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Prospective study of Computer Tomographic pattern of bone metastasis in breast cancer patients, Tikur Anbessa specialized hospital, Addis Ababa University, Addis Ababa, Ethiopia, August 2018 GC.

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List of Acronyms and Abbreviations

TASH---TIKUR ANBESSA SPECIALIZED HOSPITAL.

CT-----computed tomography.

18 FDG PET----18 -fluoro-D-glucose positron energy tomography

PET/CT---positron energy tomography/computed tomography.

SPECT-Single –photon emission computed tomography

IDC-----invasive ductal carcinoma.

ILC -----invasive lobular carcinoma.

MDL-----mixed ductal and lobular carcinoma.

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Abstract

Introduction

Bone metastasis is the most common site to which the breast cancer metastasizes. Between 30% and 55% of the patients with breast cancers will develop bone metastasis during the course of the disease. Bone is also representing the first site of metastasis for 26% to 50% of patients with metastatic breast cancer. Imaging is essential parts of the management of bone metastasis in breast cancer; however no consensus has been reached as to the optimal imaging modality. CT using the bone window offers superior skeletal detail, because of its ability to distinguish among materials of different density.

Objective

To assess the CT pattern of bone metastasis in breast cancer patients at Tikur Anbessa teaching referral hospital.

Method

Hospital based prospective cross-sectional study at Tikur Anbessa Specialized Hospital with breast cancer patient who have bone metastasis being evaluated at radiology department and who have CT imaging during the study period.

Convenience sampling technique was used.

Result

A total of 100 breast cancer patients with bone metastasis were included in the study from September 2017 to August 2018 GC. 91 of them are female and 9 of them are male. The minimum age is 21 years and the maximum age is 71 years with mean age of 42.5 years. Ductal carcinoma (87%) is the most common type of breast cancer followed by Adenocarcinoma (5%) and malignant epithelial tumor (5%). Lytic type (51%) of bone lesion is the frequent morphologic type followed by mixed (28%) and sclerotic (21%) respectively. In 87% of the patients had vertebral bone involvement followed by Pelvic bone (34% of patients) and ribs (30% of patients). There are five patients with skull bone involvement.

Conclusion

Majority of patients are female in our study with female to male ratio of 9:1 which is lower than most studies done at different countries. When seen on computed tomography, lytic lesion is the most common feature of bone lesion followed by mixed (sclerotic and lytic) and sclerotic, which is in line with most of the studies. When we come to the anatomic distribution of the affected bones from breast metastasis, vertebral bone is the most commonly affected bone followed by pelvic bone and ribs.

1. INTRODUCTION

1.1 Backgrounds of the study.

Breast cancer is the most common site-specific cancer in women and is the leading cause of death from cancer for women age 40 to 44 years. It accounts for 33% of all female cancers and is responsible for 20% of the cancer-related deaths in women. It is predicted that approximately 211,300 invasive breast cancers will be diagnosed in women in the United States in 2003 and 39,800 of those diagnosed will die from that cancer.(1)

Breast cancer was the leading cause of cancer-related mortality in women until 1985. In the 1970s, the probability of a woman in the United States developing breast cancer was estimated at 1 in 13, in 1980 it was 1 in 11, and in 2002 it was 1 in 8. Cancer registries in Connecticut and upper New York state document that the age-adjusted incidence of new breast cancer cases has steadily increased since the mid-1940s. This increase was about 1% per year from 1973 to 1980, and there was an additional increase in incidence to 4% between 1980 and 1987, which was characterized by frequent detection of small primary cancers. The increase in breast cancer incidence occurred primarily in women age 55 years or older and paralleled a marked increase in the percentage of older women who had mammograms. (1)

At the same time, incidence rates for regional metastatic disease dropped and breast cancer mortality declined. From 1960 to 1963, 5-year overall survival rates for breast cancer were 63 and 46% in white and African American women, respectively, while the rates for 1981 to 1987 were 78 and 63%, respectively(1).

More than 3/4th of the patients with breast cancer metastasis involved the bones which is the most cause for decreasing quality of the life. Most of the complication are pathological fracture, spinal cord or nerve root compression and metabolic abnormality like hypocalcaemia. The study showed the way of metastasis are haematogenous explained as the bone are hematopoietically active.(2, 3).

The bone is the most common site for distant metastasis patients with breast cancer patients with breast cancer, accounting for 65%patients with distant metastasis and representing the first site of metastasis in 50% of the patients. (4)

The study done by Hamaoka et al included as the age of breast cancer affects the outcome of the patient. Eventhough, the mortality is more rapid in the oldest age group than the youngest, the proportion of patients dying of carcinoma of the breast decreased as age increased ,97%in the group who had cancer at age 21 to 50year ,90 %of age group 51to 70 and 78%group age 71 to 100.(5)

Detection of the osseous metastasis by imaging is particularly very important and can be very challenging in patients with breast cancer. (6).

Histopathology of the Breast cancers were Invasive ductal carcinomas ,Invasive lobular carcinoma or mixed ductal and lobular in histology. With IDC accounting for 75-80%of breast cancer and ILC accounting for 10-15 %.(7-9)

Primary ILC lesion within the breast is difficult to detect than IDC on imaging studies. On FDG, PET/CT,primary lobular breast cancers demonstrate lower FDG-avidity than comparable primary invasive ductal cancer suggesting that patients that lobular breast cancers may be more apt to osseous metastasis. (10-13).

Morphology of the Osseous metastasis was classified into subtypes based on their appearance on CT and FDG PET. High attenuation osseous lesion on CT classified as sclerotic, low attenuation lucent lesion osseous lesions were classified as lytic and osseous lesion with substantial sclerotic and lytic components on CT are classified as mixed lytic/sclerotic-avid osseous metastasis without correlate on CT classified as CT occult (14)

Bone consists of different structures cortical, trabecular, and marrow components. Cortical bone which represents 80%of skeletal volume is compact and has canals containing vessels. A thin layer of compact bone surrounds trabecular bone also known as cancellous or spongy bone, which encompasses the bone marrow. Most of the red marrow is located in axial bones (e.g. Vertebrae, pelvis, and proximal femur), whereas fat marrow is found in appendicular bones (e.g., long bones). (15).

