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Original article

Role of Multislice Triphasic C.T in Assessment of Metastatic Hepatic Focal Lesion in Cancer Breast under Chemotherapy

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Abstract:

Background: A member of pattern recognition receptors is the toll-like Metastatic hepatic focal lesions in breast cancer patients undergoing chemotherapy present diagnostic challenges. This study aimed to detect hepatic focal lesion in patients with cancer breast under chemotherapy. **Methods:** This observational cross-sectional study was conducted in the Radiology department of Tanta Cancer Center and included 50 adult female patients with primary breast cancer undergoing chemotherapy. Patients were subjected to a full history taking, clinical oncological examination, routine laboratory investigation, and multi-slice triphasic CT scans. Computed tomography images were analyzed for the location, number, size, shape, borders, and enhancement pattern of hepatic focal lesions. Histopathological examination results were used as the reference standard for the diagnosis of metastasis. **Results:** A total of 95 hepatic focal lesions were detected, with the majority in segment VIII (29.47%). Lesions displayed different enhancement patterns, with the most common being a complete ring (47.36%). Triphasic CT demonstrated a significant advantage in the prediction of liver metastasis compared to MRI, with a high positive predictive value (94.59) compared to MRI (97.36). The sensitivity and specificity of CT and MRI for diagnosing liver metastasis were 90% and 94.87% for CT, and 72% and 75% for MRI, respectively. Triphasic CT showed a high positive predictive value (94.59) compared to MRI (97.36). **Conclusion:** Multi-slice triphasic CT is a valuable diagnostic tool for the assessment of hepatic focal lesions in breast cancer patients undergoing chemotherapy.

Keywords: Multi-slice Triphasic CT; Hepatic Focal Lesions; Breast Cancer; Chemotherapy; Metastasis.

Introduction

Breast cancer is the leading malignancy in Western women, with metastases causing most deaths. Early diagnosis- via mammography and adjuvant therapy- have reduced metastasis and mortality rates. Adjuvant therapy eradicates potential distant tumor cells. In women <50 years, chemotherapy increases 15-year survival by 10%; in older women, the increase is 3% [(1)].

Despite advances, 20-30% of early breast cancer patients experience distant metastasis. Risk factors include tumor size, nodal involvement, grade, lympho-vascular invasion, estrogen receptor (ER), and human epidermal growth factor receptor 2 (HER2) status. Patterns of metastasis are not fully understood [(2)].

Characteristics of the primary tumor often persist in metastases, with some associations found for lung and bone metastasis gene signatures and HER2 and ER expression status. Patterns of metastasis related to breast cancer subtypes are less studied [(3)].

Understanding metastatic patterns can impact adjuvant therapy and surveillance. Cross-sectional imaging is common during diagnosis and follow-up, including CT scans of the chest, abdomen, and pelvis [(4)].

Systemic chemotherapy is the preferred treatment for multiple metastatic liver tumors in breast cancer, but it has diverse side effects. Pseudocirrhosis is a rare complication in breast cancer, causing hepatic contour changes resembling cirrhosis radiographically but lacking classic cirrhosis attributes [(5)].

Most primary and metastatic liver tumors receive blood from the hepatic artery, reversing the typical hepatic blood supply. This forms the basis for triple-phase liver scans, aiding in imaging primary and metastatic liver tumors [(6)].

We aimed in this study to detect hepatic focal lesion in patient with cancer breast under chemotherapy.

Patients and methods

Patient population:

Our Observational cross-sectional study was performed in Tanta Cancer center, Radiology department. Patients were referred to the radiology department from the surgery or radiotherapy department for staging of their primary or recurrent disease.

This study included 50 adult female patients with primary breast cancer under chemotherapy. The patients age ranged from 40 to 60 years old, the patient's complaint from abdominal pain in 90% of cases, only minority had a different complaint as anorexia.

Inclusion criteria were no age predilection, patient known to have breast cancer by histopathological examination under chemotherapy, diagnosis of metastasis was based on clinical symptoms and physical examination.

Exclusion criteria were patient known to have other primary malignancy with metastasis to the liver, patient renal impairment who had serum creatinine level >2mg/dL, pregnant female, and patient with history of contrast allergy.

Every patient was subjected to the following:

Each patient underwent a comprehensive assessment, which included a full medical history, comparisons with other imaging modalities (ultrasound & MRI) and previous CT scans, clinical oncological examination, reference standard histopathological examination results, and routine laboratory tests encompassing; complete blood counts, random blood sugar, and assessment of liver and kidney functions; for serum creatinine levels above 2mg/dl, contrast CT scans- were contraindicated.

