Breast carcinomas: why are they missed?

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ABSTRACT

Introduction: Mammography has proven to be an effective modality for the detection of early breast carcinoma. However, 4-34 percent of breast cancers may be missed at mammography. Delayed diagnosis of breast carcinoma results in an unfavourable prognosis. The objective of this study was to determine the causes and characteristics of breast carcinomas missed by mammography at our institution, with the aim of reducing the rate of missed carcinoma.

Methods: We reviewed the reports of 13,191 mammograms performed over a five-year period. Breast Imaging Reporting and Data Systems (BI-RADS) were used for the mammographical assessment, and reports were cross-referenced with the histological diagnosis of breast carcinoma. Causes of missed carcinomas were classified.

Results: Of 344 patients who had breast carcinoma and had mammograms done prior to surgery, 18 (5.2 percent) failed to be diagnosed by mammography. Of these, five were caused by dense breast parenchyma obscuring the lesions, 11 were due to perception and interpretation errors, and one each from unusual lesion characteristics and poor positioning.

Conclusion: Several factors, including dense breast parenchyma obscuring a lesion, perception error, interpretation error, unusual lesion characteristics, and poor technique or positioning, are possible causes of missed breast cancers.

Keywords: breast cancer, mammography, missed diagnosis

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INTRODUCTION

Mammography is currently the most sensitive method for the detection of early breast carcinoma[1]. Screening mammography is used to detect clinically-occult breast carcinoma, while diagnostic mammography is performed for assessing symptomatic patients or to further evaluate an abnormality detected on screening mammography. Nevertheless, most studies have reported a sensitivity of cancer detection in the range of 68-92%[2]. Some occult cancers, even when palpable, may not be evident at mammography. Delayed diagnosis of breast carcinoma results in an unfavourable prognosis. The objective of this study was to determine the causes and characteristics of breast carcinomas missed by mammography at our institution, with the aim of reducing the rate of missed carcinoma.

METHODS

We retrospectively reviewed 13,191 reports of mammograms performed over a five-year period from January 1999 to December 2003. Two standard mammography views were performed using a dedicated film-screen unit (LoRad MIII, Damburg, CT, USA). Mammograms of each patient were interpreted immediately after imaging was completed by one of two breast radiologists. Additional mammographical views or ultrasonography (US) were performed on the same day. We used the Breast Imaging Reporting and Data Systems (BI-RADS)[3] for the mammographical assessment. Reports were cross-referenced with the histological diagnosis of breast carcinoma obtained from the records of the Department of Pathology. A false-negative mammogram was defined as one in which a patient had a pathological diagnosis of breast carcinoma within one year after a negative or benign mammographical result. A false-negative mammogram was also ascribed to cases when the

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lesion could be seen retrospectively more than a year later. We defined a true-positive mammogram as one in which the mammography was reported as BI-RADS 5 (highly suggestive of malignancy), and BI-RADS 4 (suspicious abnormality) and the patients were subsequently pathologically diagnosed to have breast cancer. The sensitivity (percentage of breast cancers that were identified with mammography) was calculated by [true-positive/(true-positive+false-negative)] ×100.

The mammograms of those with missed cancers were analysed by two breast radiologists who were aware that each patient had breast carcinoma but were blinded with respect to the location of the tumours. Causes of missed carcinomas were categorised into five types, namely: (1) Dense breast parenchyma obscuring a lesion; (2) Perception error; (3) Interpretation error; (4) Unusual lesion characteristics; and (5) Poor technique or positioning. The breast parenchymal density, features of the tumour, and location of the tumour were also recorded. We analysed the data with descriptive statistics. This study was approved by the Chiang Mai University Institutional Review Board.

RESULTS

805 patients with breast carcinoma were diagnosed from pathological reports. Of these, 362 had mammographical examinations before surgery but mammograms were available for review in only 344 patients. Of the 344 patients studied, 18 (5.2%) were considered to be missed diagnosis, according to the criteria listed in the preceding section. The mean age of the patients was 50.8 years (range 45-66 years). The overall sensitivity of mammography in identifying carcinoma was 94.7%. Five of 18 patients had diagnostic mammography and 13 had screening mammography. All five diagnostic patients presented with breast masses. Three of these five patients had multiple cysts with subtle area of architectural distortion in one, faint pleomorphic microcalcifications in one, and dense breast without mammographical abnormality in the other one. In the other two patients, one had a circumscribed mass and was misinterpreted as a complex cyst, one had synchronous breast carcinomas with lesion on one side which was missed due to poor positioning on the first examination.

