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D Bunjunwetwat

N. Dumrongpisutikul

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Mammographic breast parenchymal patterns in Thai women with breast cancers

Darunee Bunjunwetwat*

Netsiri Dumrongpisutikul*

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- Introduction** : *Dense breast parenchyma are reported as increasing risk of breast cancer from the previously study. The dense breasts have a role to consider additional MRI to the screening mammogram for early detection in women with moderately increased breast cancer risk.*
- Objective** : *To assess breast parenchymal patterns of Thai women with breast cancers.*
- Setting** : *King Chulalongkorn Memorial Hospital*
- Research design** : *A retrospective study.*
- Patients** : *Thai women who had verified of breast cancers and had bilateral mammography in King Chulalongkorn Memorial Hospital.*
- Methods** : *Seventy two Thai women with breast cancers were retrospectively reviewed for breast parenchymal patterns from the latest mammography before surgery by a skilled breast radiologist. The breast parenchymal patterns were classified according to Wolfe's classification (N1, P1, P2 and Dy).*

- Results** : *The mean age value of 72 Thai women with breast cancers is 50 years (age range 32 - 75 years). The breast parenchymal patterns of these women were 2 cases as type N1 (3%), 12 cases as type P1 (17%), 26 cases as type P2 (36%) and 32 cases as type DY (44%). The P2 and Dy breast parenchymal patterns are majority in 3 age-groups; 30 - 39 years, 40 - 49 years and 50 - 59 years. The most frequent cancer type is invasive ductal carcinoma (66 cases, 91.7%).*
- Conclusions** : *Type P2 and DY represented dense breast were the most prevalent mammographic breast parenchymal patterns in Thai women with breast cancers.*
- Keywords** : *Breast parenchymal pattern, Mammography, Breast cancer.*

Reprint request: Bunjunwetwat D. Department of Radiology, Faculty of Medicine,
Chulalongkorn University, Bangkok 10330, Thailand.

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- บทนำ** : นอกจากลักษณะเนื้อแท้เต้านมที่มีความหนาแน่นสูงจะเพิ่มโอกาสเกิดมะเร็งเต้านมแล้ว ยังมีบทบาทในการพิจารณาตรวจด้วยเอ็มอาร์ไอ (MRI) เพิ่มเติมจากการตรวจคัดกรองโรคด้วยแมมโมแกรมในผู้ป่วยที่มีความเสี่ยงที่จะเกิดโรคมะเร็งเต้านมระดับปานกลาง
- วัตถุประสงค์** : เพื่อศึกษาลักษณะเนื้อแท้เต้านมในผู้ป่วยหญิงไทยที่ป่วยเป็นมะเร็งเต้านม
- สถานที่ทำการศึกษา** : โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย
- รูปแบบการวิจัย** : การศึกษาแบบย้อนหลัง
- ผู้ป่วยที่ได้ทำการศึกษา** : ผู้หญิงไทยที่มีผลการตรวจทางพยาธิวิทยายืนยันว่าเป็นมะเร็งเต้านม และได้ตรวจแมมโมแกรมที่โรงพยาบาลจุฬาลงกรณ์ สภากาชาดไทย
- วิธีการศึกษา** : ผู้วิจัยศึกษาแมมโมแกรมก่อนเข้ารับการผ่าตัดของผู้ป่วยมะเร็งเต้านม ซึ่งเป็นหญิงไทย 72 ราย แมมโมแกรมได้รับการแปลผลโดยรังสีแพทย์ ผู้มีความเชี่ยวชาญ ลักษณะเนื้อแท้เต้านมแบ่งตามแบบของ Wolf เป็นชนิด N1, P1, P2 และ Dy
- ผลการศึกษา** : อายุเฉลี่ยของผู้หญิงไทย 72 รายที่ป่วยเป็นมะเร็งเต้านมคือ 50 ปี (ช่วงอายุ 32 - 75 ปี) ลักษณะเนื้อแท้เต้านมที่พบแบ่งเป็น N1 2 ราย คิดเป็น 3%, P1 12 ราย คิดเป็น 17%, P2 26 ราย คิดเป็น 36% และ DY 32 ราย คิดเป็น 44% ลักษณะเนื้อแท้เต้านมแบบ P2 และ Dy ซึ่งเป็นเนื้อเต้านมที่มีความหนาแน่นสูงพบมากในกลุ่มผู้ป่วยสามกลุ่ม ช่วงอายุได้แก่ 30 - 39 ปี, 40-49 ปี และ 50 - 59 ปี ชนิดของมะเร็งเต้านมที่พบมากที่สุดคือ invasive ductal carcinoma จำนวน 66 ราย (91.7%)
- วิจารณ์และสรุป** : ลักษณะเนื้อแท้เต้านมจากภาพแมมโมแกรมที่มีความทึบสูงที่สุดในผู้หญิงไทยที่ป่วยเป็นมะเร็งเต้านมคือชนิด P2 และ Dy ซึ่งมีความหนาแน่นของเนื้อแท้เต้านมสูง
- คำสำคัญ** : เนื้อแท้เต้านม, ภาพแมมโมแกรม, มะเร็งเต้านม.