Methodology:

The methodology for this study comprised several steps. It began with a comprehensive assessment that included a detailed clinical history and laboratory studies, specifically kidney function tests. Patient preparation involved fasting for 4-6 hours to ensure an empty stomach, hydration to improve visualization, and wearing loose, non-metallic clothing.

The actual imaging procedure involved triphasic CT scans using a Siemens 128-slice multi-detector spiral CT. The scans were performed in a craniocaudal direction, with images reconstructed every 5 mm to provide contiguous or overlapping sections. Patients were positioned supine with their arms raised. A non-ionic iodinated contrast agent (Omnipaque) was administered based on the patient's weight, with a saline chaser used after the contrast material injection. The CT scans included three phases: hepatic arterial, portal venous, and delayed phases, scanned at specific time intervals post-contrast injection.

The imaging technique also involved precise patient positioning in a supine orientation with their arms raised. Scout images covered the area from the diaphragm to the iliac crests, with scan extent matching this range. Some departments performed a full abdomen and pelvis scan in the portal venous phase. The scans were obtained through the liver in a craniocaudal direction, with a 5-mm collimation, a 7.5mm/s table speed, and a pitch of 1.0. Primary slice thickness was set at 5 mm, with a reconstruction interval of 2 mm.

To ensure accurate contrast injection, a bolus tracking program was used to initiate the scan following the contrast injection. A premonitory scan was taken, and a region of interest (ROI) cursor was positioned in the aorta just above the right hemi-diaphragm. The trigger for image acquisition was set at specific Hounsfield unit (HU) values. The threshold Hounsfield unit was set at 150 HU, and a volume of 100-120 mL of non-ionic contrast- was administered at a rate of 3 to 5 mL/s.

The CT scan delay times were carefully managed: the arterial phase was scanned 15-30 seconds post bolus trigger (35-45 seconds after injection), the portal venous phase was scanned 60-75 seconds post-injection, and the delayed phase was acquired 2-5 minutes after contrast injection. The resulting CT images were then analyzed for various parameters, including; the site, number, size, shape, borders, and enhancement patterns of hepatic lesions in the arterial, portal venous, and delayed phases. Hyper-vascular tumors were visible during the arterial phase due to enhanced blood supply. Hypo-vascular tumors appeared in the portal venous phase, and delayed phase images revealed lesions with specific contrast characteristics in comparison to normal liver tissue.

Approval of Ethical Committee from December 2021 to January 2023- was obtained (Approval code: Ms 11-12-2021)

Statistical analysis

The collected data was processed using IBM SPSS Statistics SPSS v26 (IBM Inc., Armonk, NY, USA), including normality testing with the Shapiro-Wilk test. Descriptive statistics such as mean and standard deviation- were computed for numerical data, while non-numerical data-were presented in terms of frequency and percentage. Analytical statistics included Student T Test for assessing differences between group means and the Chi-Square test for examining relationships between qualitative variables. The ROC Curve was used to evaluate the sensitivity and specificity, with the optimum cut-off point determined to maximize the AUC value, where an AUC above 0.9 indicates high accuracy, 0.7-0.9 suggests moderate accuracy, 0.5-0.7 reflects low accuracy, and 0.5 is equivalent to a chance result. Statistical significance was determined by a p-value < 0.05 at a 95% confidence interval.

Results

The current study carried on 50 females known to have primary breast cancer diagnosed by histopathological examination and under chemotherapy. The mean age was 50.18 years. The mean BMI

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was 27.78 kg/m^2. The diagnosis of metastasis was based on clinical symptoms and physical examination. Clinical picture represented abdominal pain in 92% of patients and anorexia in 8%. Chemotherapy used in all subjects was Fluorouracil, Adriamycin, and Cytoxan (FAC) with 6 median cycles ranging from 4 to 8 cycles for each patient, Table (1).

According to triphasic CT hepatic findings, 34% of subjects had capsular retraction, 56% had diffuse fatty pattern and 10% had a picture of pseudo cirrhosis.

Total lesions examined detected was 95 hepatic focal lesions. Their mean largest diameter was 2.48 cm. Most of the focal lesions were distributed in segment VIII (29.47%) followed by segment II (23.15%), Table (2).