The classification of breast parenchymal density in missed carcinomas was heterogeneously dense in 17 patients and homogeneously dense in one. Types of missed carcinomas are shown in Table I. Features of missed carcinomas are shown in Table II. Location of the tumours is shown in Table III. Of these 18 patients, one was invasive lobular carcinoma (ILC), four were ductal carcinoma in situ, and 13 were invasive ductal carcinoma. According to TNM tumour staging, four were stage 0, seven were stage I, and seven were stage II. Illustrative cases are shown in Figs. 1-6.

Table I. Reasons for missed carcinoma.

Reason for missed carcinoma	Number of cases
Dense breast parenchyma	5
Perception error	7
Interpretation error	4
Unusual lesion characteristics	1
Poor positioning	1
Total	**18**

Table II. Mammographical features of missed breast carcinoma.

Mammographical feature	Number of cases
Mass	4
Microcalcifications	2
Architectural distortion	5
Asymmetrical density	2
No lesion seen	5
Total	**18**

Table III. Locations of missed breast carcinoma.

Location	Number of cases
Lateral	6
Medial	1
Central	5
Retroglandular	2
Subareolar	4
Total	**18**

DISCUSSION

The proportion of cancers missed by mammography varies widely in the literature, ranging from 4% to 34%[4,6-9]. This wide range is due to the many different and variable ways it has been calculated and reported in the literature. Comparison among studies are difficult because the populations that are considered may vary, from screening of

asymptomatic patients to symptomatic patients referred for mammography. The quality of mammography and the experience of readers may also not be uniform. The failure to detect cancer on a mammogram may be caused by many factors, including dense breast parenchyma obscuring a lesion, subtle features of malignancy, perception error, interpretation error, unusual lesion characteristics such as slow-growing tumours, and poor technique or positioning[6-9].

Five of our missed breast carcinomas occurred in patients with dense breasts (Fig. 1). The abnormality was not visible, even in retrospect. In fact, missed carcinomas have been shown in multiple studies to occur more frequently in dense breasts[4-6]. Missed cancers were also reported to be less dense, relative to the immediate surrounding tissue[7]. Clinical breast examination and US are commonly used to complement mammography and more cancers are detected with these combinations[9-11]. Techniques of digital mammography, magnetic resonance imaging and nuclear medicine studies for breast cancer screening are being developed, and may have a future role in improving the detection of breast cancer in patients with dense fibroglandular tissue[9].

Although we usually perform additional US in patients with dense breasts, we still missed the diagnosis in the five patients. This may be explained by the size and type of the tumours. The smaller the tumour size, the more likely they are to be missed. Tumours were small in four screening patients that could be easily missed from both mammography and US. The other patient presented with palpable breast masses with negative mammography but US revealed multiple cysts. She was subsequently found to have ILC. ILC is known to be difficult to diagnose either by clinical examination or imaging due to the lack of a desmoplastic reaction[8]. The overall sensitivity of US in the detection of ILC was 68%[12].

Perception and interpretation errors are the most common causes of our missed carcinomas (11/18), similar to the studies by Bird et al[6] and Martin et al[13]. Perception and interpretation errors are caused by several factors, including deficient training, lack of experience, subtle features of malignancy, presence of an obvious finding, fatigue, inattention, haste, poor viewing conditions, and distractions. Subtle features of malignancy are difficult to perceive. These subtle features are small faint densities that are visible on only one of the two views (Fig. 2), faint microcalcifications, or minimal architectural distortion (Fig. 3). The presence of an obvious finding (Fig. 4) leading to overlooking of another more subtle lesion is one of the common causes of observation error[8,9]. Two of our patients who presented with breast masses were found to have multiple circumscribed masses on mammograms, leading to overlooking of the small area of