Breast cancer is the second most common cancer in Thai women. The incidence in Thailand is about 20.5/100,000 and the highest incidence rate is in Bangkok (24.3/100,000). Age-specific incidence rates in Thailand begin to rise after 35 years and reach a maximum peak at age 45, and then declining as a plateau. The incidence increased in all parts of the country in the past decade. The most common histologic subgroup of breast cancer is ductal carcinoma (76.4 - 91.2%). Stage distribution is in order as following; stage 2 (32.1%), unknown stage (25.2%), stage 3 (21.1%), stage 1 (13%) and stage 4 (8.6%).⁽¹⁾

There are different kinds of risk factors affecting chance of getting breast cancer according to the National Cancer Institute 2008 and American Cancer Society 2007 as indicated by risk factors cannot be changed such as gender, age, race, genetic risk factor, family history of breast cancer and previous breast cancer. Some factors are linked to cancer-causing factors in the environment and some factors are related to personal behaviors such as obesity, previous history of radiation or ovarian, cervix and colon cancer, previous history of repetitive trauma, early menarche, late menopause, nulliparous or first child at age > 30 years, high cholesterol, long term contraceptive pills, hormonal replacement therapy, and abnormal breast biopsy results such as proliferative lesions.^(2, 3)

Despite the risk factors mentioned above, the dense breasts are reported as increasing risk of breast cancer from the previously studies^(4, 5, 6 - 8)

Besides, the dense breasts do have a role to consider additional MRI to the screening mammogram for early detection in women with moderately increased risk (15% to 20% lifetime

risk) following the American Cancer Society's guidelines.⁽²⁾

The early detection of breast cancer improves the chances that breast cancer can be diagnosed at an early stage and treated successfully.

Since the dense breasts are the majority group in Thai women⁽⁹⁾ and MRI is not available everywhere and also expensive, the national guidelines for early detection of breast cancer in Thailand should be different from the USA guidelines.

The main interest in mammography has focused on its value as a screening method. Normal mammogram is a homogeneous pattern interspersed with islands of fatty tissue appearing as round radiolucencies in a wide variety of configuration. Fine arcs or stripes of increased density of Cooper's ligament and large lactiferous ducts converging in the retroareolar area will be visualized.

Mammographic parenchymal pattern was classified by Wolfe into 4 groups: *N1*, *P1*, *P2* and *Dy* based on the relative amounts of fat, epithelial and connective tissue and prominent duct.⁽⁵⁾

In *N1*, the breast consists of mostly fatty tissue with no visible duct. The *P1* category represents a fatty breast, with predominant ducts in the anterior portion occupying up to a quarter of the breast area. In *P2*, the breast is involuted, with prominent duct pattern of moderate to severe degree, occupying more than a quarter of the breast. The visible duct pattern may occupy the entire breast. In *Dy*, the breast parenchyma is dense, which usually denotes connective tissue hyperplasia.

The *N1* and *P1* groups are considered as low risk for malignancy. The *P2* group is considered a high risk and the *Dy* group is considered to be the

highest risk pattern.

This study aimed to determine the distribution of mammographic breast parenchymal patterns in Thai women who had histological verified of breast cancers.

Material and Method

The research was approved by the ethics committee of the Faculty of Medicine, Chulalongkorn University, Thailand. The patient's hospital data was approved for analysis by Director of the Hospital.