Examined lesions showed different enhancement patterns, 21.05% were homogenous, 10.52% were variegated, 4.26% had peripheral puddles, 47.36% showed complete ring, 5.26% showed incomplete ring and 11.52% showed no enhancement, Table (3).

The value of triphasic CT visibility of liver metastasis compared to MRI images and it showed that 84 out of 95 focal lesions were accurately diagnosed as liver metastasis compared to 87 were accurately diagnosed by MRI. Triphasic CT results showed a significant p value (<0.001) in prediction of liver metastasis, Figure (1).

The sensitivity and specificity of CT & MRI were 90%, 94.87%, 72% & 75%, respectively. Triphasic CT showed a high positive predictive value (94.59) compared to MRI (97.36%), Table (4).

Table 1. Demographic data of the studied subjects.

			Total subjects n=50
Age	M±SD		50.18±5.54
	Range		40-60
BMI	M±SD		27.78±3.87
	Range		22-35
Clinical picture			
Abdominal pain			46(92%)
Anorexia			4(8%)
Chemotherapy data			
Chemotherapy used		FAC	50(100%)
Number of cycles		Median	6
		Range	4-8

Table 2. Lesions characteristics in triphasic CT.

		Total lesions examined n=95
Largest diameter, cm	M±SD	2.48±1.45
	Range	0.09-4.96
Segment distribution of focal lesion	II	22(23.15%)
	III	6(6.31%)
	IV	14(14.73%)
	V	6(6.31%)
	VI	9(9.47%)
	VII	10(10.52%)
	VIII	28(29.47%)

CT: Computed Tomography

Table 3. CT Enhancement pattern of liver metastasis.

	Total lesions examined (n=95)	Number (%)
Enhancement pattern of focal lesions	Homogeneous	20(21.05%)
	Abnormal internal vessels	10(10.52%)
	Peripheral puddles	4(4.26%)
	Complete ring	45(47.36%)
	Incomplete ring	5(5.26%)
	No enhancement	11(11.52%)

CT: Computed Tomography

Table 4: Validity of triphasic CT and MRI in diagnosis of liver metastasis**.**

	Accuracy (%)	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
MRI	92	94.87	75	97.36	60
CT	88	90	72	94.59	33.33

MRI: Magnetic Resonance Imaging, CT: Computed Tomography

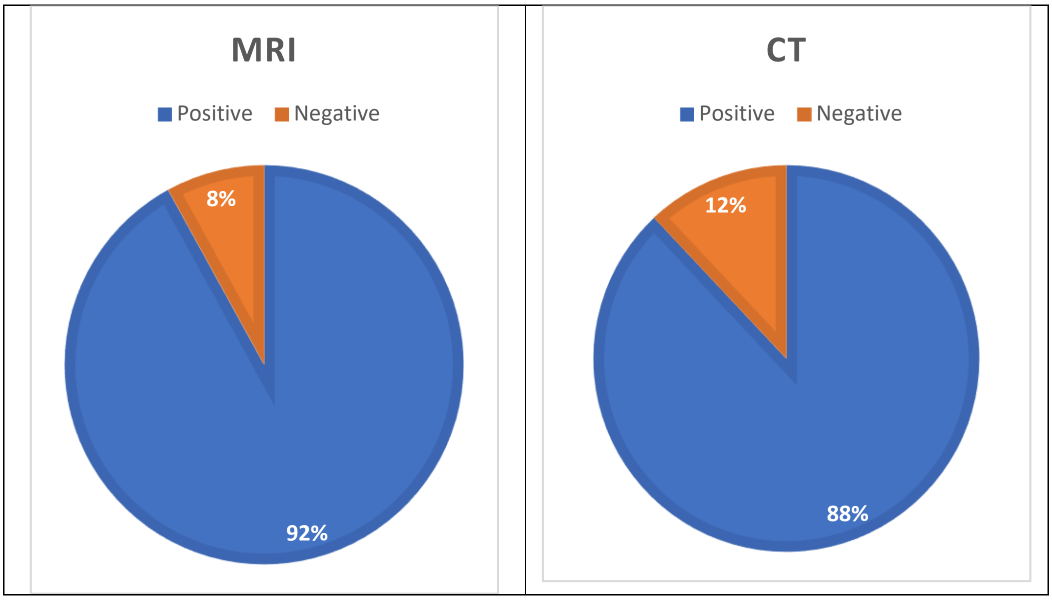

Figure 1. Validity of triphasic CT and MRI in diagnosis of liver metastasis.