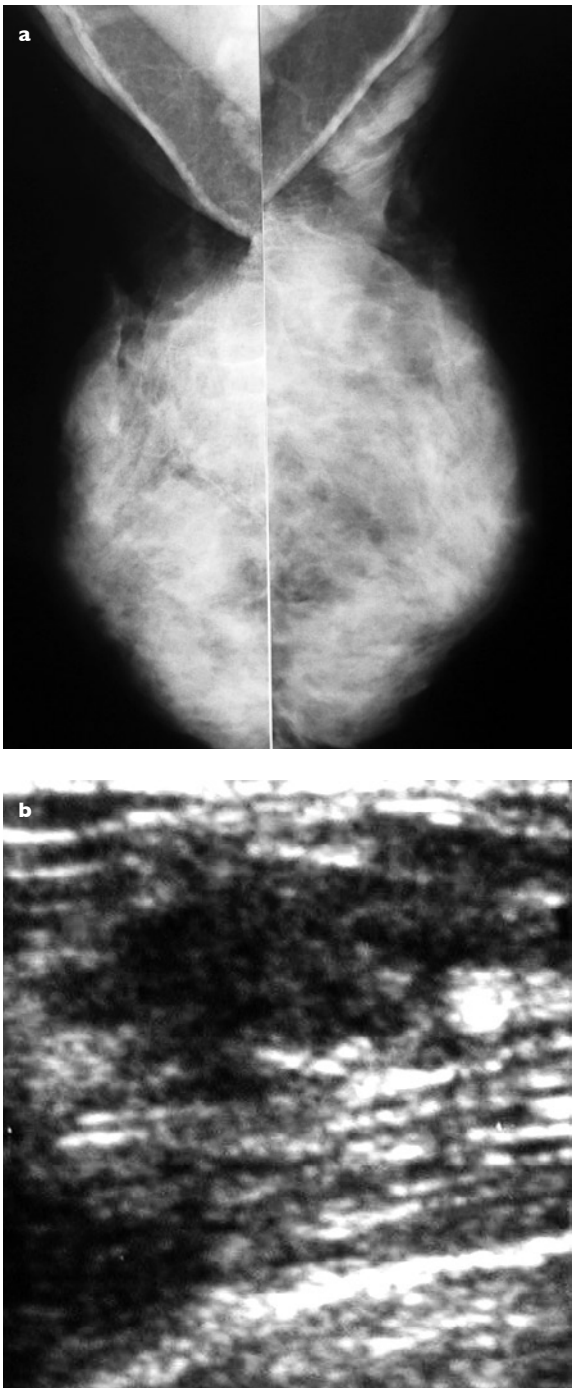


Fig. 1 Dense breast. (a) Screening bilateral mediolateral oblique mammograms of a 47-year-old woman show a dense breast without mass or microcalcifications. Two months later, she returned and complained of a palpable mass in the right upper outer quadrant (RUOQ); (b) US image of the RUOQ shows a 1.5 cm irregular hypoechoic mass. Excisional biopsy revealed intraductal carcinoma, cribriform type with microinvasion.

