Incidental breast lesions detected on CT: what is their significance?

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ABSTRACT. An increasing number of breast lesions are being detected incidentally on CT. The aim of this study was to investigate the rate of referrals to the breast unit for assessment of lesions identified on CT and the resulting yield of previously undiagnosed breast malignancies from this pathway. A retrospective review was undertaken of CT examinations conducted over a period of 14 years. All patients (with no previous history of breast cancer) whose report contained the keyword “breast” and who were referred to a specialist breast unit for assessment were reviewed. CT lesion morphology and enhancement pattern were identified and compared with the final diagnostic outcome. 70 patients were identified by retrospective analysis, yielding 78 incidental breast lesions, of which 22 (28.2%) were malignant (category B5). This gave a positive predictive value (PPV) for malignancy of 28.2%. The best morphological predictor of malignancy was spiculation (PPV, 76%) and irregularity (PPV, 58%), whereas calcification patterns (PPV, 36%) were diagnostically unhelpful. Malignant lesions were likely to be larger (mean, 28.5 mm) than benign lesions (mean, 20.2 mm; $p < 0.05$). In conclusion, 30% of incidental breast lesions in this large series of patients proved to be unsuspected breast cancers, particularly irregular spiculated masses. Referral for formal triple assessment of CT-diagnosed breast lesions is worthwhile, and careful examination of the breast should be a routine part of CT examinations.

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Over the past 10 years, there has been an exponential rise in the use of CT imaging in all diagnostic areas [1]. Multidetector, single and dual source CT can give unprecedented spatial and temporal resolution [2, 3], identifying previously unseen structures and pathology and improving diagnostic accuracy. Greater utilisation and resolution of CT also results in an increased detection of “incidental” findings unrelated to the original diagnostic query, raising issues of further investigation, diagnosis and follow-up with consequent economic and emotional cost. It has long been known that CT can identify incidental breast lesions when imaging for cardiac or respiratory disease [4]. Previous review articles have described the appearances of incidental breast lesions found on CT [5–7], but there has been no formal quantitative assessment of the impact of incidental CT-diagnosed breast lesions. With implementation of the Department of Health Cancer Reform Strategies, including the age extension to the NHS Breast Screening Programme (NHSBSP) [8] and cancer pathway targets [9], the workload of breast assessment units is rising. The impact of referral of incidental breast lesions found on CT is therefore an important issue to consider, with respect to the accurate and timely diagnosis of breast malignancy.

The aim of this study was to investigate the rate of referrals to the breast unit for assessment of lesions

identified on CT and the resulting yield of previously undiagnosed breast malignancies from this pathway.

Methods and materials

All reports of thoracic and abdominal CT examinations from 19 March 1994 to 18 March 2008 containing the key word “breast” were reviewed. The radiological report information was derived from the Hospital Information System Software (Northgate Information Solutions, Hemel Hempstead, UK) and the Computed Radiology Information System (Healthcare Software Systems, Nottinghamshire, UK). All patients with a previous history of breast cancer or benign or malignant breast surgery were excluded from the study. For all remaining patients, the radiology reports and any information held on the breast unit clinical database (the Joint Clinical Information System (JCIS)) were reviewed to ascertain details of referral to the breast unit and further investigation. All imaging (mammograms and ultrasound), needle core biopsy (CB) or surgery performed was carried out according to NHSBSP guidelines [10].

The CT examination that initially identified the breast lesion (mass, asymmetry or calcification) was reviewed by two radiologists (P.M., R.S.) who were blinded to the final outcome of the breast assessment. Lesion morphology and contrast enhancement patterns were recorded. In the absence of a formal CT lexicon for breast imaging, consensus analysis of morphology and enhancement was

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Table 1. Morphology and enhancement pattern descriptors used to describe the 78 CT-detected lesions. Adapted from the Bi-RADS[®] mammography and MRI lexicons 2003 [4,5]

Asymmetry	Focal or global
Mass shape	Oval, round, irregular or lobulated
Mass margin	Circumscribed, indistinct, microlobulated or spiculated
Calcification	Rim, coarse, fine, grouped, scattered, associated with a mass or not associated with a mass
Enhancement	Rim, homogeneous, heterogeneous, non-enhancing internal septations, enhancing internal septations or no enhancement
Skin thickening	Present, not present
Abnormal lymph nodes	Present, not present

Bi-RADS, Breast Imaging and Reporting Data System.