The study group of 72 Thai women, who had histological verified of breast cancers were retrospectively reviewed for mammographic breast parenchymal patterns from the latest bilateral mammography before surgery. All of the mammograms were performed in breast imaging unit, King Chulalongkorn Memorial Hospital. The mammograms were interpreted by more than 30 years breast radiologist on the picture archiving and communicating system (PACS). A full-field digital mammography (GE senographe 2000) was used to expose in standard two views (CC and MLO views) of bilateral breasts.

Inclusion criteria:

- All eligible Thai women who had histological verified breast cancers in King Chulalongkorn Memorial Hospital.
- All patients who had bilateral mammography before diagnosis of breast cancers in King Chulalongkorn Memorial Hospital.

Exclusion criteria:

- Male patient.
- Other nationality besides Thai.
- Women who have no histological verified of breast cancers or no bilateral mammography at

King Chulalongkorn Memorial Hospital.

Sample size

In order to calculate a sample size for this study, there are four variables to be considered: p , q , z and Δ . The formula of $(n) = Z^2 pq / \Delta^2$ was used to calculate sample size where p is a percentage of interval breast cancer in $P2+Dy$ group = 95%, q is a percentage of interval breast cancer in $N1+P1$ group = 5%, 95% CI, $z = 1.96$ and Δ is an acceptable error at 0.05e.

The p and q values come from Wolfe study group II in 1976 because this group is the most applicable distribution of breast parenchymal pattern in screening women to Thailand.

The final number of the patient in this study is 72.

The mammographic breast parenchymal patterns of 72 patients were classified by Wolfe's grade into 4 groups: $N1$, $P1$, $P2$ and Dy , based on the relative amounts of fat, epithelial and connective tissue and prominent duct.

Mammographic breast parenchymal pattern by Wolfe's grade:

- $N1$ is the breast parenchyma composed primarily of fat with at most small amounts of dysplasia. No duct is visible in this category (Figure 1).
- $P1$ is the fatty breast with prominent ducts in anterior portion up to a quarter of volume breast. There may be a thin band of ducts extending into a quadrant (Figure 2).
- $P2$ is the involuted breast, with prominent duct pattern of moderate to severe degree, occupying more than a quarter of volume of breast. The visible duct pattern may occupy the entire breast (Figure 3).

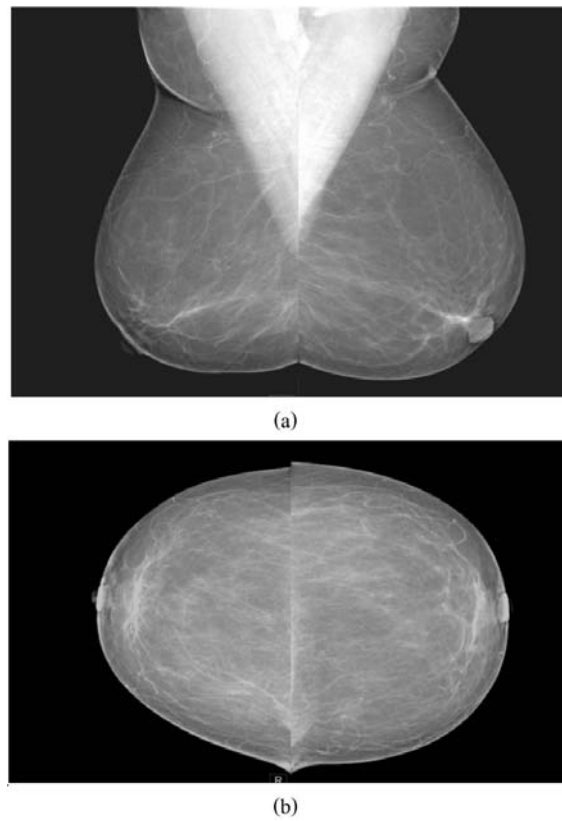


Figure 1. N1 feature; (a) mediolateral oblique view and (b) craniocaudal view.