CT using the bone window setting offers superior skeletal detail, , because of its ability to distinguish among materials of different densities. (15)

The sensitivity of the CT for the diagnosis of bone metastasis ranges from 71 to 100%. Despite the limited data that are available, CT is thought to be highly sensitive. (16).

CT can detect metastasis in the marrow, before bone destruction becomes evident. The disadvantages of CT are that in its most widely available form, only limited anatomic areas can be scanned at time. Thus, at present CT is not the most useful means of detecting abnormalities on whole body screening (17).

1.2 Statement of the problem

Bone is the most common site to which breast cancer metastasizes. Imaging-by skeletal Scintigraph, plain radiography, computed tomography, or magnetic resonance imaging-is an essential part, and PET or single-photon emission computed SPECT have a potential of evaluating bone metastases, but no consensus exists as to the best modality for diagnosing the lesion and for assessing its response to treatment. (18)

Breast carcinoma is the number one lethal cancer of females in the United States. An estimated 116,000 new cases will be diagnosed in 1984, and 37,600 will die of it.(19) The incidence of cancer of the breast is increasing at the rate of 1.8% per year. Despite various therapeutic advances and multiple diagnosis, the death rate of patients with carcinoma of the breast has remained unchanged for over(20) .

Imaging bone metastases is problematic because the lesions can be osteolytic, osteoblastic, or mixed, and imaging modalities are based on either direct anatomic visualization of the bone or tumor or indirect measurements of bone or tumor metabolism. The Although bone metastases can be treated, their response to treatment is considered "unmeasurable" according to existing response criteria. Therefore, the process by which oncologists and radiologists diagnose and monitor the response of bone metastases needs revision, and the current inability to assess the response of bone metastases excludes patients with breast cancer and bone disease from participating in clinical trials of new treatments for breast cancer (4,5)

Complication related bone involvement such as bone pain or pathologic fractures can substantially reduce the quality of life for long-term survivors. When the bones are involved there will be reactive homeostatic changes may take place and the responds forming osteolytic, osteoblastic, or mixed lesions. Thus, accurate assessment of the response of bone metastases to treatment requires visualizing not only the tumor burden but also structural changes in the bone (21)

The study done by Gunalp et al the radiographic pattern of the target lesions on the baseline CT images was classified as lytic, blastic (sclerotic), mixed and no CT abnormality on target lesion (bone marrow metastases). 86 patients with bone metastasis were imaged and the involved bones are vertebral bone, pelvic bones, ribs, sternum, scapula, extremity, skull and disseminating pattern. (22)

The study done by Dashevsky et al showed that the histological subtype of breast cancer is significantly associated with the appearance of untreated osseous metastases on FDG PET/CT. Untreated osseous metastases were more often sclerotic in patients with ILC than with IDC. Osseous metastases of patients with ILC demonstrated lower FDG-avidity than those of IDC patients and non-FDG-avid sclerotic osseous metastases were significantly more common in untreated patients with ILC, than with IDC. Since the histology of breast cancer is usually known at the time of diagnosis, this information should be considered when interpreting osseous lesions on PET/CT. The value of FDG PET may be greater for patients with IDC than with ILC, particularly when evaluating for osseous metastases (23)

The median age of females was 40 years in Ethiopia. The median duration of the presenting symptom on admission was nearly 1 year. Clinically, majority of cases had stage III disease. Invasive ductal carcinoma was the most frequent type (24). Breast carcinoma in men accounts for 0.5% of all breast cancers in the United States (25) and 2.4% to 15% in African series (26), 10.4% in the present study. The reported median age of breast cancer in men varies from 56 to 59.6 years, 55 years in this series (27)

CT provides excellent resolution of cortical and trabecular bone and is the imaging modality of choice for evaluating the ribs which have high cortex to marrow ratio (22)..

1.3 Significance of the study.

The purpose of this study is to assess the CT pattern of bone metastasis in breast cancer patients in TASH. As there is no published data regarding CT pattern of bone metastasis in breast cancer patient in Ethiopia, this study can reveal the reality. Imaging is an essential part of the management of bone metastasis in breast cancer; however, no consensus has been reached as to the optimal imaging modality for this purpose. The imaging modalities used to follow-up tumor response should be compared against the baseline images that most clearly define the bone metastases and the lesions to be monitored. Determining the common CT pattern of bone metastasis in breast cancer patients. This can also prompt those who are interested to conduct further research on this area, not only hospital based but also nationwide..

2. LITARATURE REVIEW

Breast carcinoma is the number one lethal cancer of females in the United States. An estimated of 116,000 new cases were diagnosed on 1984, the incidence of cancer of the breast is increasing at the rate of 1.8% per year (4). Despite various therapeutic advances and multiple efforts to promote mass screening and early diagnosis, the death of patients with carcinoma of breast has remained unchanged for over 40 years (5).

Melniketal studied 10,702 breast cancer patients diagnosed in Israel over 16 years (1960-1975) of the entire groups 89% died of breast cancer. Among women diagnosed under the age of 50, 91% died of breast of cancer, 86% of those 50 to 69 years old, 77% of woman 70 and older died of breast cancer. (28) The bone is the most common site for distant metastasized patients with breast cancer accounting for about 65% patients with distant metastasis and representing the first site of metastasis in 50% patients (4).

