RESEARCH ARTICLE

# Differences Between Breast Cancer Patients Younger and Older than 40 Years: Mammographic Findings

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## Abstract

**Objective: To compare the mammogarphic appearance between breast cancer patients aged <40 and ≥40 years. Methods: Needle localization and biopsy of suspicious mammographic lesions identified 1,959 breast carcinomas in a single institution from Jun 2012 to Apr 2013. According to the age, we divided patients into two groups: <40 and ≥40 years old, and analyzed mammographic appearance separately. Results: Young patients had 44.2% foci with calcification, but old patients only had 39.4% (*P*<0.001). In younger group, the ratios of cases according to mass density were 41.8% or higher, 58.2% equivalent and lower. In older group, the ratios were 55.5 % and 44.5%, respectively. There were statistical differences between high density and others (*P*<0.05). The ratios of cases according to mass margin were 13.9% circumscribed and microlobulated, 86.1% indistinct and spiculated in the younger group, as compared to 6.5% and 93.5%, respectively, in the older group (*P*<0.05). Conclusions: Mammographic findings differ between young and old patients with breast cancer, for example regarding mass density, mass margin and microcalcification ratios.**

**Keywords:** Breast cancer - mammography findings - age-dependence - mass margins - microcalcification

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## Introduction

The tumors of young breast cancer patients often show more aggressive biologic behaviors, such as advanced stage, less ER/PR positive expression, high histological grade and more peritumoral vascular invasion. Although breast cancer is uncommon in young women below the age of 40 years old, only accounting for fewer than 6.6% (Tichy et al., 2013), the incidence continues to increase yearly. Early diagnosis is of great importance. Mammography is an important method in the diagnosis of breast cancer. Differences in the mammographic appearance of malignancies at different age may be due to the biologic differences in the surrounding breast. Therefore, diagnosis of breast cancer in young individuals presents a real challenge because of their denser breast tissue in comparing with older women. In the western countries, young females with a high genetic risk of breast cancer, are often provided specialized screening by the government, including the use of Magnetic resonance imaging (MRI). MRI has evolved into an important adjunctive tool for breast cancer detection, because of its high sensitivity (Abdulkareem, 2014). However, even in the most developed countries, MRI is not only long-running, but also costly. Therefore, mammography is also a preferred method for diagnosis. The purpose of this study was trying to stratify the risks of malignancy about mammographic characteristics of young patients.

## Materials and Methods

*Patients*

Overall, we collected mammographic findings of 1959 malignant cases that underwent needle biopsies or surgical resection in Cancer Institute and Hospital of Tianjin Medical University, China, from Jun 1, 2012 to Apr 30, 2013, including 190 cases of patients less than 40 years.

*Focus Classification and Mammographic Image*

Two doctors with over 10 years experience were blinded to the pathologic outcomes of all cases. According to the Breast Imaging Reporting and Data System (BI-RADS) developed by The American College of Radiology (ACR), the mammographic appearance of carcinomas in the current study was classified as: 1) mass. The shape was further classified as round/ oval, lobular and irregular. Margin was classified as circumscribed/microlobulated, and indistinct/spiculated. Density was classified into equivalent/low and high. 2) microcalcification. Shape of calcification was tentatively classified as typically benign, intermediate concern-suspicious and higher probability malignancy. Distribution was classified as regional, grouped/clustered or linear/segmental. 3) architectural distortion.

Statistical analyses were performed using SPSS16.0. All results were considered significant at $P<0.05$.

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**Table 1. Comparison of Calcification Rate in Different Age Groups**

| | <40 (190) | ≥40 (1769) | $X^2$ | *P* |
|---|---|---|---|---|
| Focus with calcification | 84 (44.2%) | 697 (39.4%) | 19.052 | 0.000 |
| Focus without calcification | 106 (55.8%) | 1072 (60.6%) | | |

## Results

1959 case ranged in age from 22 to 87 years were referred to the study. Of these, 190 cases were below 40 years, accounting for 1% of all patients. In young patients group, 122 (64.2%) cases had a mammographic mass with/ without calcification, 23 (12.1%) cases had calcification only, 37 (19.5%) cases had architectural distortion with/ without calcification, and 8 (4.2%) cases found no abnormality. In elderly groups, the case are 1338 (75.6%), 149 (8.4%), 265 (15.0%) and 17 (1.0%) separately.