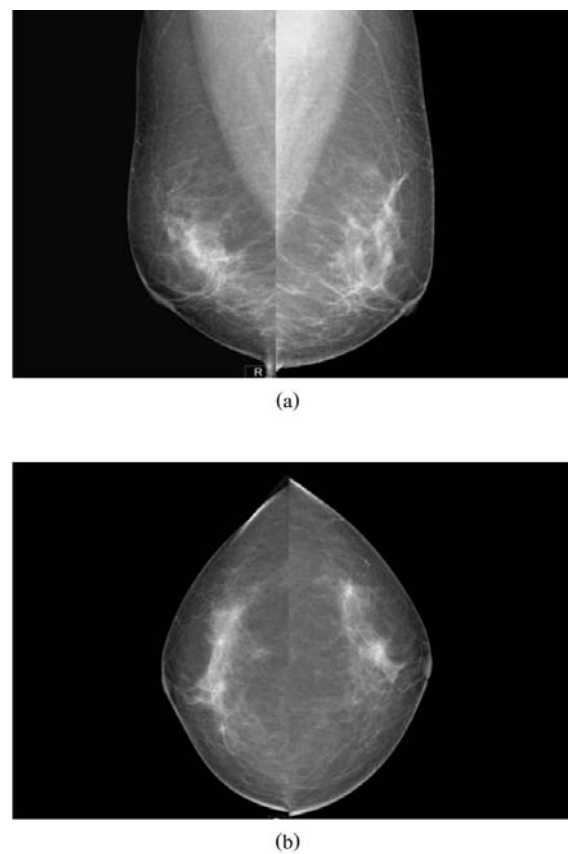
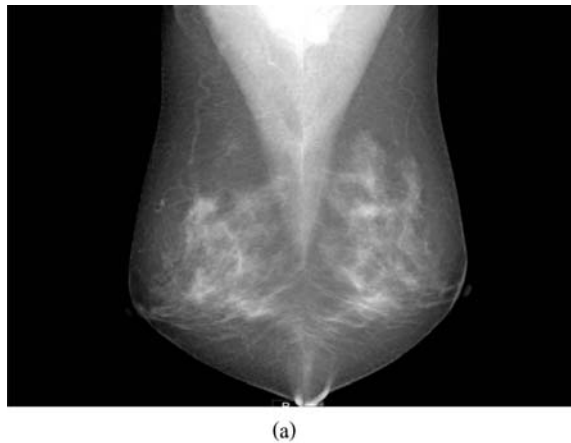
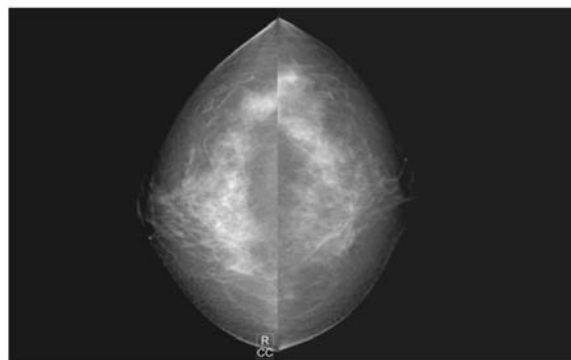


Figure 2. P1 feature; (a) mediolateral oblique view and (b) craniocaudal view.



(a)



(b)

Figure 3. P2 feature; (a) mediolateral oblique view and (b) craniocaudal view.

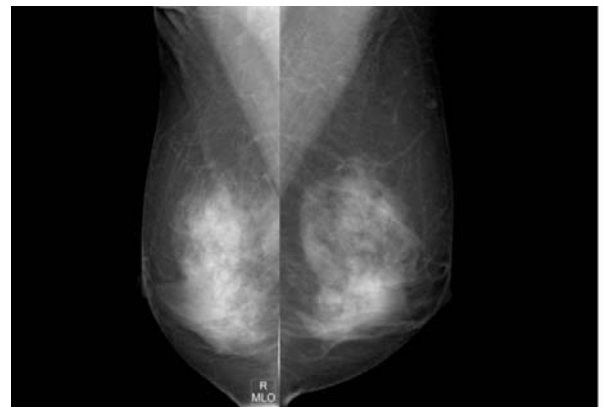
- *Dy* is the dense breast parenchyma with severe degree dysplasia that often obscures an underlying prominent duct pattern (Figure 4).

Besides, the breast parenchymal patterns were also categorized by age-groups (30 - 39 years, 40 - 49 years, 50 - 59 years, 60 - 69 years and 70 - 79 years).

