁶ For each phase of a contrast-enhanced CT of the liver, patients will get a median (P75) dose length product (DLP) of approximately 1,322 mGy-cm and a median (P75) effective dose of 19.4 mSv⁷ which has led to an attempt to reduce radiation doses while maintaining imaging quality for lesion detection.⁸ Latterly, follow-up CT scan of cancer patients after treatment have been proposed to be performed in portovenous phase only in some centers.

Thus, this study aimed to study a feasibility of using portovenous-phase CT alone to detect liver lesions in known cases of metastatic liver disease after treatment, as compared with standard multiphase contrast-enhanced CT scan. The results of the study will help in adjusting the appropriate protocol of scanning CT for such cancer patients in our department.

Materials and methods

This research was conducted as a retrospective, descriptive study. Enrollment was performed at Department of Radiology, Phramongkutklao hospital during January 2019 to December 2020. All patients who were diagnosed with metastatic liver disease and performed multiphase contrast-enhanced CT of the liver during the study period for follow-up after treatment were included. The patients were excluded in analysis if CT scan was not completely performed in all phases, or the finding was not compatible with metastatic liver disease, such as, hepatic cyst, hemangioma or primary tumor of liver. For the multiphase contrast-enhanced CT scan of liver, it was defined as scanning in non-contrast enhancement phase (NECT), hepatic arterial phase (HAP), portovenous phase (PVP) and delayed phase (DP).

Sample size estimation

Sample size was calculated based on the estimation of percentage ratio of 2-phase (NECT and PVP) vs. 3-phase (NECT, PVP and HAP) contrast-enhanced CT from the study of Yukiko et al.,⁹ using an equation:

$$n = \frac{Z^2 \alpha / 2 p(1-p)}{d^2}$$

while n = total number of lesions used in the study, p = the percentage ratio at contrast enhanced CT 2-phase (NECT and PVP) vs. 3-phase (NECT, PVP and HAP) in detecting metastatic liver lesions which was 85.11%, d = error was 0.05 and $Z\alpha/2$ = probability of type I error at $\alpha = 0.05$ (1.96). Then, the number of metastatic liver lesions to be recruited was

194.84. Therefore, the appropriate sample size of this study is at least 195 lesions.

Equipment and scanning process

After the study was approved by the Institutional Review Board Royal Thai Army Medical Department (IRBRTA; number R101h/64), permission to access medical record and PACS was made from the director of Phramongkutklao Hospital. Patients with secondary malignant neoplasm of liver and intrahepatic bile duct were then searched by using ICD-10 (C78.7). The diagnosis was re-confirmed using the aforementioned criteria.

For the multiphase contrast-enhanced CT, non-contrast enhancement phase was performed first, before injection of contrast medium. Then, hepatic arterial phase was performed by using automatic bolus-tracking program and putting 0.8-2.0 cm²-region of interest (ROI) cursor at distal thoracic aorta. Scanning was started when it triggered a threshold level of 200 Hounsfield units (HU) for 15 seconds. After that, portovenous phase and delayed phase were performed at 90 seconds and 180-300 seconds after injection of intravenous contrast medium respectively. CT scan machine used was a 16-row, 32 slice helical CT system for whole body imaging (Aquilion Lightning® and Aquilion Prime SP®).

Imaging was first retrospectively reviewed only in portovenous phase (PVP). After 7 days' interval, imaging was reviewed again in all phases (Multiphase) in a random sequence and editing of previous interpretation was not allowed. Imaging of each patient was interpreted by consensus of two radiologists specialized in advanced diagnostic body imaging.

Imaging was categorized into 2 groups, i.e., isolated-lesion group and overall-lesion group. The categorization was done according to the characteristics of the lesion (isolated or conglomerated lesions), border of the lesion (well-defined or ill-defined border) and volume of liver parenchyma involved by cancer. For the volume involved by cancer, visual semi-quantitative scale was used with a cut-value of less than or more than 25%. This threshold was chosen because there is evidence that liver involvement of more than 25% is an independent predictor of poorer survival.¹²

Statistical analysis

Personal information of the patients was collected including age at the date of diagnosis, gender and type of primary malignancy. The information was checked and saved as a data file using STATA/MP12. Then, it was analyzed using the following descriptive statistics, i.e., number, percentage, mean, standard deviation, minimum and maximum value. The number of lesions detectable in each phase of CT was compared in percentage. Subgroup analysis was performed according to primary site and type of liver parenchymal attenuation.