According to calcifications we classified the image into focus with calcifications and focus without calcification. Microcalcification was the only finding prompting biopsy in 12.1% cases, and was present in association with a mass or distortion in another 32.1% cases, giving a total of 44.2% in the whole series in young patients group. Table 1 showed that young patients had 44.2% focus with calcification, but old patients only had 39.4%. There were statistically significant differences between the two groups ($P$<0.001).

All mammographic features were classified according to BI-RADS. In younger group, the ratios of cases according to mass density were 41.8% of higher, 58.2% of equivalent and lower. In old group, the ratios were 55.5 % and 44.5%, respectively. There were statistically significant differences between higher and other density ($P$<0.05). The ratios of cases according to mass margin were 13.9% of circumscribed and microlobulated, 86.1% of indistinct and spiculated in younger groups. While in older group, the ratios were 6.5% and 93.5%, respectively. There were statistically significant differences in different age groups ($P$<0.05) (Table 2)

We also classified mass shape into round/oval, lobular and irregular, calcification type into typically benign, intermediate suspicious and high probalility of malignancy, calcifications distribution into grouped/ clustered, linear/segmental and regional, but there were no statistical differences in each classification (Table 2).

**Table 2. Comparison of Mammgraphic Features Between Two Age Groups**

| | <40 (190) | ≥40 (1769) | $X^2$ | *P* |
|---|---|---|---|---|
| Mass density | | | | |
| equivalent/low | 71 (58.2%) | 595 (44.5%) | 8.493 | 0.004 |
| high | 51 (41.8 %) | 743 (55.5 %) | | |
| Mass shape | | | | |
| round/oval | 33 (27.0 %) | 395 (29.5%) | 0.378 | 0.828 |
| lobular | 10 (8.2%) | 99 (7.4%) | | |
| irregular | 79 (64.8%) | 844 (63.1%) | | |
| Mass margin | | | | |
| circumscribed/ microlobulated | 17 (13.9%) | 87 (6.5%) | 9.335 | 0.002 |
| indistinct/ spiculated | 105 (86.1%) | 1251 (93.5%) | | |
| Calcifications | | | | |
| typically benign | 16 (19.0%) | 147 (21.1%) | 1.286 | 0.526 |
| intermediate concern, suspicious calcifications | 25 (29.8 %) | 168 (24.1%) | | |
| high probalility of malignancy | 43 (51.2 %) | 381 (54.7%) | | |
| Distribution | | | | |
| grouped/clustered | 5 (21.7%) | 59 (39.6%) | 3.46 | 0.177 |
| linear/segmental | 12 (52.2%) | 68 (45.6%) | | |
| regional | 6 (26.1%) | 22 (14.8%) | | |

## Discussion

It is known that image was decided by biological behaviors of tumors. Young patients always show different behaviors from older patients, especially poor prognosis, which may bring about different images in mammography. For breast cancer, the Breast Imaging Reporting and Data System developed by The American College of Radiology, was commonly used to describe mammographic data. Images in mammography were classified as mass, calcification and architectural distortion basically.

Because of different biological behaviors, mammographic findings had different characteristics between young breast cancer and older patients. Obviously, parenchymal pattern was the most different. As young patients always had dense breast, the ratio of mammographic abnormalities was higher than old groups. This revealed the limitation of mammography that sensitivity decreased in dense breast. Wang FL et al revealed that ultrasonography is more sensitive than mammography in women under 55 year-old, especially in those with high-density breast (Wang et al., 2013). Still there were another mammographic data of malignant tumors affected by age.

Mass was one of the primary signs, and spiculated margin was a powerful predictor for malignant tumor. Previous studies revealed that mass, accounting for the majority of mammographic images, was more powerful predictor in women in the USA and Europe (Pisano et al., 1998; Thurfjell et al., 2002). Our results revealed that the ratio of the cases detected as a mass in young groups was lower than that of older groups. In addition, mass with indistinct or spiculated margin turned out to be major predictor only for malignancies in older patients group, while young patients always showed circumscribed or microlobulated margins, and the ratio had statistically significant differences compared to older patients.

