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Research Article

Evaluation of Treatment Responses with Pre- and Post-Treatment Density Measurement Values of Breast Cancer in Thorax CT

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Abstract

Objectives: We aimed to investigate the contribution of mass CT density values to the diagnosis in the evaluation of the response of the local disease to the treatment during the treatment of breast cancer.

Methods: 40 female patients histopathologically proven to have breast cancer, had routine Thorax CT at diagnosis and the treatment stage, and whose metabolic activity was known by PET CT were included.The mean mass densities were measured from malignant breast lesions at the time of diagnosis and after treatment through the Thorax CT examinations.

Results: In our study, we found the mean mass density measurement values of breast cancer before treatment as 38.21 HU, and the average density measurement values after treatment as 20.54 HU. We showed that malignant mass densities were significantly reduced in the non-metabolic period after treatment. We found that thorax CT density values can be a guide in evaluating the response of malignant breast lesions to local treatment.

Conclusion: In conclusion, adding a quantitative CT attenuation value to breast lesions examinations increases the diagnostic accuracy of malignant lesions. We have shown that malignant lesions show significantly higher attenuation on Thorax CT and attenuation values decrease in response to treatment.

Keywords: Breast Cancer, Density Thorax CT

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Breast cancer is the most common cause of cancer-related death in women worldwide. Patients with early breast cancer have a good chance of being treated with curative surgery or topical therapy; these patients have an 85-99% 5-year survival rate.[1] Diagnosis, staging, accurately detecting distant metastases, implementation of the treatment plan, and accurate evaluation of the treatment outcome in breast cancer will help determine the prognosis. Therefore, chest CT examination plays an important role in diagnosing, staging, and treating breast cancer cases. Our study thinks that routine CT examination during the disease may be important in evaluating the breast lesion response to local treatment and the whole body.

Although most current guidelines, including the American Society of Clinical Oncology (ASCO), recommend staging breast-CT only for advanced disease, physicians treat many patients diagnosed with early-stage breast cancer using breast-CT as part of the incidental initial diagnosis and initial staging evaluation.[2]

The basic radiological methods in diagnosing breast diseases are ultrasound, mammography, and magnetic resonance imaging (MRI). In recent years, the spread of multislice computed tomography (CT) has increased the rate of incidentally detected breast lesions. Besides ultrasound, CT has gained an important place in breast cancer diagnosis. Especially the new generation multidetector computed

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tomography (MDCT) reveals structures and pathologies that could not be displayed in detail before. With the widespread use of MDCT scans, incidental breast cancer detection is increasing.[3] PET CT gives important information about whether the mass has metabolic activity according to FDG uptake. CT and PET CT are widely used for the patients' staging, the response to treatment, and the recurrence evaluation after a breast cancer diagnosis. CT density values have been used to evaluate breast cancer metastases in the literature.[4,5] PET CT costs, radiation load, and the effects of the radioactive material used cause limitations in applying the method. Therefore, we used breast density measurements of Thorax CT at routine controls to assess the local metabolic activity of breast cancer to assess post-treatment response.

In studies conducted in the literature, researchers investigated the mean CT attenuation values (HU, Hounsfield units) of lesions in patients suspected of breast cancer.[6] To the best of our knowledge, no study in the literature evaluates the metabolic activity before and after treatment in breast cancer with CT utilizing density. Our study is the first study on this subject.

Evidence must be provided on the usefulness of breast density measurements on chest CT in evaluating local disease in the breast during the disease. We aimed to investigate whether thorax CT taken during routine control evaluation is an adjunct method to PET CT to evaluate the treatment response of breast parenchymal density in the detection of metabolic and non-metabolic mass lesions without the need for additional examination.