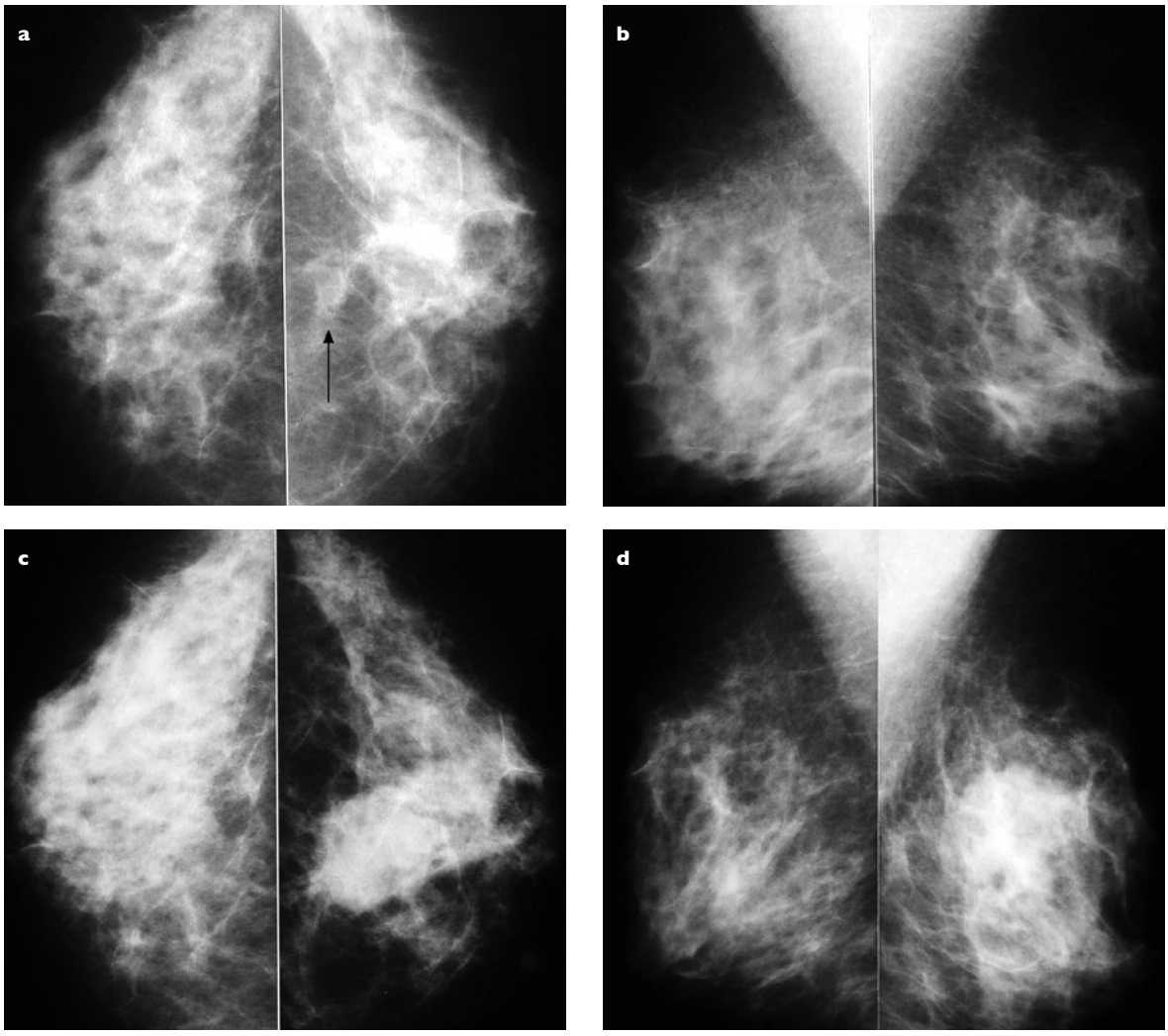


Fig. 2 Perception error: lesion seen on one view. Screening mammograms of a 45-year-old woman. (a) Bilateral craniocaudal (CC) views, and (b) bilateral mediolateral oblique (MLO) views, show dense breast and a faint focal increased density (arrow) in the left retromammary region seen on the CC view. Seven months later, she returned and complained of a palpable mass in the left breast. (c) Bilateral CC views, and (d) bilateral MLO views, show a 3-cm, ill-defined mass in the left retromammary region.