Spicules are extensions with a pyramidal base, spreading out from the masses. By causing a retractile phenomenon, fibrosis and elastosis are responsible for the stellate aspect of breast cancer. Tumor cells often gather at the base of spicules, far fewer at the extremities (Cherel et al., 2005). Therefore, the very thin spicules may due to a fibrous reation, but the short thick ones around the central mass could for the most part of cells infiltrating the connective tissue. This can also be demonstrated indirectedly by radial scar, which is also present with long and thin spicules but belongs to one of benign hyperplasia of breast (Taneja et al., 2008). In our study, young patients had less spicules than older patients with following reasons: firstly, the extremities of the spicules were sometimes difficult to detect and it was necessary to take films with spot compression, especially in dense breast; secondly, several studies demonstrated that triple-negative breast cancers often affected younger patients,

while older patients were Luminal A/B subtypes mostly (Bauer et al., 2007). Boisserie-Lacroix et al. (Boisserie-Lacroix et al., 2013) found that triple-negative breast cancers, which were associated with aggressive clinical course and poorer prognosis, often present with benign imaging features on images, but less typical findings of malignances. At the same time, Taneja et al. (Taneja et al., 2008) also found that groups characterized by hormone receptor positive had significantly more spiculated mass at mammography.

Our study also showed that masses in young patients performed equivalent/low density mostly, while older patients had high density mass. The main reason was parenchymal pattern. With a fatty background, tumor margins can be distinguished from normal tissue. On the contrary, the margins could not easily display in dense breast. Therefore, in the published literatures, the sensitivity of mammography had been reported to be lower in dense breast of young patients, ranging from 45% to 90% ( Shaw de Paredes et al., 1990; Brand et al., 1993; Ciatto et al., 1994).

For breast cancer, calcification was another primary signs. And mammography was the best image method for displaying calcification. Previous literatures consistently showed that the presence of calcifications, either as an isolate finding or in combination with a mass or distortion, was very frequent, ranging from 38% to 66% cases (Shaw de Paredes et al., 1990; Ferranti et al., 2000; Zadelis & Houssami, 2003; Tamaki et al., 2012). In our study, the rate was 44.2% in young age group, which is coincident with literatures. Besides, there were statistically differences of calcification performance rate between different age groups. Proved by pathology, microcalcifications revealed by mammography in young patients were more frequently a manifestation of DCIS (Hermann et al., 1988; Papatestas et al., 1990; Evans et al., 1997). Even invasive malignancies presenting as calcifications also associated with extensive intraductal carcinoma (Healey et al., 1989; Schmidt-Ullrich et al., 1993). These intraductal parts often performed a wide range and unpalpable, so they had high rate of positive margin in the surgery. Further more, without a clear margin, local recurrence turned out to be more frequent. Malignant calcifications represent necrosis, probably due to high cell turn over and inadequate blood supply, this may explain intraductal component often present as microcalcifications. These calcifications characterized by fine linear, linear branching or coarse-granular patterns. Lesions of this type were usually c-erbB-2 and Ki-67 positive, showed a high proliferative activity and were less frequently hormone receptor positive. All these denoted that microcalcification was an unfavourable sign of invasive breast tumors. As Young patients with high rate of microcalcifications, they may have poor prognosis. Finally, image performance was coincident with biological behaviors. Therefore, the value of mammography in young breast cancer could be increasing.

In conclusion, mammographic findings had different performance in young patients and in older patients, including mass density, mass margin and calcification positive rate. Especially, calcification had special significance for breast cancer, which demonstrated an unfavorable sign and was relevant with poor prognostic factors. This may be a prognostic factor from image aspect which needs us to have further study.

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## References

Abdulkareem ST (2014). Breast magnetic resonance imaging indications in current practice. *Asian Pac J Cancer Prev*, **2**, 569-75.