Methods

This study was approved by Elazığ Fırat University Non-Interventional Clinical Research Ethics Committee (approval number: 2021/13-23). We retrospectively reviewed the radiological images of 63 breast cancer cases treated and followed in our hospital between January 2020 and October 2021. The images obtained during the patient's routine oncological treatment were retrospectively evaluated, and no additional examination or procedure was performed. Forty patients who underwent PET CT examination during staging and evaluation of response to treatment and who met the criteria for histopathological breast cancer diagnosis were included in the study. Patients with a visible breast mass on Thorax CT images, FDG uptake in PET CT confirmed the localization of their mass, and patients receiving post-diagnosis oncology treatment were included in the study. During the retrospective examination, 40 breast cancer patients who did not show FDG uptake in the mass lesion in the post-treatment PET CT, were successfully treated, and had thorax CT before and after the treatment were selected. The mass density values of these 40 patients before the treatment and the mass density values of these 40 patients during the period when they did not show FDG uptake in PET CT after receiving treatment were measured.

Patients who showed FDG uptake or progression with PET CT findings after 3 months of treatment were not included in the study. Patients who had undergone breast surgery during their treatment, had previous RT treatment, had secondary primary cancer, and had completely regressed breast mass after treatment were excluded from the study. Patients who were regularly followed up before and after treatment and had routine CT scans were particularly selected. Mass lesions in the breast were detected on non-contrast Thorax CT in correlation with the areas of FDG uptake in PET CT. The mean densities of the defined masses were measured by ROI.

Density values were measured and noted on Thorax CT images taken for the initial diagnosis and staging of patients with breast cancer. Oncology treatment was given to the patients after diagnosis. Control PET CT and Thorax CT images were examined at the 3rd month after the treatment. After the treatment, patients who did not have metabolic activity in PET CT were selected. The density values were measured and recorded in routine Thorax CT images of these patients.

Patients were scanned in the supine position with 64-detector sequential CT (64, Siemens Medical Solutions, Forchheim, Germany). Our standard protocol included unenhanced MDCT taken from the lung apex: 2.5 mm slice thickness, 2.5 mm reconstruction interval, 0.75 second rotation speed, 1.05–1.25 interval, and 120 kVp; the effective tube current × time product was in the 150–200 mAs range. Images were generated using a standard soft tissue algorithm (window width, 350 HU; level, 40 HU) and a retrospective lung algorithm (window width, 1000 HU; level, -700 HU). Mass localization was detected in non-contrast images, a manually drawn region of interest (ROI) was placed, and (HU) values were measured. All ROIs were placed as close to the central part of the lesion as possible. Obtained density values were noted. An ethics committee approval was obtained for our study.

In calculating the sample size of this study, which was conducted for the purpose of "comparison of the Density Values (HU) of the patients before and after the treatment", Power was determined by taking at least 80% and Type-1 error of 5% for each variable. Shapiro-Wilk ($n<50$) and Skewness-Kurtosis tests were used to check whether the continuous measurements in the study were normally distributed, and because the measurements were normally distributed, Parametric tests were applied. Descriptive statistics for the variables in the study; expressed as mean, standard deviation, minimum and maximum. The "Paired T-test" was used to compare the pre-treatment and post-treatment Density (HU) values of the measurements. Pearson correlation coefficients were calculated to determine the relationship between age and HU values. The statistical significance level was taken as 5% in the calculations and the SPSS (IBM SPSS for Windows, ver. 26) statistical package program was used for analysis. If the P-value found as a result of a hypothesis test is below 0.05, it is said that "the relationship/difference found as a result of the comparison is statistically significant ($p<0.05$)".

Results

40 female patients with breast cancer were included in our study. The mean age of the patients participating in the study was 51. The mean age of the patients included in the study is shown in Table 1. All of these patients were histopathologically diagnosed with breast cancer. Their breast masses were detected in their CT scans for initial diagnosis and staging. The average sizes of the masses were between 10 and 32 mm. All of the patients had PET CT for distant metastasis screening after the first CT, and all identified breast cancer masses were metabolically active and showed FDG uptake.