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Ethical consideration

All patients gave permission to disclose confidential information from their treatment history (OPD record) and their data were protected as we used a code instead of patient name or hospital number (HN) throughout data collection.

Results

A total of 274 patients were diagnosed with secondary malignant neoplasm of liver and intrahepatic bile duct by ICD-10 coding during the study period (1 January 2019 to 31 December 2020) at Phramongkutklao hospital. After reviewing the medical records, 23 patients were excluded due to a miscoding. Thirty-one patients were excluded because they had primary hepatic neoplasm and 73 patients were excluded because a CT scan was not performed or incompletely performed. The 147 patients included in the study were comparable in terms of the number of males (73 patients) and females (74 patients) with a mean age of 61.58 years (30-86 years). Among these 147 patients, 117 patients had normal liver parenchymal while the remaining 23 patients had low- and 7 patients had high attenuation.

For the distribution of primary site of malignancies, most was colorectal cancer (84 patients, 57.14%), followed by breast cancer (31 patients, 21.09%) and other primary malignancies (32 patients, 21.77%), as described in Table 1.

According to the categorization described above, there were 80 patients with 245 lesions categorized as isolated-lesion group and 67 patients were in overall-lesion group.

Isolated-lesion group

In the isolated-lesion group, most of the lesions, and regardless of primary sites, 90.2% (221 lesions) could be seen conspicuously in PVP, followed by 26.5% (65 lesions) in HAP, 14.2% (35 lesions) in DP and 2.9% (7 lesions) in NECT as shown in Table 2.

Although PVP had the highest detection rate for metastatic liver lesion regardless of primary site, there were some lesions in specific primary site that were missed in PVP. These were 19 lesions in 6 breast cancer patients, 2 lesions in 2 colorectal cancer patients, 2 lesions in 1 glucagonoma patient and 1 lesion in 1 nasopharyngeal/laryngeal cancer patient.

Table 1: Distribution of primary sites of malignancy

Primary sites of malignancy	Overall (n = 147)	Male (n = 73)	Female (n = 74)
Colorectal cancer	84	56	28
Breast cancer	31	0	31
Lung cancer	8	3	5
Pancreatic cancer	6	3	3
Nasopharynx-larynx cancer	5	5	0
Gastric cancer	4	2	2
Bladder cancer	1	0	1
Cervical cancer	1	0	1
Endometrial cancer	1	0	1
Esophageal cancer	1	1	0
Ovarian cancer	1	0	1
Poorly differentiation cancer	1	0	1

Table 2: Isolated-lesion group.

Primary malignancy	Lesion (n(%)) (n = 245)	Patients (n(%)) (n = 80)	Conspicuous phase (lesions/%)			
			NECT	HAP	PVP	DP
Colorectal cancer	118 (48.2)	46 (57.5)	2 (1.7)	30 (25.4)	116 (98.3)	25 (21.2)
Breast cancer	67 (27.4)	17 (21.3)	4 (5.9)	21 (31.3)	48 (71.6)	2 (3.0)
Nasopharynx-larynx cancer	16 (6.5)	4 (5.0)	1 (6.3)	2 (12.5)	15 (93.8)	2 (12.5)
Gastric cancer	11 (4.5)	3 (3.8)	-	5 (45.4)	11 (100.0)	-
Pancreatic cancer	10 (4.1)	3 (3.8)	-	2 (20.0)	8 (80.0)	-
Ovarian cancer	9 (3.7)	1 (1.2)	-	-	9 (100.0)	3 (33.3)
Lung cancer	5 (2.0)	3 (3.8)	-	-	5 (100.0)	-
Bladder cancer	4 (1.6)	1 (1.2)	-	3 (75.0)	4 (100.0)	3 (75.0)
Thymic cancer	3 (1.2)	1 (1.2)	-	-	3 (100.0)	-
Renal cell carcinoma	2 (0.8)	1 (1.2)	-	2 (100.0)	2 (100.0)	-