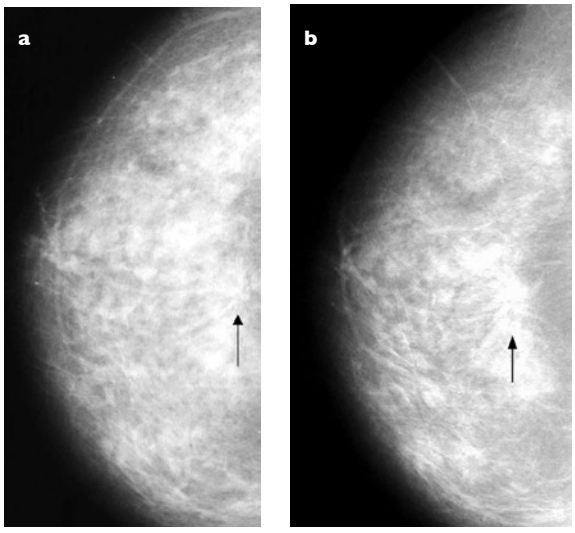
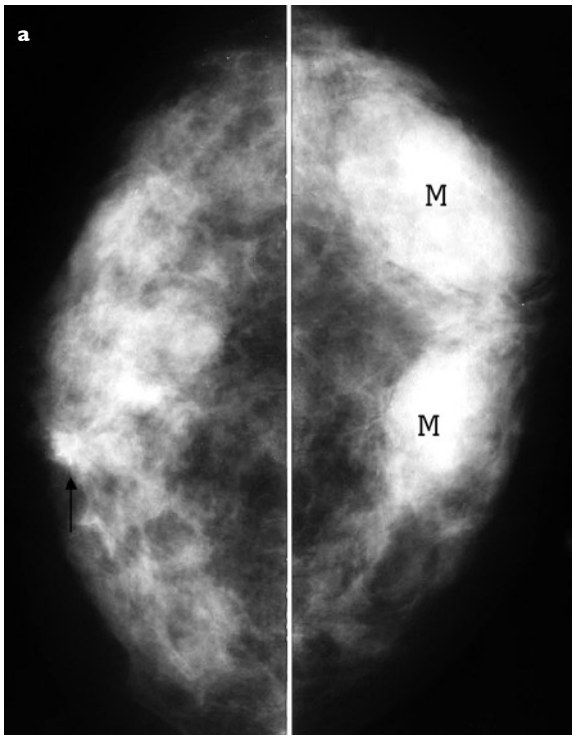


Fig. 3 Perception error: subtle architectural distortion. Screening mammograms of a 54-year-old woman who had history of left mastectomy for breast carcinoma three years ago. (a) Right CC view taken two years after left mastectomy shows a subtle architectural distortion (arrow); (b) Right CC view obtained one year after (a) clearly shows the lesion.

architectural distortion in one case and faint pleomorphic calcifications in another case.

Misinterpretation occurs when an abnormality is observed but is interpreted as being a benign or probably benign lesion. We had four misinterpretations. Of these, two had a benign-appearance mass (Fig. 5), one had faint pleomorphic microcalcifications, and the other one had an area of distortion seen on one view. They were interpreted as probably benign lesions and were suggested to have a follow-up study. Training and experience are essential for radiologists responsible for mammographical interpretation. To avoid perception and interpretation errors, radiologists who interpret mammograms should have special training in mammography. Right and left breast mammograms of each standard projection should be mounted back-to-back on view boxes. Careful attention to mirror image abnormalities or focal abnormalities is important, in order to identify



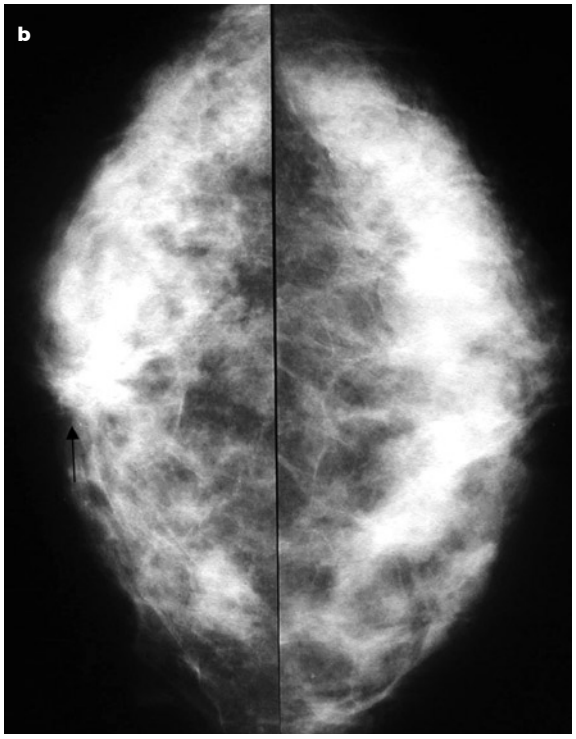


Fig. 4 Perception error, presence of obvious lesions. Bilateral CC views of the same breast in a 51-year-old woman who presented with left breast masses in (a) 1999 and (b) 2000, show benign-appearing masses in the left breast (M) that were found to be cysts on US. An area of architectural distortion in the right areola (arrows in a,b) was overlooked in 1999. Histology revealed invasive ductal carcinoma.

the subtle features of malignancy. Additional views may be needed to better verify the lesion. The margins of masses and characteristics of microcalcifications are best evaluated with spot-compression and magnification views.