One study done inJapan showed bone metastasis from breast cancer was present in 149 patients. The media patient age at diagnosis was 60years (31-85)years. Bone metastasis was classified according to their CT findings osteoblastic 16 patients, osteolytic31, mixed in 21 and negative in 20. The final diagnosis of CT-negative patients was made as follows,6 patients confirmed by bone biopsy,4 by MRI and 10 by later study. From 88 patient's histology of breast cancer Invasive ductal cancer 76, invasive lobular cancer 7 and others. (29)

One study in western Virginia showed, Ninety-five of the 687(13.8%) breast cancers patients developed distant metastasis to bone n =42 and visceral (n=53). Of the patients 439(71.8%) were 50 years older and 194(28.2%) were younger than 50 years old. The mean age at the time of diagnosis of the patients who remained free of distant metastasis was 58.7 years and for those with bone or visceral metastasis it was 53.6 and 56 years respectively. (30, 31).The breast cancer were most commonly IDC and ILC or mixed ductal and lobular (MDL) in histology. (30)

Study done by Tulinius et al showed the histology of the breast cancer patient were IDC accounting for 75-80% of primary breast malignancies and ILC accounting for 10-15%. Primary ILC lesions within the breast are more difficult to detect than IDC on imaging studies. On FDG PET/CT, primary lobular breast cancer demonstrates lower FDG-avidity than comparable primary invasive ductal cancer suggesting that patients that lobular breast cancer may be has more osseous metastasis. (32)

There is one study done in Hino,Tokyo, Japan Lesions of bone metastases on CT scan were visually classified by multi-slice CT based on the degree of osteoblastic and osteo lytic change into four types: osteoblastic, osteolytic,mixed and negative (not detectable) for the four CT-based types are. The sensitivity 93%(15/16) for the osteoblastic type 90%(28/31) forosteo lytic, 100% (21/21) for mixed, and 70% (14/20) for negative. (33)

There is one study done in India high incidence of bone metastasis to spine and pelvis. In pelvis, SI joints and Ilium and in long bones and sternum, proximal parts were commonly involved Bone metastases were seen

n in 23.42% (241/1029). Of these, 10.06% (31/308) EBC, 25.60% (169/660) locally advanced BC (LABC) and 63.93% (39/61) of metastatic BC (MBC) patients had BM. Most common sites of BM were spine and pelvis. In long bone and sternum, proximal part was commonly involved. (34)

One research done in Department of Radiology, Weill Cornell Medical College, New York, NY Department For the 74 patients with IDC, the most common CT morphology of the osseous metastases was lytic (n = 29/74, 39%), followed by occult (n = 22/74, 30%), sclerotic (n = 14/74, 19%), and mixed (n = 9/74, 12%) Notably, all IDC patients with osseous metastases demonstrated at least one osseous metastasis that was FDG-avid, even among patients with osseous metastases classified as sclerotic. Thus, all 74 patients had osseous metastases that were apparent by FDG PET.(32)

For the 8 patients with MDL, the most common CT morphology of the osseous metastases was mixed (n = 4/8, 50%), followed by occult (n = 3/8, 38%), and lytic (n = 1/8, 12%). There were no patients with MDL classified as sclerotic. All MDL patients with osseous metastases demonstrated at least one osseous metastasis that was FDG-avid. Thus, like IDC patients, all MDL patients had at least one osseous metastasis that was apparent on FDG PET.(33)

For the 13 patients with ILC, the most common CT morphology of the osseous metastases was sclerotic (n = 7/13, 54%), followed by mixed (n = 4/13, 31%), and lytic (n = 2/13, 15%). There were no patients with ILC classified as having only CT occult osseous metastases. All ILC patients with mixed and lytic CT morphology of their osseous metastases demonstrated at least one osseous metastasis that was FDG-avid, and thus were apparent on FDG PET (6/6, 100%). However, only 3 of 7 patients with ILC (43%) classified as having sclerotic osseous metastases demonstrated an FDG-avid osseous metastasis. (34).

One study done in Turkey showed Confirmed bone metastases were present in 86 patients (57.3%) and absent in 64 (42.7%). Bone metastases were present in 86 (57.3%) and absent in 64 patients (42.7%) by the reference standard. Based on the CT appearance, metastatic lesions were sclerotic, lytic or had mixed pattern in 40%, 26%, and 34% of patients, respectively. Based on the CT appearance, metastatic lesions were sclerotic, lytic or had mixed pattern in 40%, 26%, and 34% of patients, respectively and the location of lesions in 86 patients with bone metastases.(22)

There is other study done in Ireland within the spine, most metastases are located in the lumbar spine, less frequently in the thoracic spine, and rarely in the cervical spine (52%, 36% and 12%) respectively. Less frequent metastatic sites include the mandible, patella, and distal extremities (35)

One study in Lagos Nigeria of the 67 eligible breast cancer patients, one is male and 66 are female. The average age of the patients was 46 years old, ranging from 28 to 77-year-old. Among the 67 patients who received radiotherapy, 58 (87%) have bone metastases. The most common sites of bone metastases are spine (61%), pelvis (22%), and long bones (22%).(36) Thirty-one patients had osteoblastic lesions, 24 patients had osteolytic lesions and 2 patients had mixed osteolytic and osteoblastic lesions. (37).

3. OBJECTIVES

3.1 General objective

- To assess the pattern of bone metastasis in breast cancer patients at Tikur Anbessa teaching referral hospital.

3.2 Specific objectives.

- To describe the socio demographic characteristics of breast cancer patients with bone metastasis at Tikur Anbessa teaching referral hospital.
- To see the correlation of histopathology of the breast cancer patients with pattern of bone metastasis at Tikur Anbessa teaching referral hospital.
- To describe pattern of the affected bone in metastatic breast cancer patients at Tikur Anbessa teaching referral hospital.
- To describe distribution of bone metastasis in breast cancer patients at Tikur Anbessa teaching referral hospital.

3.Methods and Materials

3.1 Study areas and study population.

3.1.1 Study area

The study was conducted at TASH, College of health science, Addis Ababa University, Addis Ababa Ethiopia. TASH is located in the Ethiopian capital, Addis Ababa, and is the largest referral as well as the main teaching hospital and the only radiotherapy center in the country. The study was conducted from September 2017 to August 2018 G.C.

3.1.2 Source population.

All patients with breast cancer who were imaged at radiology department, TASH.

3.1.3. Study subjects

All patients with breast cancer having bone metastasis who were imaged at the radiology department, TASH from September 2017 to August 2018 G.C.

3.2. Study design

A prospective cross-sectional study was conducted to assess CT pattern of bone metastasis in breast cancer patients at Tikur Anbessa teaching referral hospital.