Among the lesions that were the most conspicuously in NECT, all of them were found in patients with high liver parenchymal attenuation. Whereas, some lesions were best seen in HAP because of a better delineation between lesion and its peripheral enhancement. Apart from this, some lesions

had iso-attenuation in PVP, especially small lesions ranging from 4-14 mm and lesions of patients with abnormal liver parenchymal attenuation were also better seen in HAP. Lastly, DP showed no superiority over PVP in term of conspicuity in all lesions, as shown in Figure 1-3.

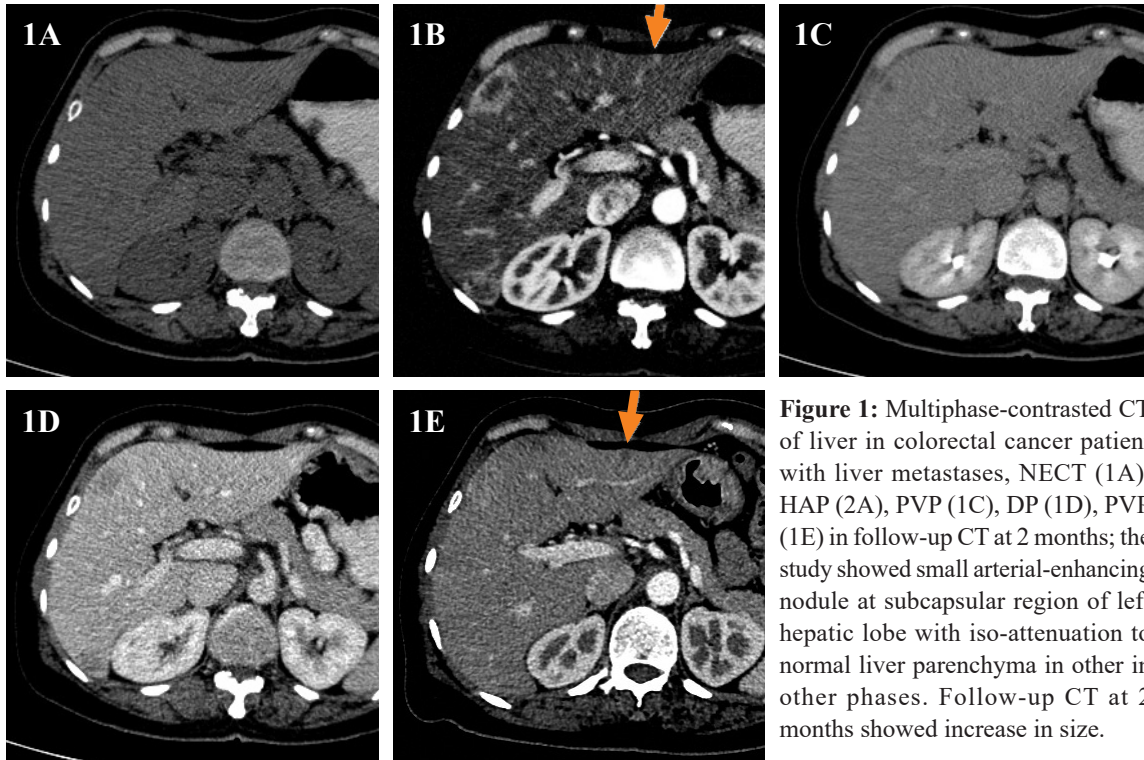


Figure 1: Multiphase-contrasted CT of liver in colorectal cancer patient with liver metastases, NECT (1A), HAP (2A), PVP (1C), DP (1D), PVP (1E) in follow-up CT at 2 months; the study showed small arterial-enhancing nodule at subcapsular region of left hepatic lobe with iso-attenuation to normal liver parenchyma in other in other phases. Follow-up CT at 2 months showed increase in size.