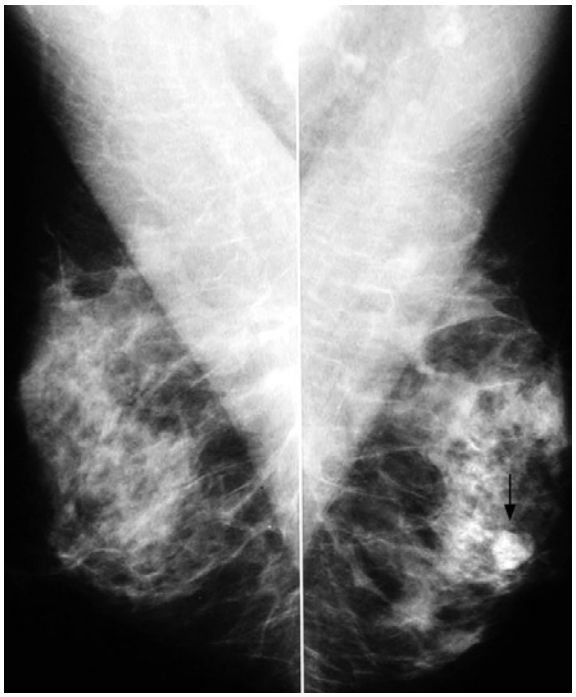


Fig. 5 Interpretation error, benign appearing mass. Bilateral MLO screening mammograms of a 44-year-old woman show a 1 cm well-circumscribed mass in the left subareola region. The lesion was interpreted as a cyst. Four months later, she returned and complained of a palpable lump in the left subareola. Excisional biopsy revealed intraductal carcinoma.

A circumscribed carcinoma should always be considered in peri- or postmenopausal women who present with a circumscribed solid mass, since fibroadenoma is not common in this age group.

Whenever feasible, the current mammographical examination should be compared with previous mammograms to look for a new or progressive increase in density. Optimal viewing conditions needed for reading mammograms include view boxes with adequate luminance, reduced extraneous light, and low ambient room light. Distractions, such as the telephone and checking of other non-mammographical examinations, should be minimised. Double reading has been shown to allow detection of an additional 5%-15% of cancers[14,15]. Nevertheless, there is a lack of manpower in many places and the cost of increased manpower is also a problem. Computer-aided detection and diagnosis (CAD) represent a relatively new technology that may emerge in some mammography facilities for double reading. The CAD systems increase the sensitivity of breast cancer detection by radiologists by up to 20%[16,17].

Unusual lesion characteristics, such as a lesion that is located in the deep retroglandular region, benign appearance, lack of desmoplastic reaction,