Cases:

In case 1, a 46-year-old female patient who previously had a left mastectomy and was undergoing chemotherapy presented with laboratory findings indicating a creatinine level of 0.9. On CT imaging, multiple well-defined, rounded lesions were observed in both the right and left hepatic lobes. These lesions exhibited a characteristic pattern of rapid vascular enhancement in the arterial and portal venous phases, followed by contrast washout in the delayed phase, Figure (2).

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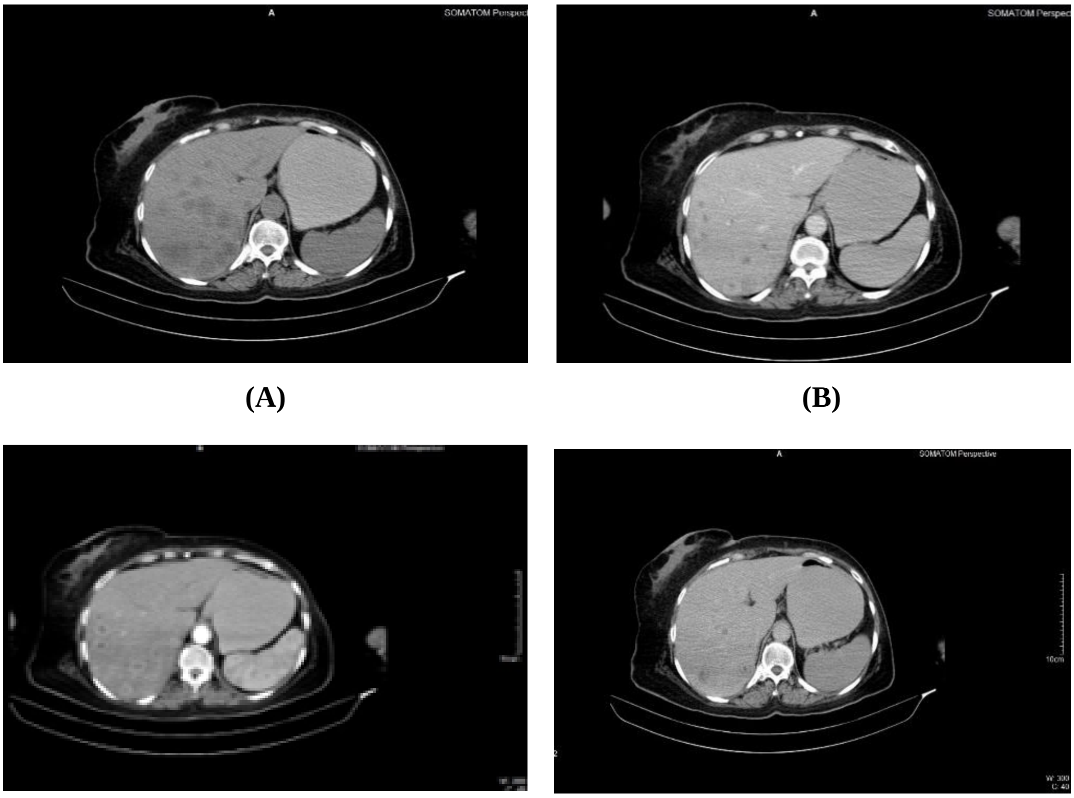