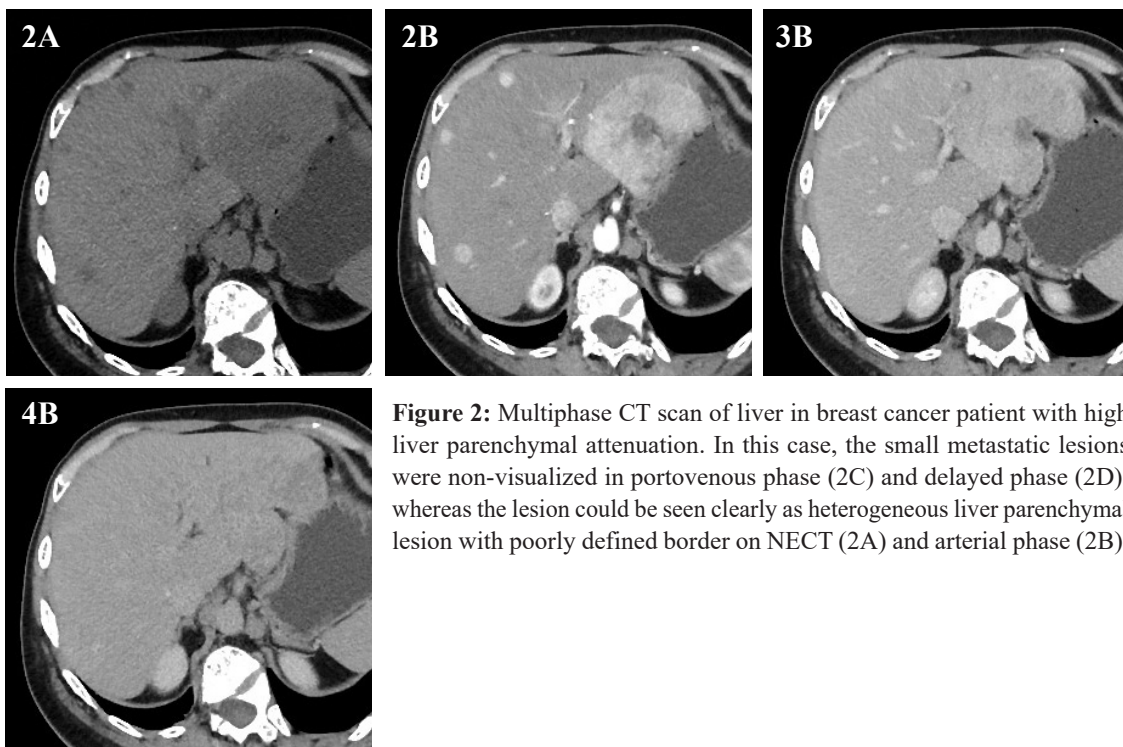


Figure 2: Multiphase CT scan of liver in breast cancer patient with high liver parenchymal attenuation. In this case, the small metastatic lesions were non-visualized in portovenous phase (2C) and delayed phase (2D), whereas the lesion could be seen clearly as heterogeneous liver parenchymal lesion with poorly defined border on NECT (2A) and arterial phase (2B).