made by adapting the Breast Imaging and Reporting Data System (Bi-RADS[®]) terminology for mammography and MRI lexicon 2003 (Table 1) [5, 11, 12]. Axillary lymph nodes, if included in the examination field, were reviewed and deemed abnormal if their longest-shortest axis ratio was <2 , or their cortex was irregular or eccentric [13]. During the 14 year study period, CT examinations were performed on a variety of machines, with slice thicknesses of 2–5 mm, a variety of contrast timings and for a wide range of clinical indications. In chronological order, the machines used were: Siemens Somatom plus single slice spiral, Siemens Somatom single slice spiral plus 4, Siemens Somatom 4 slice multidetector CT (MDCT), Siemens Somatom Sensation 16-slice MDCT and Siemens Somatom sensation 64-slice MDCT (all Siemens Medical Solutions, Erlangen, Germany). The contrast medium used for each procedure was 100 ml of Niopam 300 (61.2% w/v iopamidol equivalent to 300 mg iodine ml^{-1} ; Bracco, Milan, Italy) administered via a pump injector. The arterial phase was performed at 3–4 ml s^{-1} , with imaging triggered after a bolus of contrast medium had reached the pulmonary artery. In the portal venous phase, contrast was given at 2–4 ml s^{-1} with a standard 70 s delay. Unlike dedicated CT mammography studies [14, 15], these examinations were not optimised for breast pathology, and therefore variation in contrast medium administration was anticipated. The positive predictive value (PPV) for malignancy was calculated for all breast lesions and for each of the individual morphological descriptive terms: enhancement pattern, nodal status and lesion size. This study formed part of a retrospective audit, registered and approved by the hospital audit department and, according to our institution policy, not requiring the approval of the local research ethics committee.

Results

Demographics and study cohort

A total of 105 372 thoracic and/or abdominal CT examinations were performed between 19 March 1994 and 18 March 2008. 5679 radiological reports containing the keyword “breast” in any context were found.

91 patients (89 females and two males) with no history of breast disease were reported to have one or more breast lesions on CT. Of those 91, eight CT studies could not be reviewed owing to corrupt data. Of these eight patients, four had been referred for subsequent breast assessment with either normal or benign outcome (two

had normal mammograms, one had benign cysts and one had fibrocystic change) and were discharged. One patient was referred to another institution where a diagnosis of breast cancer was confirmed. The remaining three patients were not referred to the breast unit and the Regional Cancer Registry has no record of their having developed breast cancer. 13 patients with breast lesions were excluded from referral because they were either too unwell with concomitant illness ($n=10$) or corroboration with recent breast imaging satisfactorily explained the CT lesion as benign ($n=3$). The remaining 70 patients (68 female and two male) had a subsequent formal breast assessment and constitute the cohort of patients examined in this study. 63 patients had a solitary lesion, six patients had two lesions and one patient had three breast lesions. A total of 78 incidental breast lesions were therefore analysed for this study over a 14 year period.

Overall referral rates

The incidence of breast lesions referred to the breast unit has increased with time; the highest incidence was 18 patients in 2006. The 2007 figure dropped slightly to 15 patients referred, but in the first 3 months of 2008, after which the study closed, 15 such patients had been referred to the breast unit (Figure 1). Figure 1 shows the referral rate to the breast unit via incidental CT findings over time.

Assessment findings

70 patients were referred for formal breast assessment. 35 patients with 43 lesions were deemed either “normal” or to have benign appearances (Bi-RADS[®] category 2) following clinical examination and mammography and/or ultrasound, and were therefore discharged.

The remaining 35 patients underwent ultrasound-guided CB of 35 lesions. 22 (63%) yielded breast carcinoma (category B5), most commonly invasive ductal carcinoma. One patient was diagnosed as having a granular cell tumour (category B3, a rare neoplasm that follows a relatively benign clinical course. 11 patients (31%) had biopsy-proven benign disease (category B2) and 1 revealed normal breast tissue (category B1); all were discharged (see Table 2). Therefore, of 78 breast lesions, 22 were malignant and 56 were normal or benign, giving a PPV for malignancy of 28.2%. Patients with malignancy were significantly more likely to be older (average age, 73 years; range, 43–94 years) than those with benign disease (average age, 62 years; range, 27–87 years; $p<0.05$).