3.3. Study period

Data was collected from September 2017 to August 2018 from patients who were seen at TASH radiology department

3.4 Inclusion and exclusion criteria

3.4.1 Inclusion criteria

All patients with breast cancer who have bone metastasis and CT imaging at radiology department, TASH during the study period.

Patients with histological confirmed breast cancer.

3.4.2 Exclusion criteria

Breast cancer patient who were diagnosed to have other malignancy concomitantly. Patients those who don't have biopsy result and those who were on treatment .

3.5. Study variables

- ✓ Age
- ✓ sex
- ✓ Histopathology of breast cancer
- ✓ Morphology of bone metastasis
- ✓ Distribution of bone metastasis

3.6. Sample size and sampling technique

All breast cancer patients who had CT imaging with bone metastasis during the study periods were included in the study. The convenience sampling method was used where subjects are selected because of their convenient accessibility.

3.7. Data collection

A modified structured questionnaire was used to collect information from patient's charts. At the beginning of the study the responsible body will be informed about the objective of the study and importance of giving appropriate information. Data was collected by principal investigator and other radiology residents and supervision was done by principal investigator and Advisors

3.7.1 Pre-test

Pre-test of the questionnaire was carried out among study group who are not selected for the study on about 5% of the study population. Modification of the questionnaire was done based on the result of the pretesting.

3.7.2 Data quality control

The research advisors have reviewed the modified structured questionnaire before the study is conducted. Pretesting of the questionnaire was done and based on the result of the pretesting it was modified.

3.8. Data Analysis

After filling the data on to Microsoft excel, it was imported to SPSS version 23 and analyzed. Tables and figures are drawn using SPSS and Microsoft Excel.

Frequency distribution and percentages are obtained for:

- Socio-demographic data (age, sex)
- Cross tabulation is used to describe the frequency and percentage of the histopathologic feature, type of bone lesion and bone distribution

3.9 Ethical Consideration.

Permission was obtained from the radiology department ethical board.

4. Results

4.1 Socio demographic characteristics of the patients

A total of 100 breast cancer patients with bone metastasis were included in the study from September 2017 to August 2018 GC. 91(91%) of them are female and 9(9%) of them are male (figure 1.1).

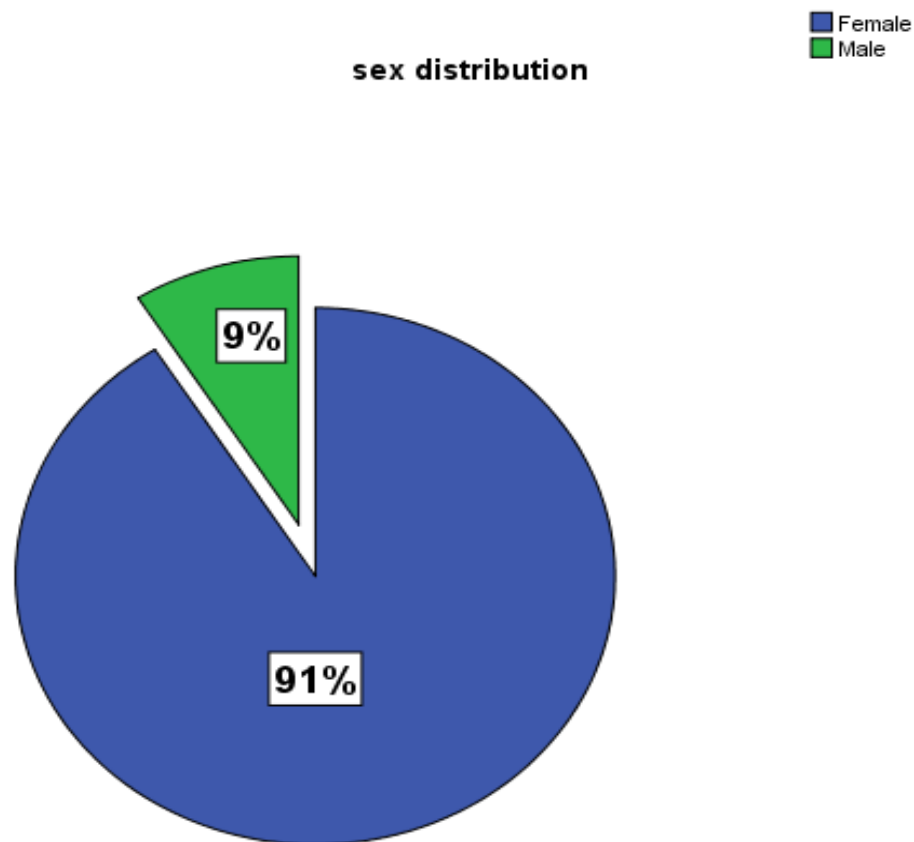


Figure 1.1 Sex distribution of breast cancer patients with bone involvement at TASH, Ethiopia from September 2017 to August 2018 GC.

The minimum age is 21 years and the maximum age is 71 years with mean age of 42.5 years. The most commonly affected age group is from 30 to 39 years 36(36%) followed by 40 to 49 years 30(30%) and 50 to 59 years 17(17%) (Figure 1.2)