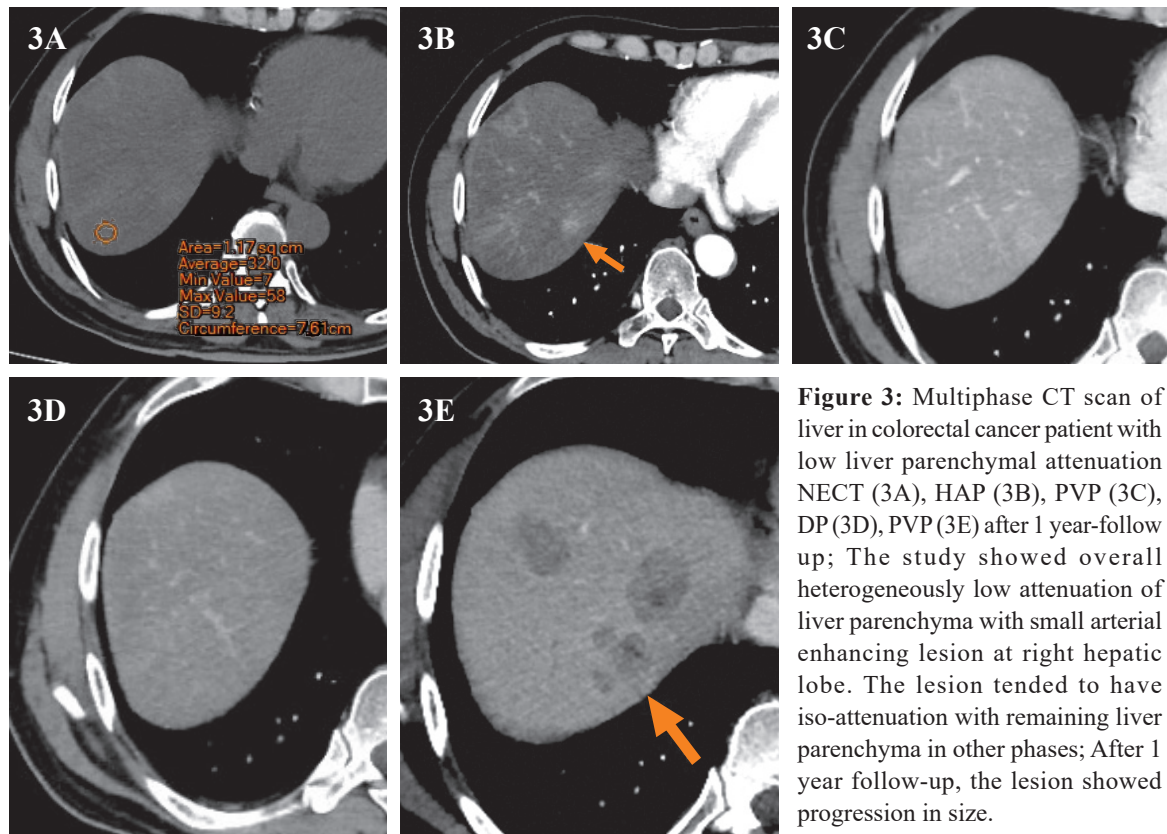


Figure 3: Multiphase CT scan of liver in colorectal cancer patient with low liver parenchymal attenuation NECT (3A), HAP (3B), PVP (3C), DP (3D), PVP (3E) after 1 year-follow up; The study showed overall heterogeneously low attenuation of liver parenchyma with small arterial enhancing lesion at right hepatic lobe. The lesion tended to have iso-attenuation with remaining liver parenchyma in other phases; After 1 year follow-up, the lesion showed progression in size.

Overall-lesion group

In the overall-lesion group, CT scan in PVP had the best detection rate (85%, 57 patients), followed by HAP (14.9%, 10 patients) while NECT and DP showed no superiority in lesion detection. Metastatic lesions of some primary site tended to have more conspicuous in arterial-phase CT scan than PVP, i.e., breast cancer (3 patients), colorectal cancer (3 patients), cervical cancer (1 patient), gastric cancer (1 patient), glucagonoma (1 patient) and poorly differentiation cancer

(1 patient), as described in Table 3. In addition, there was one colorectal cancer case with heterogeneously low liver parenchymal attenuation that all phases of CT scan showed very poor conspicuity. In this case, although the lesion was most visualized on arterial phase, its border was still poorly defined as shown in Figure 4-6. Percentage of lesions found in each phase is summarized in Chart 1.

Table 3: Overall lesion interpretation groups.

Primary malignancy	Patients (n = 67)	Most conspicuous phase (patients)	
		A-phase	P-phase
Colorectal cancer	38 (56.7%)	3 (7.9%)	35 (92.1%)
Breast cancer	14 (20.9%)	3 (21.4%)	11 (78.6%)
Lung cancer	5 (7.5%)	-	5 (100.0%)
Pancreatic cancer	3 (4.5%)	1 (33.3%)	2 (66.7%)
Cervical cancer	1 (1.5%)	1 (100.0%)	-
Esophageal cancer	1 (1.5%)	-	1 (100.0%)
Gastric cancer	1 (1.5%)	1 (100.0%)	-
Nasopharynx-larynx cancer	1 (1.5%)	-	1 (100.0%)
Endometrial cancer	1 (1.5%)	-	1 (100.0%)
Poorly differentiation cancer	1 (1.5%)	1 (100.0%)	-
Prostate cancer	1 (1.5%)	-	1 (100.0%)

Chart1. Percentage of lesions found in each phase.