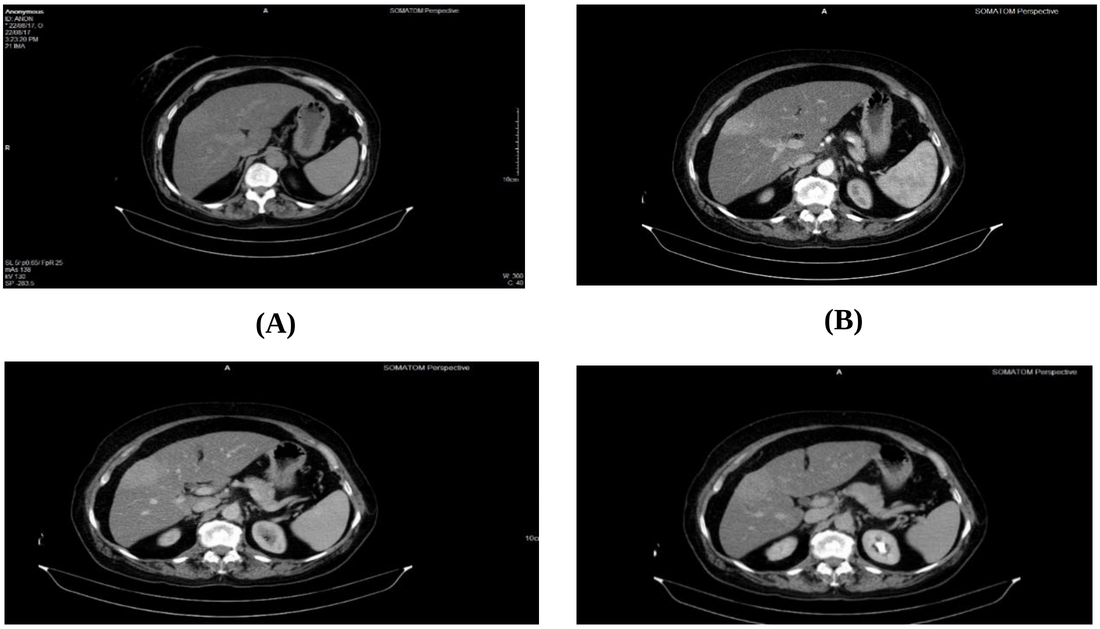
(A) **(B)**

(C) **(D)**

Figure 2: Triphasic CT demonstrated rounded lesions in right & left hepatic lobes showing contrast enhancement in arterial phase (A) portovenus enhancement (B) and washout in delayed phase(c).

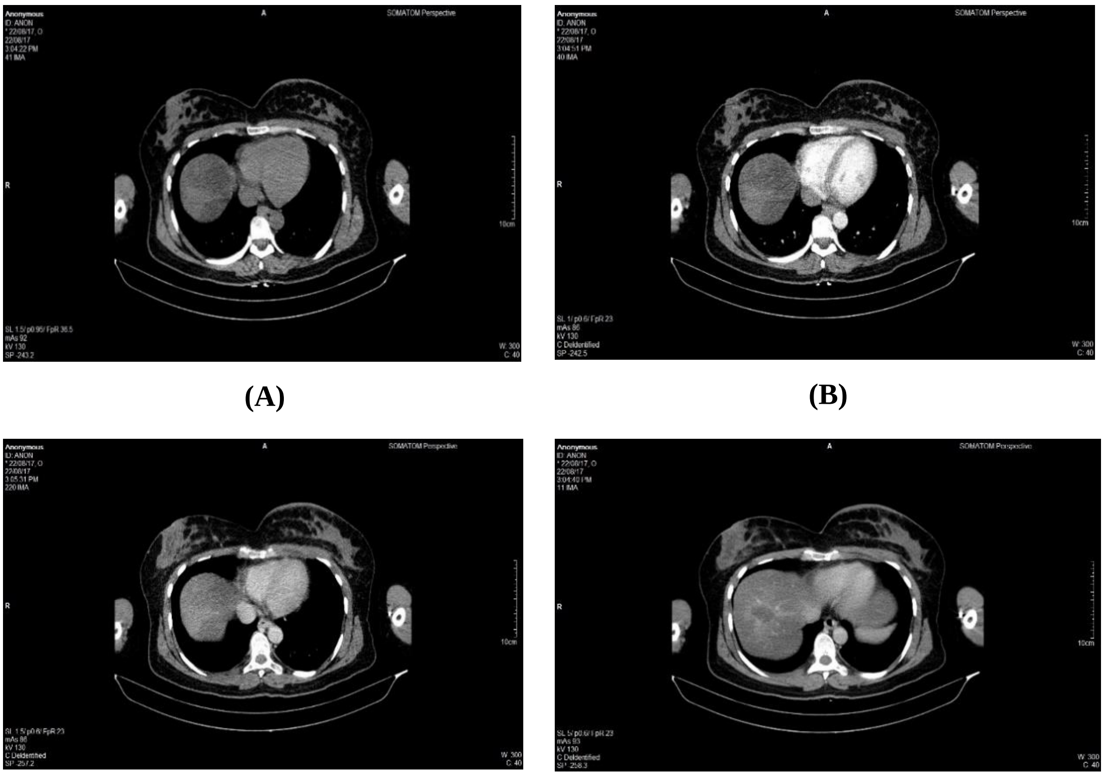
In case 2, a 46-year-old female patient who previously had a left mastectomy and was undergoing chemotherapy, presented with laboratory findings indicating a creatinine level of 0.9. On CT imaging, the liver appeared enlarged and displayed a homogenous hypodense appearance, suggestive of fatty changes. Additionally, a large hyperdense lesion was noted subcapsular at segment IV of the liver. This lesion demonstrated rapid vascular enhancement in the arterial and portal venous phases, followed by contrast washout in the delayed phase. The nature of this lesion was deemed likely to be metastatic or a hemangioma, which merited further investigation with MRI, Figure (3).