Bauer KR, Brown M, Cress RD, et al (2007). Descriptive analysis of estrogen receptor (ER)-negative, progesterone receptor (PR)-negative, and HER2-negative invasive breast cancer, the so-called triple-negative phenotype: a population-based study from the California cancer Registry. *Cancer*, **9**, 1721-8.

Boisserie-Lacroix M, Macgrogan G, Debled M, et al (2013). Triple-negative breast cancers: associations between imaging and pathological findings for triple-negative tumors compared with hormone receptor-positive/human epidermal growth factor receptor-2-negative breast cancers. *Oncologist*, **7**, 802-11.

Brand IR, Sapherson DA, Brown TS (1993). Breast imaging in women under 35 with symptomatic breast disease. *Br J Radiol*, **785**, 394-7.

Cherel P, Becette V, Hagay C (2005). Stellate images: anatomic and radiologic correlations. *Eur J Radiol*, **1**, 37-54.

Ciatto S, Rosselli del Turco M, Catarzi S, et al (1994). The contribution of ultrasonography to the differential diagnosis of breast cancer. *Neoplasma*, **6**, 341-5.

Evans WP, 3rd, Starr AL, Bennos ES (1997). Comparison of the relative incidence of impalpable invasive breast carcinoma and ductal carcinoma in situ in cancers detected in patients older and younger than 50 years of age. *Radiology*, **2**, 489-91.

Ferranti C, Coopmans de Yoldi G, Biganzoli E, et al (2000). Relationships between age, mammographic features and pathological tumour characteristics in non-palpable breast cancer. *Br J Radiol*, **871**, 698-705.

Healey EA, Osteen RT, Schnitt SJ, et al (1989). Can the clinical and mammographic findings at presentation predict the presence of an extensive intraductal component in early stage breast cancer? *Int J Radiat Oncol Biol Phys*, **6**, 1217-21.

Hermann G, Janus C, Schwartz IS, et al (1988). Occult malignant breast lesions in 114 patients: relationship to age and the presence of microcalcifications. *Radiology* , **2**, 321-4.

Papatestas AE, Hermann D, Hermann G, et al (1990). Surgery for nonpalpable breast lesions. *Arch Surg*, **3**, 399-402.

Pisano ED, Fajardo LL, Tsimikas J, et al (1998). Rate of insufficient samples for fine-needle aspiration for nonpalpable breast lesions in a multicenter clinical trial: The Radiologic Diagnostic Oncology Group 5 Study. The RDOG5 investigators. *Cancer* , **4**, 679-88.

Schmidt-Ullrich RK, Wazer DE, DiPetrillo T, et al (1993). Breast conservation therapy for early stage breast carcinoma with outstanding 10-year locoregional control rates: a case for aggressive therapy to the tumor bearing quadrant. *Int J Radiat Oncol Biol Phys*, **3**, 545-52.

Shaw de Paredes E, Marsteller LP, Eden BV (1990). Breast cancers in women 35 years of age and younger: mammographic findings. *Radiology*, **1**, 117-9.

Tamaki K, Ishida T, Miyashita M, et al (2012). Retrospective

analysis of mammographic findings for Japanese women: a potential predictor for breast malignancies. *Cancer Sci*, **3**, 472-6.

Taneja S, Evans AJ, Rakha EA, et al (2008). The mammographic correlations of a new immunohistochemical classification of invasive breast cancer. *Clin Radiol*, **11**, 1228-35.

Thurfjell MG, Lindgren A, Thurfjell E (2002). Nonpalpable breast cancer: mammographic appearance as predictor of histologic type. *Radiology*, **1**, 165-70.

Tichy JR, Lim E, Anders CK (2013). Breast cancer in adolescents and young adults: a review with a focus on biology. *J Natl Compr Canc Netw*, **9**, 1060-9.

Wang FL, Chen F, Yin H, et al (2013). Effects of age, breast density and volume on breast cancer diagnosis: a retrospective comparison of sensitivity of mammography and ultrasonography in China's rural areas. *Asian Pac J Cancer Prev*, **4**, 2277-82.

Zadelis S, Houssami N (2003). Mammographic features of breast cancer in young symptomatic women. *Australas Radiol*, **4**, 404-8.