Table 2. Core biopsy pathology of the 35 CT-detected lesions

Core biopsy category 3					
B1 (Normal)	B2 (Benign)	B3 (Suspicious, probably benign)	B4 (Suspicious, probably malignant)	B5 (Malignant)	Total
1 (3%) Concordance with imaging	11 (31%) Fibroadenomas (6) PASH (1) Haemangioma (1) Fibrofatty/fibrocystic change (3)	1 (3%) Granular cell tumour (1)	0	22 (63%) IDC (12) ILC (4) Mixed IDC/ILC (1) Mucinous (3) NHL (1)	35

IDC, invasive ductal carcinoma; ILC, invasive lobular carcinoma; NHL, non-Hodgkin's lymphoma; PASH, pseudoangiomatous stromal hyperplasia. % = percentage of lesions

Lesion characteristics

Table 3 shows the PPV values for malignancy in relation to the shape and margin description. The descriptor "spiculated" has the highest PPV of 76% (see Figure 2), followed by "irregular" with a PPV of 58%. The converse is true of descriptive terms associated with benignity: an oval shape has a PPV for malignancy of 0% (see Figure 3) and a circumscribed margin has a PPV of 4%.

CT measurement of lesion size revealed that malignant lesions were likely to be larger (average, 28.5 mm; range, 10–72 mm) than benign lesions (average, 20.2 mm; range, 5–48 mm; $p < 0.05$).

11 (14%) of the 78 CT studies contained calcification, of which 4 were malignant (PPV for malignancy = 36%). Half of the malignant calcifications (2/4) were associated with a mass lesion (Figure 4). Of the calcifications associated with malignancy, three were punctate and one was coarse in nature. Overall, five of the six coarse calcifications were benign, and both the lesions with rim calcification were benign. Only one patient with focal asymmetry proved to have a malignant lesion; the rest were benign (Figure 5). Two patients had skin thickening on CT, but neither was caused by malignancy.

Contrast enhancement

66 lesions were analysed following administration of intravenous contrast medium according to the enhancement pattern in relation to the phase of study acquisition (Table 4). Six CT studies were unenhanced. Six CT studies had only calcification with no additional mass to measure enhancement; therefore, these were not included. The highest PPV for malignancy was given by a heterogeneous enhancement pattern, in both the arterial (PPV = 76%) and venous (PPV = 56%) phases. There was no rim enhancement of a lesion in the arterial phase (0/2 patients), but this occurred in 2/2 patients in the portal venous phase.

Axilla

The axilla was within the CT field of view in 53 of the 70 patients reviewed. 9 (17%) of 53 patients had abnormal ipsilateral axillary lymph nodes, with a longest–shortest

axis diameter ratio of <2 or an irregular or eccentric cortex [6]. Eight of these patients were subsequently found to have malignant lesions within the breast; however, only five patients had pathologically proven axillary lymph node metastases (see Figure 6), and, in three, the nodes were reactive or normal.

Discussion

Malignancy rate

In 70 patients with a total of 78 lesions referred for triple assessment in a specialist breast unit, 28.2% of lesions proved to be unsuspected breast carcinoma. Meller et al [7] reported on incidental breast lesions found on CT over a period of one year and found 12 breast masses in 1208 body CTs of women over the age of 21 years. All had formal breast assessment and 6 (50%) were found to have breast cancer. From this incidence, they extrapolated a rate of five breast cancers per 1000 CT examinations in adult women. In our study, our cancer detection rate would be 2.8 per 1000 persons, much lower than the above rate. This may be caused by perception bias, with malignant lesions not being identified owing to the spatial and temporal resolution of the older CT scanners, or the breasts not being reviewed at the time of reporting and lesions not being perceived. The NHSBSP reported an incidence of 8.1 breast cancers per 1000 women screened in 2004–2005 [16]. We would not expect our CT breast cancer rate to be as high as this because, currently, CT does not have the resolution to image malignant microcalcifications, and therefore excludes breast cancers which are detected by calcification alone; CT is, therefore, not a suitable screening examination, even in dense breasts [5].

Pathology of CT-detected breast cancers

The pathology of the lesions in our series identified a higher percentage of invasive lobular carcinoma (18%) than the general incidence rate of 5–10% of all breast cancer [17]. Lobular carcinoma can be difficult to diagnose, both clinically and on mammography, because it can spread diffusely through the breast and may present only as subtle distortion. In our series, one lobular cancer was identified as a focal asymmetry and

Figure 1. Graph showing the number of patients referred to a specialist breast unit for further assessment of 78 incidental breast lesions detected on CT over the 14 year study period.

the remainder as masses. 13% of cancers in our series were of mucinous type, again higher than the general incidence rate of 1–4% [18]. This type of cancer is slower growing, has a generally good prognosis, is often well defined and, clinically, can feel benign. Invasive ductal carcinoma remains the most common pathological type: 54% in our series compared with the 70–80% general incidence rate [17]. No *in situ* cancers were detected, which most likely reflects the lack of CT resolution for fine microcalcification, as discussed above.