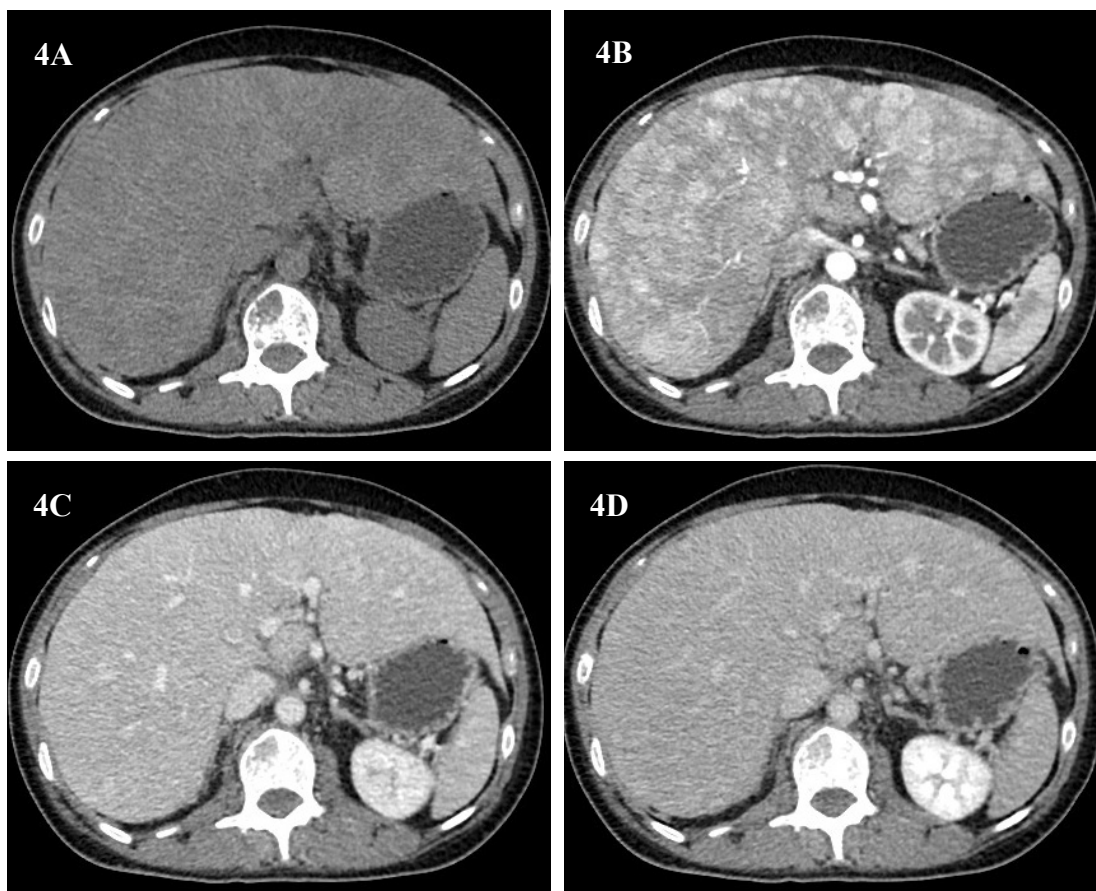
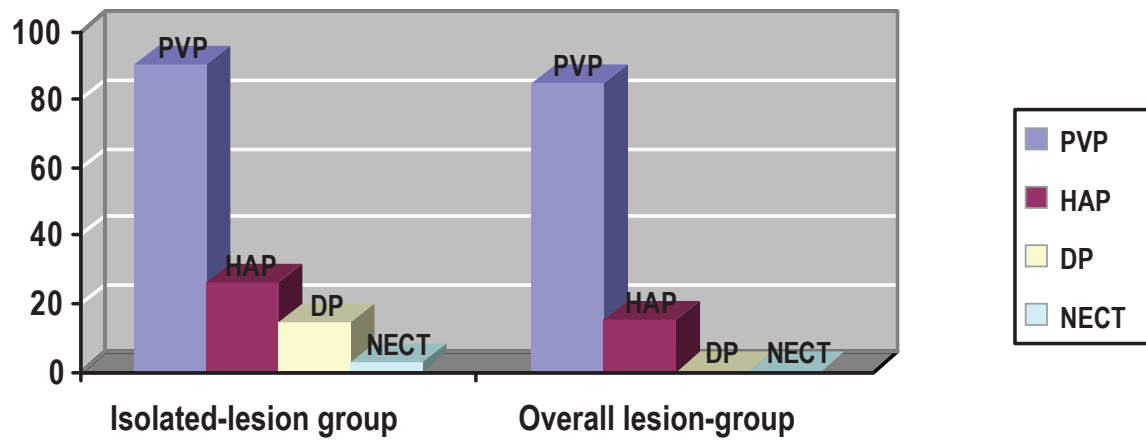