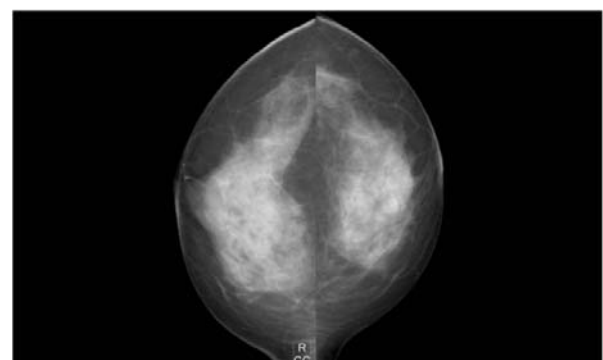
The histologic details were recorded from King Chulalongkorn Memorial Hospital computer-based medical database.

Result

This study reveals mean age value of 72 Thai women with breast cancer which is 50 years (age



(a)



(b)

Figure 4. DY feature; (a) mediolateral oblique view and (b) craniocaudal view.

range 32 - 75 years). About 71% of patients, breast cancer occurred between age-groups of 40 - 59 years and peak age-group is at 40 - 49 years.

The parenchymal pattern distribution according to Wolfe's classification of 72 Thai women with breast cancers reveals the most common to be *Dy* (44%). Next in decreasing order of occurrence were *P2* (36%), *P1* (17%) and *N1* (3%) as shown in figure 5.

The most frequent *DY* feature was more found in 40 - 49 years (56.3%). The second frequent feature *P2* was more found in two age-groups, 40 - 49 years (46.2%) and 50 - 59 years (50%). The third frequent feature *P1* was more found in 60 - 69 years (50%)

and the least frequent feature *N1* was more found in two age-groups, 60 - 69 (50%) and 70 - 79 years (50%).

Of the 72 screening mammograms, the different breast parenchymal patterns between age-groups were found, 30 - 39 years (total 9 cases, figure 6) had *P1* feature 1 case (11%), *P2* feature 1 case (11%) and *DY* feature 7 cases (78%), 40 - 49 years (total 31 cases, figure 7) had *P1* feature 1 case (3%), *P2* feature 12 cases (39%) and *DY* feature 18 cases (58%), 50 - 59 years (total 20 cases, figure 8) had *P1* feature 1 case (5%), *P2* feature 13 cases (65%) and *DY* feature 6 cases (30%), 60 - 69 years (total 8

cases, figure 9) had *N1* feature 1 case (13%), *P1* feature 6 cases (74%) and *DY* feature 1 case (13%) and 70 - 79 years (total 4 cases, figure 10) had *N1* feature 1 case (25%) and *P1* feature 3 cases (75%).

The most frequent cancer type is invasive ductal carcinoma (91.7%). The other cancer types are invasive ductal carcinoma with paget's disease (1.4%), Ductal carcinoma in situ (DCIS) (2.8%), invasive lobular carcinoma (1.4%), mucinous carcinoma (1.4%) and papillary carcinoma (1.4%) as shown in figure 11.

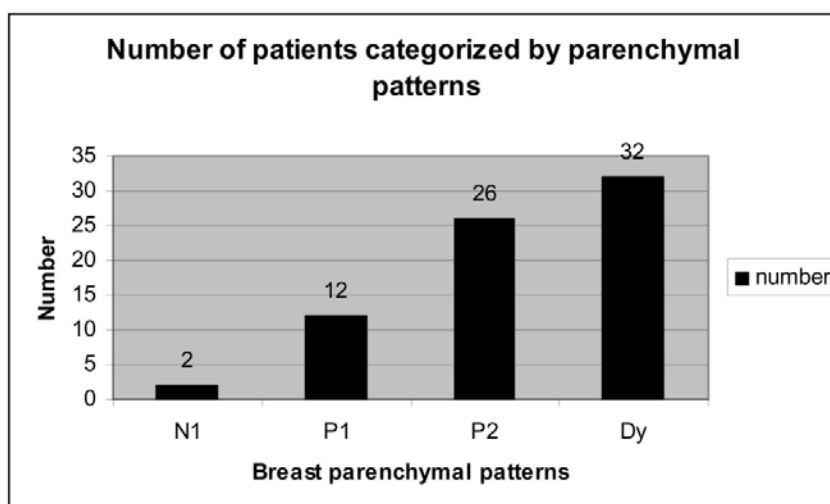


Figure 5. Number of patients categorized by parenchymal patterns.