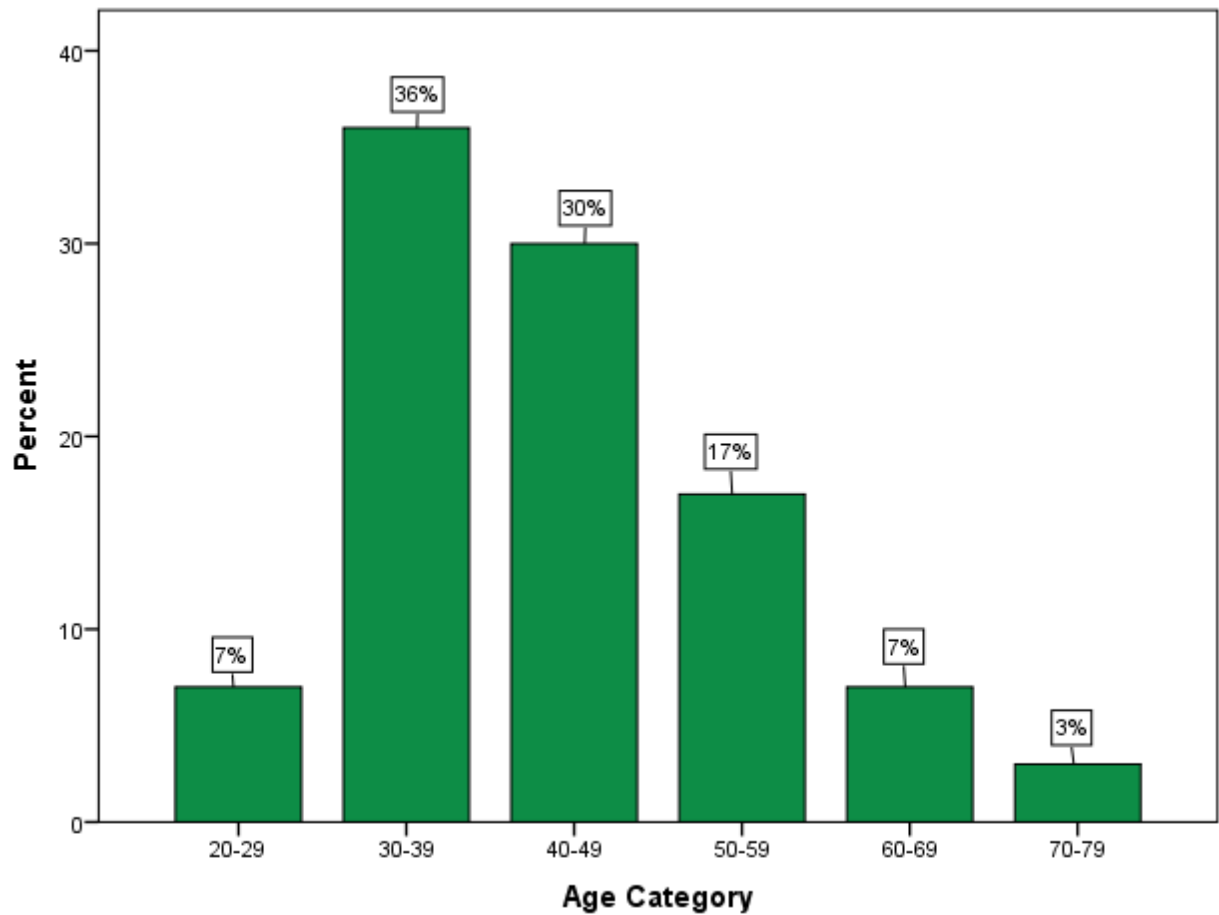


Figure 1.2 Age category of breast cancer patients with bone metastasis at TASH, Ethiopia from September 2017 to August 2018 GC.

4.2 Histopathology of the breast cancer

Ductal carcinoma 87(87%) is the most common type of breast cancer followed by Adenocarcinoma 5(5%) and malignant epithelial tumor 5(5%) (Table 1.1)

Table 1.1 Histopathology of the breast cancer patients at TASH, Ethiopia from September 2017 to August 2018 GC.

Histopathology		Frequency	Percent
	Ductal Carcinoma	87	87.0
	Adenocarcinoma	5	5.0
	malignant epithelial	5	5.0
	Lobular carcinoma	1	1.0
	Neuroendocrine	1	1.0
	squamous cell carcinoma	1	1.0
	Total	100	100.0

4.3 Morphology of the affected bones

Lytic type 51(51%) of bone lesion is the commonest morphologic type followed by mixed 28(28%) and sclerotic 21(21%) respectively (table 1.1)

Table 1.2 Morphologic feature of affected bones from breast metastasis at TASH, Ethiopia from September 2017 to August 2018 GC.

Morphology	Frequency	Percent
Lytic	51	51
Mixed	28	28
Sclerotic	21	21
Total	100	100

Table 1.3 Morphologic feature by Gender of affected bones from breast metastasis at TASH, Ethiopia from September 2017 to August 2018 GC

Gender	Type of bone lesion		
	Lytic	Mixed	Sclerotic
Female	48	23	20
	52.7%	25.3%	22%
Male	3	5	1
	33.3%	55.6%	11.1%
Total	51	28	21

Table 1.4 *Morphologic feature by histopathology feature of affected bones from breast metastasis at TASH, Ethiopia from September 2017 to August 2018 GC*

Type of lesion	Histopathology							Total
	Adenocarcinoma	Ductal Carcinoma	Epithelial	Lobular carcinoma	Malignant epithelial	Neuroendocrine	squamous cell carcinoma	
Lytic	2	45	0	1	2	1	0	51
Mixed	1	25	0	0	1	0	1	28
Sclerotic	2	17	1	0	1	0	0	21
Total	5	87	1	1	4	1	1	100

4.4 Distribution of the affected bones

In 87(87%) of the patients there is vertebral bone involvement which makes vertebral bone the most commonly affected bone followed by Pelvic bone 34 (34%) o and ribs 30(30%) of patients. There are five patients with skull bone involvement (Figure 1.3)