The mean density of malignant breast lesions of 40 patients before treatment was calculated as 38.21 HU. After completing the 3-month oncology treatment protocols of the patients, PET CTs taken to evaluate the treatment were re-evaluated. Malignant breast cancers without metabolic activity were determined in control PET CTs. Thoracic CT scans taken simultaneously from these patients were retrospectively evaluated. Density measurements of malignant masses in the breast were repeated after the treatment. The mean density values of breast masses of 40 patients who were metabolically inactive after treatment and did not show FDG uptake were calculated as 20.54 HU. As a result, the average density of malignant lesions of breast cancer was 38.21, and the average density of metabolic breast cancer masses was 20.54. Comparative results of "patients' pre- and post-treatment HU measurements" are shown in Table 2. A statistically significant change/difference was observed between the "Density Values (HU)" measurement before and after treatment ($p<0.05$). In this context, it is seen that the "Density Values (HU)" value decreased after the treatment. This difference after treatment is 17.67 units. When the data were examined, no statistically significant relationship was found between "Age" and "Pre-treatment HU value" ($p>0.05$). Similarly, no statistically significant relationship was found between "Age" and "Post-Treatment HU value" ($p>0.05$). In other words, the HU values of the patients do not change according to age.

We identified that the malignant mass lesions densities were higher than the normal parenchymal density and benign lesions determined in the literature. After the treatment, a significant decrease in the measured density values of malignant breast masses was observed. As a result of the findings we obtained in non-contrast CT, we found that the densities of malignant breast masses were high, and the densities of malignant kits decreased significantly after treatment (Fig. 1). We found that the density values we found were correlated with the PET CT metabolic activity of the patients (Fig. 2). We found that Thorax CT density values of malignant breast masses can be a quantitative measure of regression of malignant breast masses.

Table 1. General descriptive statistics of measurements

	Mean	Standart Deviation	Min.	Max.
Density Values Before Treatment (HU)	38.21	5.08	25.00	46.00
Density Values After Treatment (HU)	20.54	5.07	12.00	32.00
Age	51.21	11.99	29.00	76.00

Table 2. Comparative results of pre- and post-treatment HU measurements

	N	Mean	Standart Deviation	Min.	Max.	P
Density Values Before Treatment (HU)	40	38.21	5.08	25.00	46.00	0.001
Density Values After Treatment (HU)	40	20.54	5.07	12.00	32.00	

Significance level according to paired T-test results.

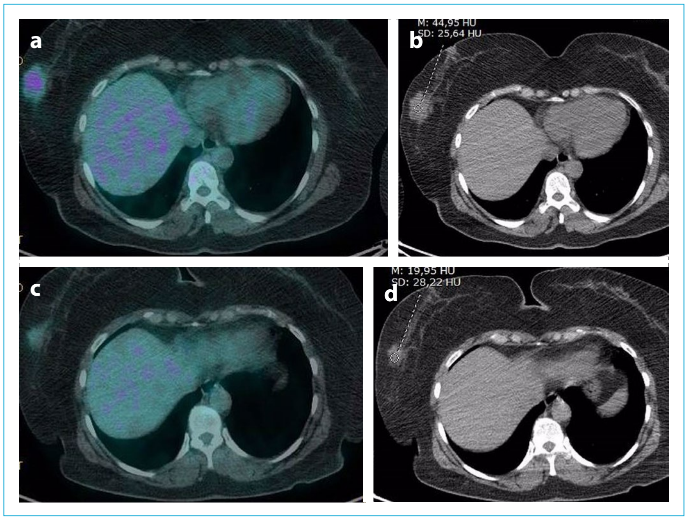

Figure 1. (a) 50-year-old with female breast cancer. PET CT shows increased [18F]FDG uptake in the breast mass. **(b)** Pre-treatment density measurement values of the mass in the patient's right breast on axial non-contrast chest CT M: Mean SD: Standard Deviation HU: Hounsfield Units. **(c)** The mass lesion in the right breast after treatment does not show FDG uptake on PET CT. **(d)** Post-treatment density measurement values of the mass in the patient's right breast on axial non-contrast chest CT. Decreased density measurement values of the mass in the right breast.