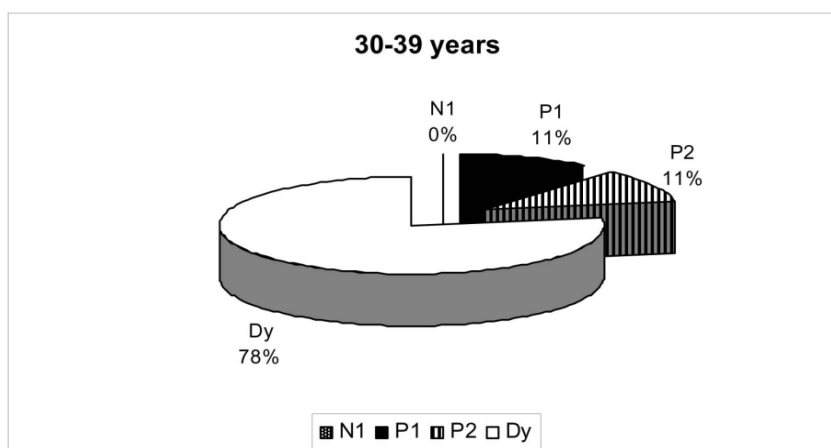


Figure 6. Breast parenchymal patterns (percentile) in women 30 - 39 years old.

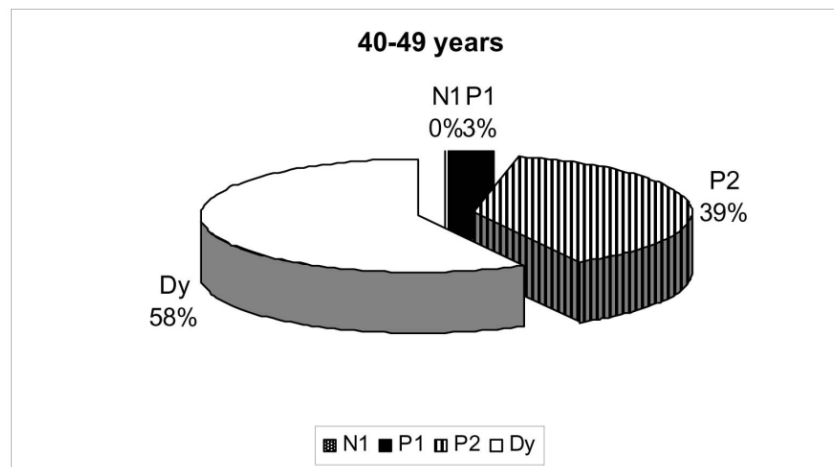


Figure 7. Breast parenchymal patterns (percentile) in women 40-49 years old.

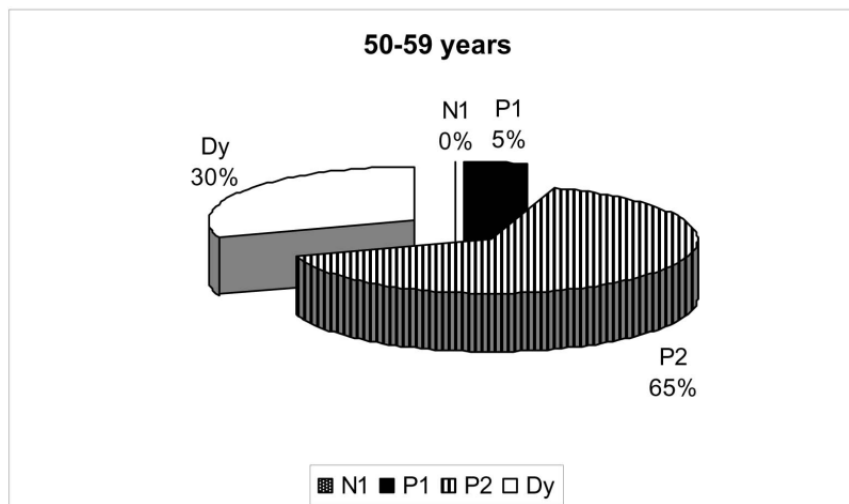


Figure 8. Breast parenchymal patterns (percentile) in women 50-59 years old with cancer.