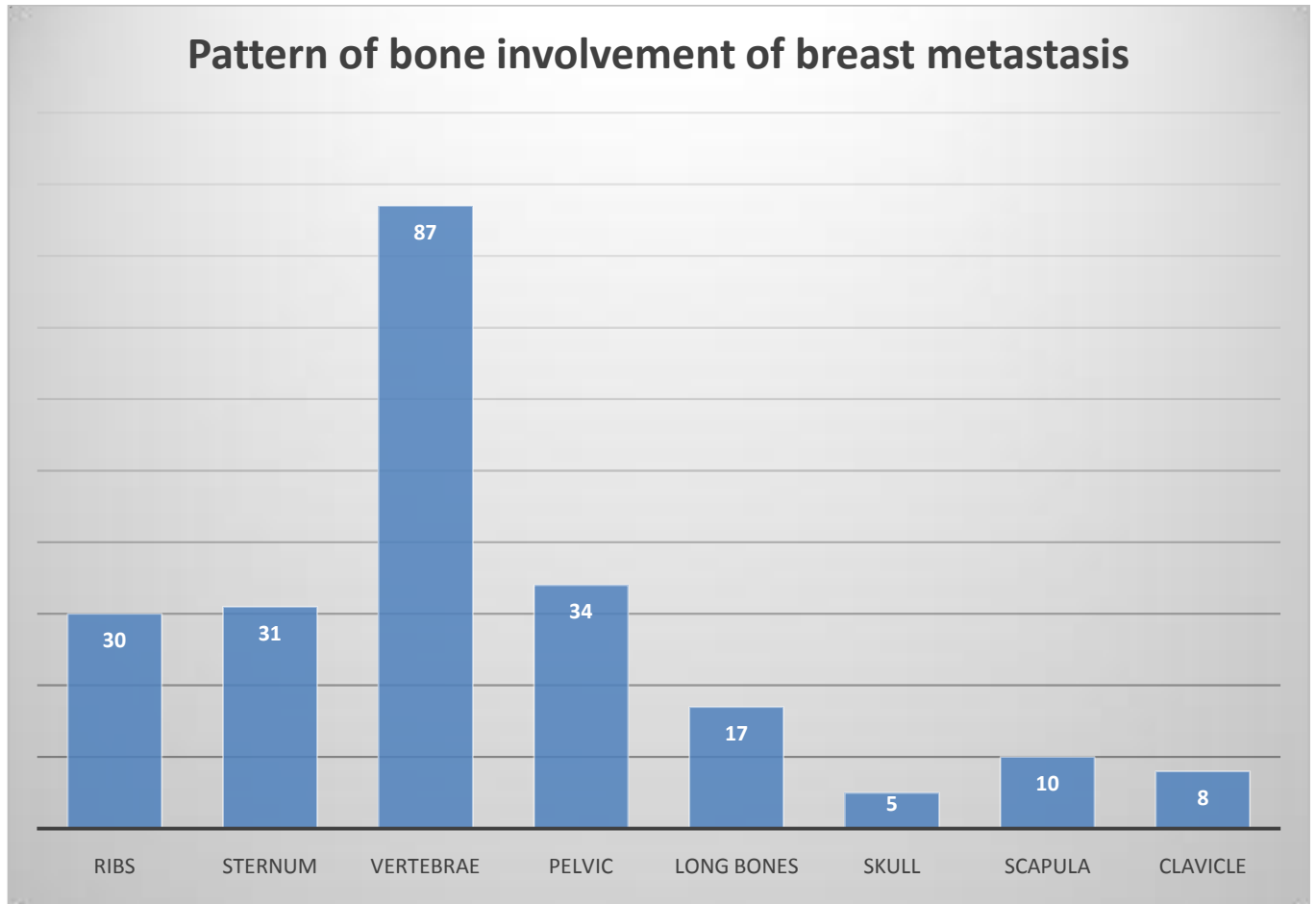


Figure 1.3 Bone involvement pattern of breast cancer patients at TASH, Ethiopia from September 2017 to August 2018 GC.

5. Discussion

Breast cancer is the most common site-specific cancer in women and is the leading cause of death from cancer for women age 40 to 44 years (1). Up to 80% Of patients with metastatic breast cancer develop bone metastasis which often cause significant morbidity and skeletal complication such as bone pain, pathological fracture, spinal cord or nerve root compression and hypocalcaemia. Metastasis to bone can occur via direct extension, anterior or venous gas spread with better representing the most common form (2, 3). Bone is the third most common organ affected by metastasis, surpassed only by the lungs and liver (34-36). Bone is the most common site for distant metastasis in patients with breast cancer, accounting for 65%patients with distant metastasis and representing the first site of metastasis in 50% of the patients. (4)

Breast carcinoma in men accounts for 0.5% of all breast cancers in the United States (24)and 2.4% to 15% in African series (25). In our present study the prevalence of breast cancer is 9% which is in contrary to the prevalence in United States and in line with the study in Africa.

The median age at diagnosis is 42.5 in our study and but the median age at diagnosis is 60 years in one study done in Japan. This could be due to the difference of average life expectancy between Japan and Ethiopian Population. The reported median age of breast cancer in men varies from 56 to 59.6 years, 55 years according to a research done by Ersumo T., Breast cancer in an Ethiopian population (24) which is somewhat in line with our present study. When we see the age distribution of breast cancer, the most commonly affected age group is 30-39 (36%) followed by 40-49 (30%) and 50 to 59 (17%) respectively which is similar to a study done in TASH by Abate.SMet al (38). See table 1.3.

Table 1.5 Comparison of Age distribution of breast cancer at TASH, 2018 and TASH, 2016.

Age category	This study (%)	<i>Abate SM.et al (%)</i>
<20	0	0.23
20-30	7	10.10
30-39	36	32.02
40-49	30	29.02
50-59	17	16.29
60-69	7	9.13
>70	3	3.82

In the current study, ductal carcinoma (87%) is the most common type of breast cancer followed by Adenocarcinoma (5%) and malignant epithelial tumor (5%) which is almost similar with the study done in Japan, Ductal carcinoma (86.44%) and Tulinius. H et al, Vona-Davis L. et al (29, 30, 32). In one study done in Turkey, the most common histologic type is Ductal carcinoma but lobular and mixed types are the commonest next to ductal respectively (33) unlike that of our study, in which adenocarcinoma and malignant epithelial tumor are the commonest histopathology next to ductal carcinoma respectively.

In this study the most frequent type of bone lesion is Lytic type (51%) followed by mixed (28%) and sclerotic (21%) respectively which is more or less similar with that of the study done in Japan which says osteolytic (35.2%) is the most common CT finding followed by mixed (23.88%) and osteoblastic (18.2%) respectively (23). One research done in Department of Radiology, Weill Cornell Medical College, New York, NY Department for 74 patients with Intra Ductal Carcinoma, the most common CT morphology of the osseous metastases was lytic (n = 29/74, 39%), followed by occult (n = 22/74, 30%), sclerotic (n = 14/74, 19%), and mixed (n = 9/74, 12%) (26-28). A study done in Turkey, based on CT appearance, sclerotic, lytic and mixed pattern are seen in 40%, 26%, and 34% of patients (20), respectively which is in contrary to our current study. One study in Lagos Nigeria of the 67 breast cancer patients, thirty-one patients had osteoblastic lesions, 24 patients had osteolytic lesions, and 2 patients had mixed osteolytic and osteoblastic lesions. (36, 37)

According to research done by Munelik et al, bone is the most common site for distant metastasized patients with breast cancer accounting for about 65% patients with distant metastasis and representing the first site of metastasis in 50% patients (4).