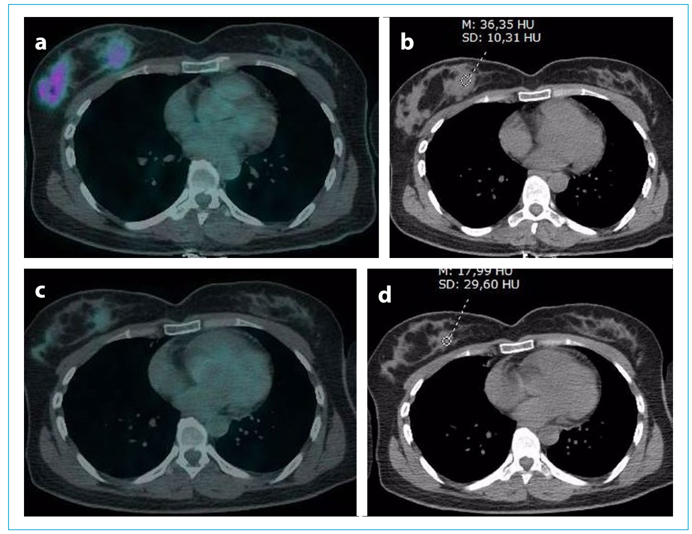

Figure 2. (a) A 43-year-old with female breast cancer. PET CT shows increased [18F]FDG uptake in the breast mass. **(b)** Pre-treatment density measurement values of the mass in the patient's right breast on axial non-contrast chest CT. Increased density measurement values of the mass in the right breast. **(c)** The mass lesion in the right breast after treatment does not show FDG uptake on PET CT. **(d)** Post-treatment density measurement values of the mass in the patient's right breast on axial non-contrast chest CT. Decreased density measurement values of the mass in the right breast. After the treatment, a decrease in the size of the mass was observed.

Discussion

The prognosis of breast cancer depends on the biological characteristics of the detected tumor and the stage of the disease. Baseline assessment for the regional staging of breast cancer patients includes clinical examination, mammography, ultrasound, and PET CT. Distant metastasis staging is done with chest (CT) and PET CT.[7] The advantages of chest CT over PET CT are its ability to detect distant metastases and evaluate local disease in the same session, in addition to its lower cost, shorter examination time, and no need for radiopharmaceuticals.[8] Therefore, we evaluated the usefulness of CT in evaluating the activity of existing breast cancers, as it is easier and cheaper to access in routine practice, can be used frequently in routine controls, and does not require exposure to radiopharmaceuticals. We found that the density values determined before and after breast cancer treatment can be a guide in evaluating the course of the disease.

Today, several studies have evaluated the performance of MDCT devices in evaluating breast lesions.[8, 9] In the literature, it has been shown that chest CT can indicate malignant lesions, distinguish malignant-benign in most cases, and make a significant contribution to the diagnosis.[10] However, histopathological confirmation of the diagnosis of the masses with biopsy is required. In the literature, Inoue et al. reported that CT was superior to mammography and sonography in detecting breast tumors and demonstrating tumor invasion.[9] They suggested using CT in preoperative examination and staging. Inoue M et al. suggested that CT is indicated to detect multifocal lesions, evaluate the extent and staging of breast cancer, especially in preoperative patients with breast cancer.

Through these studies found in the literature, we showed that we could evaluate the morphological features of malignant breast lesions with CT, distinguish lesion densities from malignant and benign lesions, evaluate staging and preoperative multifocal lesions, and obtain information about the breast masses metabolic activity with simultaneous pre- and post-treatment density changes.

Inoue et al. suggested that radiation exposure, a disadvantage of CT, can be ignored in cases with a breast cancer diagnosis.[11] In our study, the harms of radiation were not ignored. As a result of reducing the PET CT requirement in our patients, a reduction in the total amount of radiation received during the treatment is achieved.