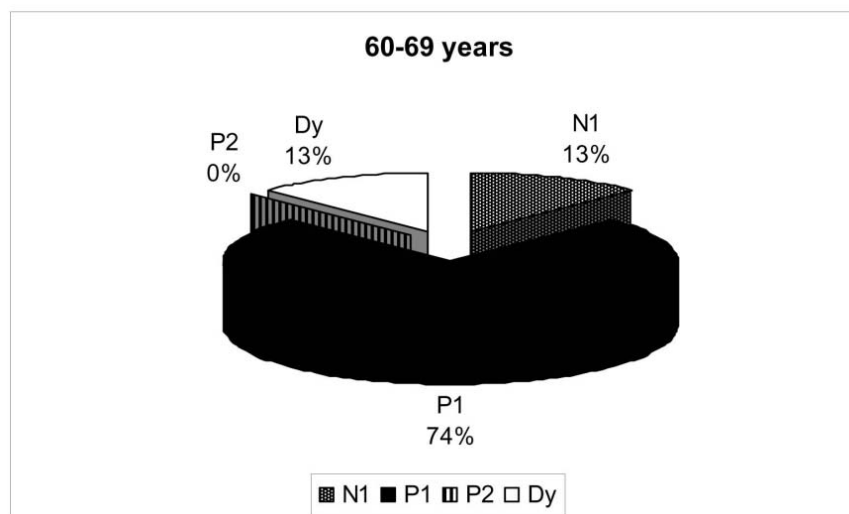


Figure 9. Breast parenchymal patterns (percentile) in women 60-69 years old with breast cancer.

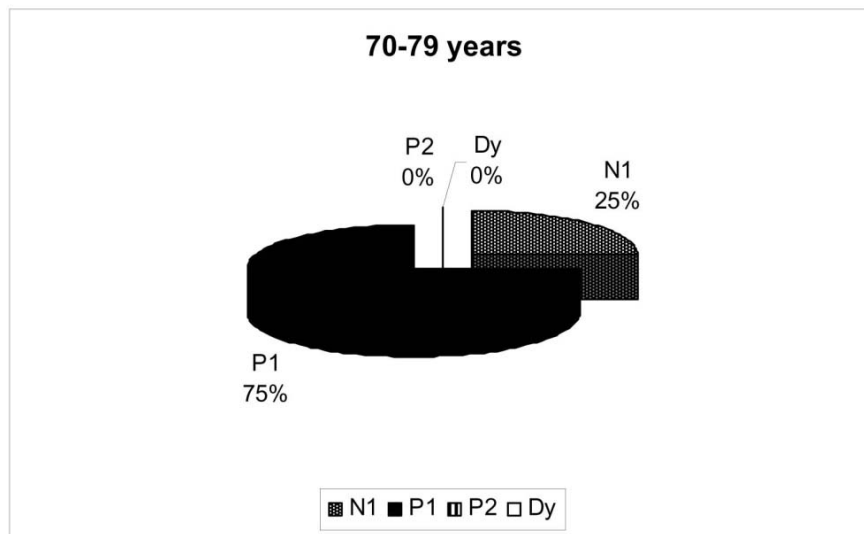


Figure 10. Breast parenchymal patterns (percentile) in women 70 - 79 years old with breast cancer.