In this current study, in 87% of the patients there is vertebral bone involvement which makes vertebral bone the most commonly affected bone followed by Pelvic (34% of patients) and ribs (30% of patients). There are five patients with skull bone involvement. In one study done in India, there is high incidence of bone metastasis to spine and pelvis which is in line with our current study. In this same study, among patients with pelvic metastasis, SI joints and Ilium and in long bones and sternum, proximal parts were commonly involved (29). In another study done in Nigeria, Turkey and Ireland, the most commonly affected bones affected from breast cancer metastasis are vertebrae, pelvic bone and ribs respectively which is the same with that of our study (22, 33, 35, 36, 37).

In this current study ,in 87(87%) of the patients histopathology was ductal carcinoma , the most common CT morphology of the osseous metastases was lytic (n=45/87,51%) followed by mixed (n=25/87,28.5%) and sclerotic (n=17/87,19.5%) which is lower compared with study be done at New York, NY Department For the 74 patients with IDC, the most common CT morphology of the osseous metastases was lytic (n = 29/74, 39%), followed by occult (n = 22/74, 30%), sclerotic (n = 14/74, 19%), and mixed (n = 9/74, 12%).(32)

6. Conclusion

Majority of patients are female in our study with female to male ratio of 9:1 which is lower than most studies done at different countries. The most common histopathology feature of the breast cancer is ductal carcinoma followed by adenocarcinoma. The commonest CT pattern from breast cancer patient with commonest histopathology of ductal carcinoma is lytic which is lower than most studies done in different country.. When seen on computed tomography, lytic lesion is the most common feature of bone lesion followed by mixed (sclerotic and lytic) and sclerotic, which is in line with most of the studies. When we come to the anatomic distribution of the affected bones from breast metastasis, vertebral bone is the most commonly affected bone followed by pelvic bone and ribs. This finding is also similar to most studies done at different part of the world.

7. Recommendation and limitation

Limitation of the study:

- Only limited anatomic areas can be scanned at time.
- CT is not the most useful means of detecting abnormalities on whole body screening. Negative CT result doesn't rule out bone metastasis.
- CT is also not best the imaging modality as compared to the other imaging modality like FDG/PET/CT, scintigraphyMRI (for bone marrow).

Recommendations.

- To have advanced best imaging modality like FDG/PET/CT, Scintigraph MRI (for bone marrow).
- Its better to scan the whole body in all breast cancer patient if possible .
- Further research should be conducted as this study is the first study conducted in the country.
- Similar service providing hospitals in other corner of the country should be strengthened in terms of infrastructure advanced imaging and human resources since patients are coming from each corner of the country.

8. References

1. Schwartz's principles of surgery, 8th edition
2. ColumnR.potential use of Bisphosphonates in prevention of metastasis in early stage of breast cancer CLIN Breast cancer .2007 ;7(supply1): S29-S39
3. Lipton A. Implication of bone metastasis and the benefits of bone targeted therapy's oncol.2010;37(supply 2): S15-S29.
4. Lee YT. Patterns of metastasis and natural courses of breast carcinoma.Cancer and Metastasis Reviews. 1985 Jun 1; 4(2):153-72.)
5. HamaokaMadewellJE,Podoloff,DAHortobagyiGN,UenoNT.Bone imaging in metastatic breast cancer.Jclin oncol2004;22:2942-53
6. RubensRD.Bone metastasis--the clinical problem.Eur Jcancer.1988; 34:210-3
- 7.TuliniusH,BjarnasonO,sigvaldasonH,BjarnadottirG,OlafsdottirG.TumoursinIceland
- 10.Malignant tumours of the female breast .A histological classification ,laterality, survival and epidemiological consideration s. APMIS 1988;96:229-38.
- 8.Caldarella A,BuzzoniC,CrocettiE,BianchiS,vezzosiV,ApicellaP,et al. Invasive breast cancer ,a significant correlation between histologic types and molecular subtypes cancer Res clinOncol 2013 139:617-23
9. LiCI, Uribe DJ Daling JR Clinical characteristics ofdifferenthistologic types of breast cancer Br J cancer 2005; 93:1046-52
- 10.Avirl N Rose CA,SchellingM,DoseJ,KuhnW,Bense S t al.Breast imaging with PET and fluorine -18 fluorodeoxyglucose :use and limitation ,JClin Oncol.2000,18:3495-502.
11. AvirlN,MenzelM,DoseJ,Schelling N Weber W,Janicke F, et al. Glucose metabolism of breast cancer assessed by 18F-FDG PET :histologic and immunohistochemical tissue analysis ,JNucl Med ,2001;42:9-16
12. BosR, Van Der HoevenJJ, van Der Wall E Vander GroepP, vanDiest PJ ,comans EF ,et al .Biologic correlates of (18)fluorodeoxyglucose uptake in human breast cancer measured PET. JClinOncol .2002; 20:379-87
13. Buck A. SchirrmierH.KuhnT.Shen C KalkerT.KotzerkeJetal.FDG up take in breast cancer: correlation with biological and clinical prognosis parameters EurJNucl Med MolImaging 2002; 29:1317-23.
14. Eur J Nucl Med Mol Imaging .Authormanuscript; available in PMC 2016 October 01.