In case 3, a 40-year-old female patient undergoing chemotherapy presented with a creatinine level of 0.9. The CT imaging revealed an enlarged liver displaying a homogenous hypodense texture. Within the liver, a large hyperdense lesion with ill-defined outlines was observed in segment VIII. This lesion exhibited a characteristic pattern of rapid vascular enhancement in the arterial and portal venous phases, followed by contrast washout in the delayed phase, Figure (4).



(A) **(B)** **(C)** **(D)**

Figure 3: Triphasic CT demonstrated single faint lesion in right hepatic lobe segment IV showing rapid contrast enhancement in arterial phase (A) portovenus enhancement (B) and washout in delayed phase(c).



(A) **(B)** **(C)** **(D)**

Figure 4: Triphasic CT demonstrated an ill defined lesion in right hepatic lobe showing contrast enhancement in arterial phase (A) portovenus enhancement (B) and washout in delayed phase (c).

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Discussion

Breast cancer is a prevalent and significant cause of morbidity and mortality worldwide, with liver metastasis being a common occurrence [7]. Managing liver metastasis in breast cancer patients is complex and relies on factors such as disease extent and patient prognosis. Radiological imaging, especially computed tomography (CT), plays a crucial role in diagnosis and monitoring [8]. Computed tomography (CT), particularly with a triphasic protocol, offers high-resolution liver images and has shown promise in detecting liver metastases, although its accuracy can vary based on lesion characteristics and underlying liver conditions [9]. Assessing treatment response in breast cancer patients undergoing chemotherapy through CT and MRI remains a subject of debate. This study aimed to detect hepatic focal lesions in breast cancer patients undergoing chemotherapy, addressing these diagnostic and monitoring challenges.

This observational cross-sectional study was conducted in the Radiology department of Tanta Cancer Center and included 50 adult female patients with primary breast cancer undergoing chemotherapy. Patients were subjected to a full history taking, clinical oncological examination, routine laboratory investigation, and multi-slice triphasic CT scans. computed tomography (CT) images were analyzed for the location, number, size, shape, borders, and enhancement pattern of hepatic focal lesions. Histopathological examination results were used as the reference standard for the diagnosis of metastasis.

Regarding patients' demographic data, the finding that abdominal pain was the predominant symptom in patients with metastatic breast cancer to the liver- is consistent with previous studies. A study found that abdominal pain was the most common symptom in 86.4% of patients with liver metastases from breast cancer [10].

Similarly, a study reported that abdominal pain was the most common symptom in 94.4% of patients with liver metastases from breast cancer [11].

Moreover, the mean age of the patients in the current study is similar to the findings of other studies. A study reported a mean age of 50.6 years in patients with breast cancer and liver metastasis, while a study reported a mean age of 51.2 years [10, 12].

In the current study, Chemotherapy was used in all subjects was Fluorouracil, Adriamycin, and Cytoxan (FAC) with 6 median cycles ranging from 4 to 8 cycles for each patient.

Several studies have reported the use of the FAC regimen in breast cancer patients. A study evaluated the efficacy and safety of the FAC regimen in comparison to the Fluorouracil, Epirubicin and Cyclophosphamide (FEC) regimen in early-stage breast cancer patients. The study showed that both regimens had similar efficacy and toxicity profiles, and the FAC regimen was found to be a reasonable alternative to FEC in the adjuvant treatment of breast cancer patients [13].

Another study investigated the use of the FAC regimen in the neoadjuvant setting for locally advanced breast cancer. The study showed that the FAC regimen was effective in reducing the size of the tumors and improving the pathological complete response rate [14].

Similarly, a study evaluated the efficacy and safety of the FAC regimen in the adjuvant treatment of breast cancer patients with positive axillary lymph nodes. The study showed that the FAC regimen was well-tolerated and had a favorable efficacy profile, with a significant improvement in disease-free survival compared to the Cyclophosphamide, Methotrexate, and Fluorouracil (CMF) regimen [15].