Morphology analysis

Morphology analysis of lesions shows that the Bi-RADS® features with the highest PPV for malignancy were spiculated margins (PPV, 76%) and irregular shape (PPV, 58%). These findings are in keeping with the current literature. Liberman et al [19] reported a mammographic PPV for malignancy of 81% for spiculated margins and 73% for irregular shape. Inoue et al [15] used dynamic dedicated breast CT to look at diagnostic features of malignancy, with a PPV of 100% for spiculated margins and a PPV of 99% for irregular shape. Stavros et al [20] described the use of sonographic morphology to distinguish between benign and malignant lesions. Spiculated lesions on ultrasound had a PPV for malignancy of 91.8%. Thus, across all modalities,

including non-dedicated CT, features of spiculated margins and irregular shape are suspicious for malignancy. In contrast, we have shown low PPV values for malignancy for the descriptive terms classically associated with benignity, such as oval shape (PPV = 0%) and circumscribed margin (PPV = 4.0%). These are, again, similar to the work of Liberman et al [19] on mammography, who reported PPVs for oval and circumscribed lesions of 8% and 9%, respectively [12]. Stavros et al [20] demonstrated that ultrasound lesions with an ellipsoid shape had a PPV of 28.6%, with a sensitivity of 97.6% and specificity of 51.2%. Overall, our data are in keeping with the literature in concluding that oval lesions are more likely to be benign. Other terms such as “round”, “lobulated” and “indistinct” have more indeterminate PPVs, as these features can commonly be seen in both benign and malignant breast disease.

Calcification analysis

Breast calcifications on CT have shown a low PPV for malignancy, with most calcifications in our series being associated with benign changes. Nearly all calcification seen on CT is benign because of the limited spatial resolution. Small (0.5 mm) calcifications, which have a higher probability of malignancy, are rarely identified, and therefore calcification identified by size criteria alone is most likely benign [5]. In work by Lindfors et al [21], even dedicated cone beam CT of the breast is significantly worse at detecting microcalcification than film–screen mammography.

Enhancement pattern

Most work on enhancement patterns in breast lesions has been performed with dynamic enhanced MRI using gadopentetate dimeglumine. Dedicated breast CT also uses dynamic acquisitions, imaging pre and post iodinated contrast medium [8, 7]. It is well known that malignant breast tumours have rapid contrast medium uptake and washout (type 3 curve) owing to tumour angiogenesis of a chaotic nature and with arteriovenous shunts [22]. Extrapolating these results to our data is problematic: (i) the timing of intravenous iodine administration was

Table 3. The PPV values for malignancy in relation to the description of the shape and margin of the 68 mass lesions detected by CT

Description	Malignant	Benign	PPV for malignancy (%)
Shape			
Oval	0	26	0
Round	4	9	31
Irregular	14	10	58
Lobulated	2	3	40
Margin			
Circumscribed	1	25	4
Indistinct	3	8	27
Microlobulated	3	11	21
Spiculated	13	4	76

PPV, positive predictive value.

Figure 2. (a) A 56-year-old female patient was referred for CT as part of her investigation for haemoptysis. A post-intravenous contrast-enhanced CT scan demonstrates an incidental finding of a spiculated right breast mass, morphologically highly suspicious for malignancy (arrow). Subsequent assessment and core biopsy confirmed an invasive ductal cancer. (b) T_1 weighted post-intravenous gadolinium breast MRI of the same patient illustrates the corresponding irregular spiculated mass (arrow).

variable, with imaging performed either 25 s or 70 s after injection; (ii) there was only one reference time-point; and (iii) the number of lesions with different enhancement patterns was too small for statistical analysis. One difference from all other studies published to date was our finding that heterogeneous enhancement had a high PPV for malignancy of 67% and homogeneous enhancement had a PPV for malignancy of 11%, which is the opposite to studies with MRI and dedicated CT. Inoue et al [15], using dedicated breast CT, showed homogeneous enhancement with a PPV of 93% and heterogeneous enhancement with a PPV for malignancy of 63%. Liberman et al [23] with the use of MRI showed homogeneous enhancement with a PPV for malignancy of 36% and heterogeneous enhancement with a PPV for malignancy of

22%. Our results may be due to early image acquisition, and it is possible that the lesions we studied would have become more homogeneous in their enhancement over time. Overall, in our experience, enhancement characteristics of a lesion were not helpful in predicting malignancy.