15. Vinholes J, Coleman R, Eastell R: Effects of bone metabolism : Implications for diagnosis , Imaging and assessment of response to cancer treatment . *Cancer Treat Rev* 22:289,1996-331.
16. Kido DK , Gould R, Taati F, et al : comparative sensitivity of CT scans, radiographs and radionuclide bone scans in detecting metastatic calvarias lesions . *Radiology* 128:371,1978-375
17. Rosenthal DI radiologic diagnosis of bone metastasis. *Cancer* 80:1595, 1997-1607
18. Bellamy EA, Nicholas D, Ward M, Coombes RC, Powles TJ, Husband JE (1987) Comparison of computed tomography and conventional radiology in the assessment of treatment response of lytic bony metastases in patients with carcinoma of the breast. *Clin Radiol* 38: 351–355
19. Silverberg E: Cancer Statistics, 1984. *Ca-A Cancer J Clin* 34: 7–23, 1982
20. Pollack ES, Horm JW: Trends in cancer incidence and mortality in the United States, 1969–76. *J Nat'l Cancer Inst* 64: 1091–1103, 1980
21. Hamaoka T, Costello CM, Madewell JE, Liu P, Berry DA, Islam R, Theriault RL, Hortobagyi GN, Ueno NT. Tumour response interpretation with new tumour response criteria vs. the World Health Organisation criteria in patients with bone-only metastatic breast cancer. *British journal of cancer*. 2010 Feb 16; 102(4):651-7.)
22. Gunalp B, Oner AO, Ince S, Alagoz E, Ayan A, Arslan N. Evaluation of radiographic and metabolic changes in bone metastases in response to systemic therapy with 18FDG-PET/CT. *Radiology and oncology*. 2015 Jun 1; 49(2):115-20. (1)
23. Dashevsky BZ, Goldman DA, Parsons M, Goñen M, Corben AD, Jochelson MS, et al. Appearance of untreated bone metastases from breast cancer on FDG
24. Ersumo T. Breast cancer in an Ethiopian population, Addis Ababa. *East and Central African Journal of Surgery*. 2006; 11(1):81-6
25. American Cancer Society. Cancer facts and figures- 1991. New York. American Cancer Society; 1991: 5PET/CT: importance of histologic subtype. *Eur J Nucl Med Mol Imaging*. 2015;42:1666–73.
26. Silverberg E: Cancer Statistics, 1984. *Ca-A Cancer J Clin* 34: 7–23, 1982.
27. Pollack ES, Horm JW: Trends in cancer incidence and mortality in the United States, 1969–76. *J Nat'l Cancer Inst* 64: 1091–1103, 1980.

28. Melnik Y, Slater PE, Katz L, Davies AM: Breast cancer in Israel, 1960–1975. II. Effects of age and origin on survival. *Europ J Cancer* 16: 1017–1023, 1980.
29. Sugihara T, Koizumi M, Koyama M, et al. Bone metastases from breast cancer: associations between morphologic CT patterns and glycolytic activity on PET and bone scintigraphy as well as explorative search for influential factors. *AnnalsofNuclear Medicine*.2017;31(10):719-725. doi:10.1007/s12149-017-1202-3.
30. Vona-Davis L, Rose DP, Gadiyaram V, Ducatman B, Hobbs G, Hazard H, Kurian S, Abraham J. Breast cancer pathology, receptor status, and patterns of metastasis in a rural appalachian population. *Journal of cancer epidemiology*. 2014 Jan 9; 2014
31. J. James, A. J. Evans, S. E. Pinder et al., “Bone metastases from breast carcinoma: histopathological—radiological correlations and prognostic features,” *British Journal of Cancer*, vol. 89, no. 4, pp. 660–665, 20032009
- 32.Tulinius H, Bjarnason O, Sigvaldason H, Bjarnadottir G, Olafsdottir G. Tumours in Iceland. 10. Malignant tumours of the female breast. A histological classification, laterality, survival and epidemiological considerations.*APMIS*.1988; 96:229–38.
33. Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histologic types of breast cancer. *Br J Cancer*.2005; 93:1046–52.
34. Doddala SM, Suryadevara A, Chinta SK, Madisetty AL. Incidence and pattern of bone metastases at presentation in Indian carcinoma breast patients. *Indian Journal of Cancer*. 2016 Jul 1; 53(3):360
35. Talbot JN, Paycha F, Balogova S. Diagnosis of bone metastasis:recent comparative studies of imaging modalities. *Q J NuclMedMol Imaging* 2011; 55: 374-410.
36. David JJ, Deborah AF, Frank JF. Metastatic Disease to Bone. *Hospital Physician*. November 2004
37. Ukihide T, Cristina G, Shaheenah D, et al. Bone Metastases in Patients withMetastatic Breast Cancer: Morphologic and Metabolic Monitoring of Response toSystemic Therapy with Integrated PET/CT, doi: 10.1148/radiol.2471070567 April 2008*Radiology*, 247:189-
38. Abate SM, Yilma Z, Assefa M, Tigeneh W, Trends of Breast Cancer in Ethiopia, *International Journal of Cancer Research and Molecular Mechanisms*, Feb 2016.

9. ANNEX

9.1 QUESTIONNAIRE

ADDIS ABEBA UNIVERSITY

SCHOOL OF GRADUATE STUDIES

DEPARTMENT OF RADIOLOGY

CT patterns of bone metastasis in breast cancer patient

1, Age _____

2, Sex M ____ F ____

3, Card No. _____

4, Clinical presentation

5. Does the patient have documented CT scan? Yes ____ No ____

6. Year of radiologic intervention A, 2016 G.C B, 2017 G.C C, 2018 G.C

7. Characterizations of bone metastasis on CT

7.1 lytic ____

7.2 sclerotic ____

7.3. mixed _____

7.4. Negative but evidenced with other imaging modality or biopsy ____

8. Distribution of the involved bone

8.1. vertebral bone if a. Yes ____ 1a. posterior element involvement

1b. Single or multiple vertebrae

1c. Associated soft tissue mass

1d. fracture- dislocation.

b. No ____

8.2. pelvic bone a. Yes ____ b. No ____

8.3. Ribs a. Yes _____ b. No _____

8.4. longbone a. Yes _____ b. No _____

if your answer is yes, specify_____

8.5. Others ,specify

9.Does the patient have documented histology of the breast cancer?

9.1 a. yes _____ b. No _____

If yes write the type of histo pathology result

9.2 Histological diagnosis _____