Figure 4: Multiphase CT scan of liver in breast cancer patient, NECT (4A), HAP (4B), PVP (4C), DP (4D). The lesion showed most conspicuity in arterial phase.

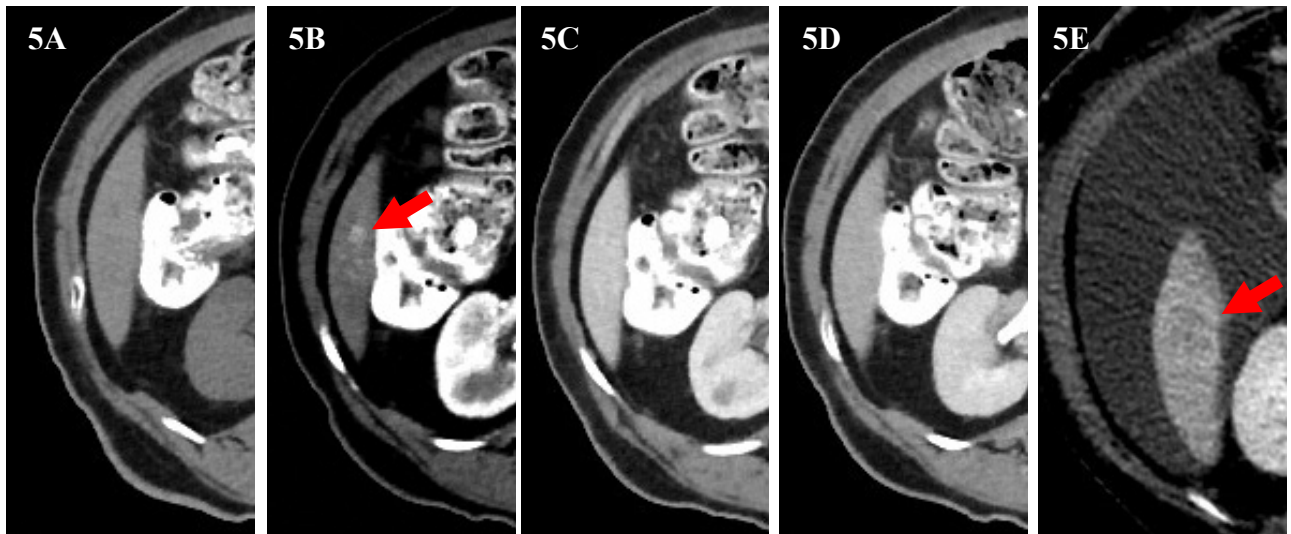


Figure 5: Multiphase CT scan of liver in colorectal cancer patient, NECT (5A), HAP (5B), PVP (5C), DP (5D), PVP (5E), at 6 months follow-up; The study showed a new arterial- enhancing nodule at hepatic segment 6 which iso-attenuation on other phases which had progression on follow-up study at 6 months interval.