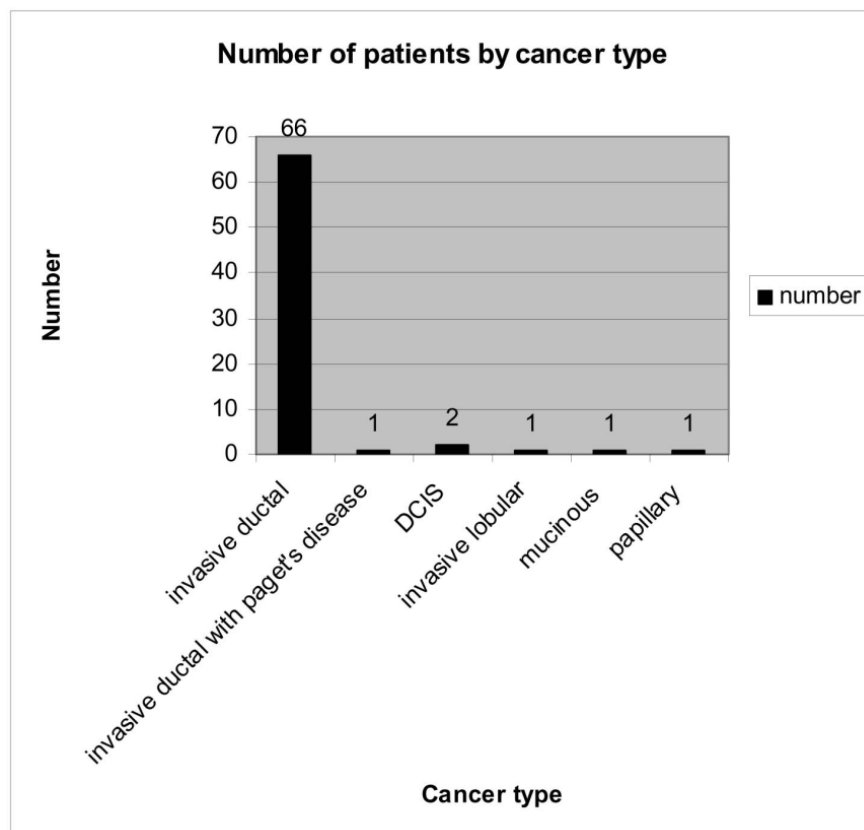


Figure 11. Cancer type (number) in 72 Thai women with breast cancer.

Discussion

The most prevalence breast parenchymal pattern in screening population in Thailand is the *P2* and *Dy* groups, whereas the results from the western countries are the *N1* and *P1* groups. The previously result in Thailand⁽⁹⁾ shows that the *P2* and *Dy* breast parenchymal patterns are the most prevalence patterns in younger age group similar to the western countries.

Reported by Wolfe identify higher rate of prevalent cancer in the *P2* and *Dy* breast parenchymal patterns.⁽⁷⁾ Wolfe found a relative risk of 31 for incident cancers in the *Dy* pattern compared with the *N1* pattern, and a relative risk of 6 for *P2* and *Dy* patterns compared with the *N1* and *P1* patterns.⁽⁴⁾

Moskowitz, et al. study shows no statistically significant short-term risk markers in dense breast parenchymal patterns.⁽¹⁰⁾

The combined data confirms that breast density, measured using either Wolfe grade or percentage density, is strongly associated with breast cancer risk, as determined by general population studies of either incident or prevalent cancer risk. In prevalence studies, Relative risks (RRs) are expected to be underestimated, as there is lower mammographic sensitivity and, hence, more false negative in dense breast rather than fatty breast.⁽⁶⁾

In this series, nearly 4 times as many tumors developed in *P2* and *Dy* as in *N1* and *P1* breasts parenchymal patterns. The *P2* and *Dy* breast parenchymal patterns are responsible for 80% of Thai women with breast cancer.

With increasing age, there is a reduction in the prevalence of *P2* and *Dy* breast parenchymal patterns in screening population, with corresponding

rise in *N1* and *P1*.⁽¹¹⁾ So, there are fewer *P2* and *Dy* breast parenchymal patterns in prevalence breast cancers in the older age groups. However, there is no significant difference in prevalence of *P2* and *Dy* breast parenchymal patterns in breast cancer patients between our study and Wolfe's study on 1976⁽⁷⁾ ($p>0.05$).

In this study, maximum peak is in age-group of 40-49 years and then followed by decline corresponding with maximum peak age at 45 years from National Cancer Institute of Thailand.⁽¹⁾

Due to problems in medical data collection in Thailand and time limitation, this study was designed to be a retrospective study and a relative risk cannot be calculated. Further prospective study in large population to identify risk of breast parenchymal patterns in Thai women with breast cancer will lead to more accurate results.

Conclusion

The *P2* and *Dy* breast parenchymal patterns are responsible for 80% of Thai women with breast cancer.

Mean age value of our study is about 50 years (range 32 - 75 years). About 71% of breast cancer patients are between age-groups of 40 - 59 years.

The *P2* and *Dy* breast parenchymal patterns are the majority in 3 age-groups; 30 -39 years, 40 - 49 years and 50 - 59 years. The Invasive ductal carcinoma is the most frequent breast cancer types (91.7%).

P2 and *Dy* are the most prevalent breast parenchymal patterns in Thailand. This study may lead to application that the women with high risk group should be watched and examined very carefully for development of breast cancer. Particularly in

women with *P2* and *Dy* breast parenchymal patterns, annual screening mammography should be strictly considered.

Changes should aim at improving screening sensitivity for dense parenchymal patterns and the diagnosis of high grade tumors.

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