Axillary lymph node analysis

Axillary lymph node status is one of the most important prognostic indicators in breast cancer. Evaluation of axillary nodes before sentinel lymph node biopsy may be performed by ultrasound [24]. CT can detect local and distant lymph nodes, but it has been well documented that the sensitivity and negative predictive

Figure 3. (a) A 27-year-old female patient was referred for CT as part of a staging examination for newly diagnosed metastatic teratoma. A post-intravenous contrast-enhanced CT scan demonstrates an incidental finding of an oval well-defined circumscribed breast mass (arrow). (b) Biopsy confirmed this circumscribed breast mass as a fibroadenoma.

Table 4. Comparison of the types of intravenous enhancement of lesions on CT with final histology

Phase of intravenous contrast	Pattern of enhancement	Final histology		PPV for malignancy (%)
		Malignant	Benign	
Arterial (41 lesions)	Homogeneous	3	20	13
	Heterogeneous	11	4	73
	Rim enhancing	0	2	0
	Non-enhancing internal septations	0	1	0
Venous (25 lesions)	Homogeneous	1	12	8
	Heterogeneous	5	4	56
	Rim enhancing	2	0	100
	Non-enhancing internal septations	0	1	0
Combining both phases (66 lesions)	Homogeneous	4	32	11
	Heterogeneous	16	8	67
	Rim enhancing	2	2	50
	Non-enhancing internal septations	0	2	0

PPV, positive predictive value.

value of CT-detected nodes in malignancy are low [25]. This is reflected in our results, with only five of the eight morphologically abnormal nodes having proven metastases.

Age analysis

The strongest risk factor for breast cancer after gender is increasing age. Four out of every five new cases are diagnosed in women aged 50 years and over, with cases peaking in the 55–69 year age group [26]. Therefore, it is not surprising that in our series the average age of the patients with malignant lesions was higher than for those with benign lesions. There was a statistical difference in the sizes of benign and malignant tumours, with the larger lesions more likely to be malignant. When assessing incidental lesions, the perception of larger lesions is easier, especially in relation to the resolution of

distinguishing overlying normal breast tissue and pathology.

This is the largest published series of incidental breast lesions found on CT. The main limitations are a potential perception bias, with malignant breast lesions either missed or unreported. However, this study was designed to address the workload and yield resulting from the referral of reported lesions, and their pathway through the breast unit. In addition, descriptive analysis of small numbers within lesion subsets may be less reliable.

Referral rates

Our figures confirm the perceived rise in breast unit workload as a result of referrals from CT, with increased reporting of incidental breast lesions on CT from 2003 onwards, rising to 18 referrals in 2006 and 15 referrals in

(a)

(b)

Figure 4. (a) An 87-year-old female patient presented with acute shortness of breath and was referred for CT as part of her investigations for suspected pulmonary embolus. A lobulated mass containing coarse calcification was demonstrated in her left breast (arrow). (b) This scan demonstrates the sonographic findings of the same lesion at subsequent assessment, and a core biopsy confirmed a mucinous carcinoma.

Figure 5. A 63-year-old female patient was referred for a CT as part of her staging investigation for uterine cancer. A post-intravenous contrast-enhanced CT scan demonstrates an incidental finding of multiple oval and round masses in the left breast causing asymmetry (arrows). Subsequent assessment and core biopsy confirmed benign fibrocystic change.

the first three months of 2008. This is most likely to be caused by a combination of new multidetector CT machines installed in June 2002 and November 2004. This not only gave increased resolution and hence perception of breast lesions, but doubled the body CT workload in our institution (from 9374 body CTs in 2004 to 18 405 body CTs in 2008 (internal audit data)). The rise in body CT workload will predictably result in increased demand for breast unit assessment of such lesions.

Conclusions

In conclusion, the breast is an important review area on CT, and a dramatic rise in the use of CT imaging has led to the increased detection of incidental breast lesions. Referral for formal triple assessment is worthwhile, as nearly 30% of incidental breast lesions in this large series of patients proved to be unsuspected breast cancers, particularly irregular spiculated masses.

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Figure 6. A 49-year-old female was referred for CT as part of her staging investigation for fallopian tube cancer. A post-intravenous contrast-enhanced CT scan demonstrates an incidental finding of a large right breast mass with some speculations and coarse calcification (arrow). There are two ipsilateral axillary lymph nodes. Subsequent assessment and core biopsy confirmed intraductal carcinoma with positive lymph nodes (arrow).

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