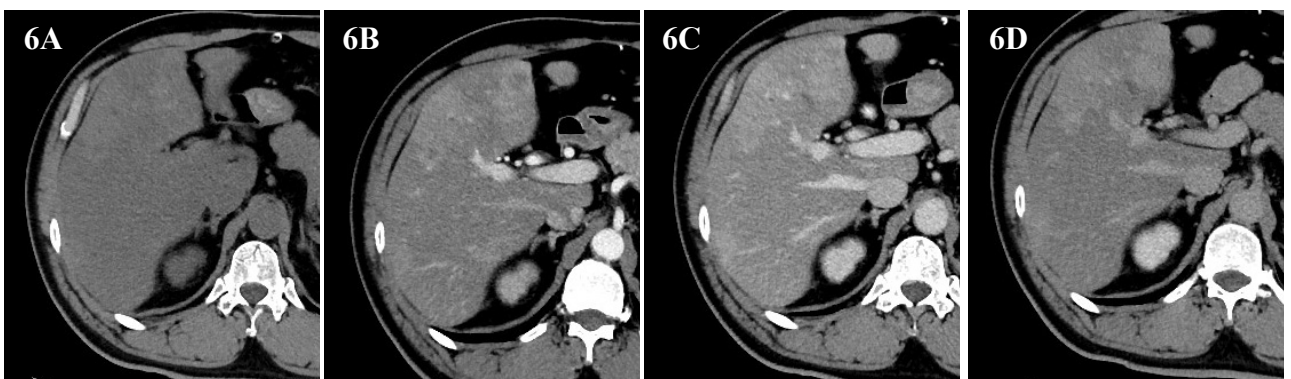


Figure 6: Multiphase CT scan of liver in colorectal cancer patient with heterogeneously low liver parenchymal attenuation NECT (6A), HAP (6B), PVP (6C), DP (6D), PVP (6E). Even though the lesion showed most conspicuity in arterial phase, the border was still poorly defined causing difficulty to measure an actual size that is crucial for follow-up cancer treatment.

Discussion

Multiphase CT scan of liver is a reliable diagnostic method to follow-up treatment response in metastatic liver disease. To optimize radiation dose to patients, this study was designed to evaluate the feasibility of using portovenous phase alone to follow-up treatment response in cancer patients with metastatic liver lesions. It was found that portovenous phase had the highest lesion detection rate regardless of primary site, especially colorectal cancer patients which corresponded with many previous studies.^{4,10,11}

Hypervascular metastases typically arise from hypervascular primary tumors and could be due to hepatic neovascularization or desmoplastic reaction around the metastases.

In this study, arterial phase was the second most conspicuous phase due to peripheral enhancement, which was

beneficial in hypervascular metastases and patients with abnormal liver parenchymal attenuation.¹³ Some metastatic lesions were not well detected using only PVP. Additional lesions were seen when arterial phase was added, especially in breast cancer patients accounting for one-third of all patients.

Delayed phase had no beneficial over portovenous phase in both lesion detection rate and conspicuity of lesion. As compared with portovenous phase, non-enhanced CT had lower performance in lesion detection for most patients except in a small number of patients with high attenuation of liver parenchyma that NECT was better.

There were a few patients with heterogeneously low parenchymal attenuation of liver in which CT scan showed poor performance in both lesion detection and conspicuity in all

phases. And there were a few lesions seen as new arterial-enhancing lesions with iso-attenuation on other phases that progressed in follow-up imaging. In this case, further study such as an MRI scan should be considered to rule out liver metastases.^{14,15}

However, there were some limitations of this study. Firstly, distributions of subtype of primary malignancy are mainly colorectal cancer and breast cancer with small number of other primary malignancies. Secondly, this study was retrospective, and CT scanners or software used may vary and may have affected image quality and interpretation of results.

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Conclusion

In most malignancies, PVP was the best phase of CT scan in terms of both detection rate and conspicuity, especially in colorectal primary. However, HAP should be added in some specific kinds of malignancies to increase the lesion detection rate, especially in breast cancer and in the preexisting study that showed good conspicuity on HAP. NECT and DP had no superiority over other phases in term of lesion detection rate in follow-up CT scan of metastatic liver disease.

Conflict of interest

The authors declare no conflict of interest