Furthermore, compared to non-contrast CT and mammography, chest CT with contrast was superior in differentiating malignant lesions from benign lesions and malignant calcifications. Nicolas et al. found the density of malignant lesions higher than benign lesions.[12] Consistent with the literature, our study found the density of breast cancer lesions higher than the density of benign breast lesions reported in the literature. We showed that the density of breast malignant mass lesions decreased significantly after treatment. To the best of our knowledge, no other study evaluating breast densities and mass metabolic activity has been reported in the literature.

Ishibashi et al. found that thyroid gland density decreased in CT after radiotherapy treatment was applied to head and neck cancers, and this may be an indicator of hypothyroidism. In addition, it has been determined that the CT density of the thyroid gland decreases in hypothyroidism caused by chronic thyroiditis and other conditions.[13] Similar to this study, we showed that the local lesion density in the breast after treatment decreased after treatment.

In previous studies, Lindfors and Prionas et al. aimed to quantify the HU increase value of lesions identified by specific breast CT.[3] Although the importance of morphology and CT enhancement pattern in differentiating breast tumors has been reported in the literature, PET CT as a result of chemotherapy treatment in breast cancer did not provide significant data on the changes in CT densities as a result of treatment of metabolically inactive masses. Following the literature, we determined the changes in the CT intensities of the breast mass lesion before and after chemotherapy for breast cancer. In addition, we verified the accuracy of our findings with the current PET CT metabolic activity and FDG uptake.

In the studies conducted by Lin et al., the mean pre-contrast density of the index tumor on CT was 35 HU, and the mean post-contrast density of the tumor was 57 HU. At the same time, they showed that although HU values are affected by various factors such as the device used, the type of contrast agent, the presence of calcification, and the duration of imaging, the threshold values they found can guide decision-making in practice.[3] We also found the mean density of malignant lesions on CT without contrast to be similar.

One of the limitations of our study is that although we found a correlation between CT density measurement values and PET CT metabolic activity in a few patients with progression, we could not include these patients in the study. We could not include it in our study because we could not reach the sufficient number of patients in this group, we could not obtain PET CT and CT results during the prolonged treatment period of this patient group, and we determined that some of this patient group did not receive regular oncology treatment. Our study was a retrospective study performed on known malignant breast lesions. We included patients with PET CT, Thorax CT, oncological treatment, and metabolically inactive patients who showed regression. The group of cases simultaneously meeting these conditions was not very large. We think randomized studies with larger sample sizes are needed to establish the relationship between CT density values and malignancy.

Radiological imaging is important in evaluating the treatment response in breast cancer and is considered a powerful tool in the early prediction of treatment response in breast cancer. Early evaluation of the response to the first treatment in breast cancer allows changing the ineffective treatment and increasing the patient's chance of survival. Our study showed that the density values of malignant breast lesions before and after treatment could be an important indicator in evaluating the response to treatment in the early stage of the disease and contribute to disease management. Radiologists can contribute to the clinician in the treatment process by adding the density values in the routine CT performed during breast oncological patients' initial diagnosis, staging, and treatment response stages. In conclusion, adding a quantitative CT density value to the breast lesions examinations and its routine use can be an important guide in the diagnostic accuracy of malignant lesions and the evaluation of the effectiveness of the response to treatment.

Conclusion

We found that the mass densities were high in breast cancer cases at the first diagnosis. We found that breast density values decreased significantly in patients whose metabolic activity decreased and regressed after treatment. The mean density of malignant breast lesions is 38.21 HU at first diagnosis and 20.54 HU after treatment. These values correlate with changes in the PET CT FDI uptake of the mass.

Disclosures

Ethics Committee Approval: This study was approved by Elazığ Fırat University NonInterventional Clinical Research Ethics Committee (approval number: 2021/13-23).

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

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