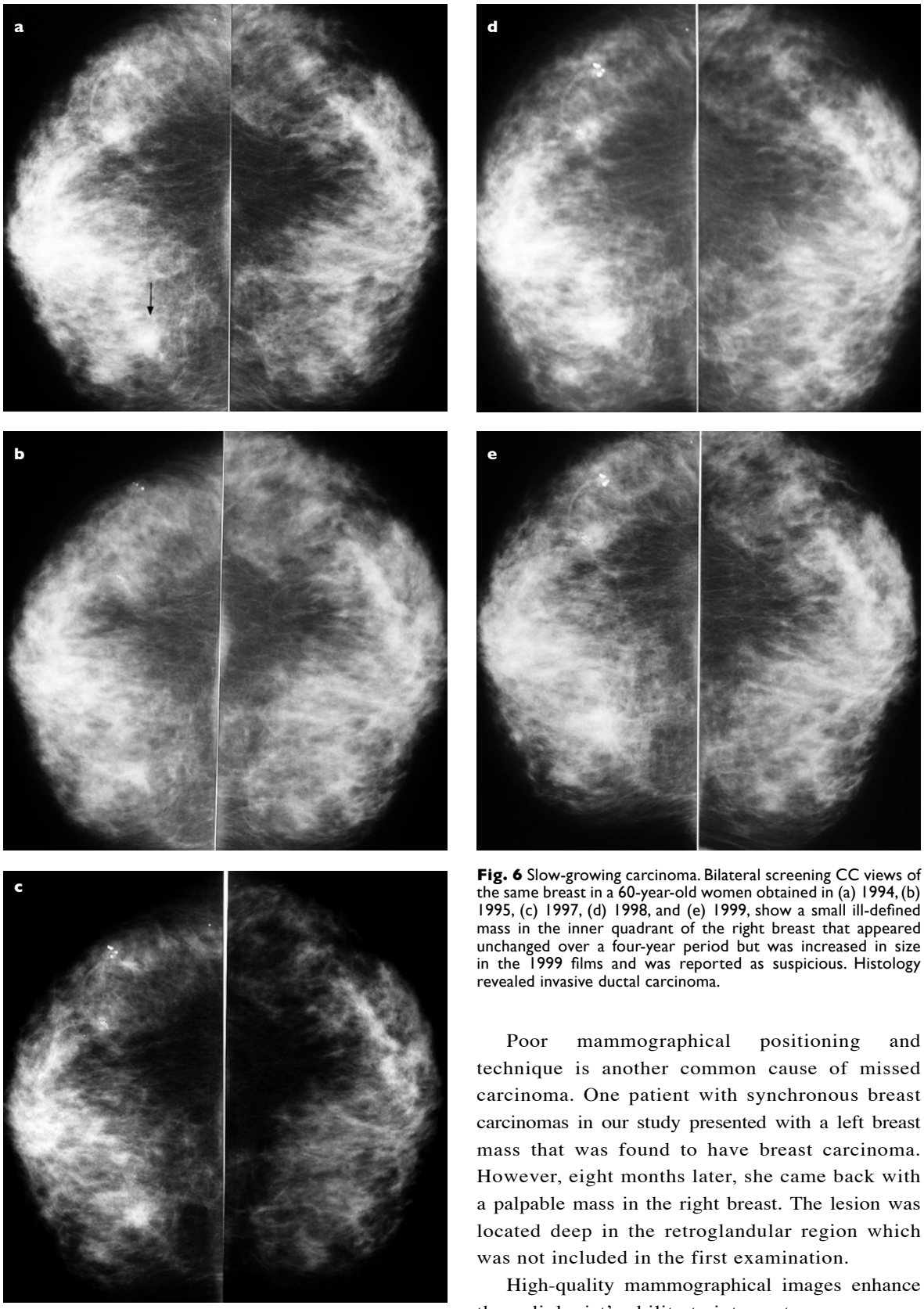


Fig. 6 Slow-growing carcinoma. Bilateral screening CC views of the same breast in a 60-year-old women obtained in (a) 1994, (b) 1995, (c) 1997, (d) 1998, and (e) 1999, show a small ill-defined mass in the inner quadrant of the right breast that appeared unchanged over a four-year period but was increased in size in the 1999 films and was reported as suspicious. Histology revealed invasive ductal carcinoma.

and slow or no growth, may be overlooked or missed during interpretation. In our study, one patient had a lesion that was unchanged over a four-year period (Fig. 6).

Poor mammographical positioning and technique is another common cause of missed carcinoma. One patient with synchronous breast carcinomas in our study presented with a left breast mass that was found to have breast carcinoma. However, eight months later, she came back with a palpable mass in the right breast. The lesion was located deep in the retroglandular region which was not included in the first examination.

High-quality mammographical images enhance the radiologist's ability to interpret mammograms with high sensitivity and specificity. Imaging should be free from artifacts, and performed with adequate exposure, high contrast, high resolution, proper compression, and inclusion of the maximum amount of breast tissue[8,9,18].

A well-positioned mediolateral oblique view is indicated by visualisation of the pectoralis muscle to the level of the nipple, a convex appearance of the pectoralis muscle, visualisation of the retroglandular fat, breast tissue that is well-compressed and positioned in an up-and-out orientation, and an open inframammary fold. Findings on the craniocaudal view that indicate proper positioning include visualisation of the retroglandular fat, a nipple that is profiled, inclusion of all the medial fibroglandular tissues, and the lateral fibroglandular tissue of the breast extends beyond the edge of the film. The difference between the posterior nipple line measurement on the mediolateral oblique and craniocaudal views should not exceed 1 cm[19]. In conclusion, recognition of these various factors is instructive and will help to decrease missed carcinomas in the future.

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