According to triphasic CT hepatic findings, 34% of subjects had capsular retraction, 56% had diffuse fatty pattern and 10% had a picture of pseudo cirrhosis.

Our result keep matching with the study evaluated the CT imaging features of hepatic metastases from breast cancer in 200 patients and found that capsular retraction was present in 24% of cases [16].

As well as, Another study reported that diffuse fatty infiltration was seen in 48% of patients with hepatic metastases from breast cancer [17].

Pseudo cirrhosis, which is defined as diffuse nodular transformation of the liver parenchyma, has also been reported in patients with hepatic metastases from breast cancer. In a study, 7 out of 34 patients (20.6%) with hepatic metastases from breast cancer showed a picture of pseudo cirrhosis on CT imaging [18].

In the current work, the total lesions examined detected was 95 hepatic focal lesions. Their mean largest diameter was 2.48 cm. Most of the focal lesions were distributed in segment VIII (29.47%) followed by segment II (23.15%).

Another study investigated the relationship between the size and location of hepatic focal lesions and the risk of malignancy. They found that lesions located in segments II, III, and IV were more likely to be malignant, while lesions in segments VI, VII, and VIII were more likely to be benign [19]. This study also reported a mean diameter of 2.5 cm for hepatic focal lesions.

Examined lesions showed different enhancement patterns, 21.05% were homogenous, 10.52% were verigated, 4.26% had peripheral puddles, 47.36% showed complete ring, 5.26% showed incomplete ring and 11.52% showed no enhancement.

In the current work, the value of triphasic CT visibility of liver metastasis was discovered and it showed that 84 out of 95 focal lesions were accurately diagnosed as liver metastasis. Triphasic CT results showed a significant p value (<0.001) in prediction of liver metastasis.

Several studies have compared the diagnostic accuracy of CT and MRI for detecting liver metastasis. A meta-analysis reported that CT had a pooled sensitivity of 70% and specificity of 93% for detecting liver metastasis. The study also found that the diagnostic accuracy of CT varied depending on the primary tumor site and lesion size [20].

Another study compared the diagnostic accuracy of CT for detecting liver metastasis in patients with colorectal cancer. The results showed that CT had a sensitivity of 86% and specificity of 93% [21].

In the present work, the sensitivity and specificity of CT were 90%, 72%, respectively. Triphasic CT showed a high positive predictive value (94.59).

There have been numerous studies comparing the sensitivity and specificity of CT in detecting liver metastasis. One study reported a sensitivity of 84.8% and specificity of 96.7% for CT [22].

Another study reported a sensitivity of 90.9% and specificity of 85.7% for CT [23].

Regarding the positive predictive value (PPV), a study reported a PPV of 94.2% for CT [24]. However, it should be noted that the PPV is dependent on the prevalence of liver metastasis in the study population, and therefore may vary in different patient populations.

In our study, we encountered a subset of breast cancer patients under chemotherapy who were presented with clinical symptoms and imaging findings suggestive of liver pseudocirrhosis. These patients demonstrated diffuse nodularity of the liver parenchyma, irregular liver surface, and signs of portal hypertension, such as splenomegaly and ascites. The appearance of pseudocirrhosis on CT scans can be challenging to distinguish from true cirrhosis, especially when clinical history and other imaging modalities are not readily available.

It is crucial to recognize liver pseudocirrhosis early, as it can have significant implications for patient management. Firstly, misdiagnosis as cirrhosis may lead to unnecessary interventions, such as liver biopsy or

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transplantation evaluations. Moreover, the presence of pseudocirrhosis can impact the chemotherapy regimen, as the liver's impaired function may alter drug metabolism and clearance, potentially leading to drug toxicity [(25)].

The pathogenesis of liver pseudocirrhosis is not fully understood, and it remains uncertain whether specific chemotherapeutic agents or cumulative dose play a role in its development [(25)].

Conclusion

In conclusion, the current study highlights the value of multi-slice triphasic CT in the assessment of hepatic focal lesions in breast cancer patients under chemotherapy. The findings demonstrate that triphasic CT is an effective tool for detecting and characterizing liver metastases, with a high sensitivity and specificity compared to MRI. Moreover, the results suggest that triphasic CT can provide important diagnostic information on the extent and distribution of liver metastases, which is important for treatment planning and monitoring of disease progression.

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Author contribution

Authors contributed equally in the study**.**

Conflicts of interest

No conflicts of interest

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