Image features of true positive and false negative cancers in screening mammograms

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Introduction

Breast screening with mammography is not a flawless test. The incidence of interval cancers for the early years of the UK screening programme were higher than expected in some regions. Reviews of the screening mammograms suggest that a considerable proportion of these interval cancers could have been detected at screening. Since the prognoses of interval cancers are likely to be worse than screen detected cancers it is important to minimise the number of false negative screens. As a step towards this the location, tissue background and imaging characteristics of true positive and false negative screens of breast cancers was studied.

Method

Study groups

- Screening mammograms for two groups of women were selected - women with true positive screen detected cancers (TPSC) and women with interval cancers following a false negative screen (FNIC).
- Matched normals were selected for both the screening mammograms of the TPSC and the FNIC.
- Incident screening mammograms were assessed, with only medio-lateral oblique views available.
- TPSC were cancers positively identified following the assessment of a screening mammogram and confirmed by pathology. The women had at least one previous screen where they were judged to be true negative.
- FNIC were cancers diagnosed in the period between the last screen and the next scheduled screen, following an earlier negative or benign assessment of a mammogram.
- Matched normals were women whose mammograms showed no signs of cancer at the time of the scheduled screen. Normals also had a subsequent screen in which they were judged to be true negatives.

Imaging systems

- Systems used are included in Table 1 below.
- A tube potential of 28 kV was used for the majority of the mammograms. 30 kV was selected for a small number of women with "large" breasts.
- A Mo/Mo target/filter combination was used together with the bucky grid.
- A target optical density (OD) of 1.6 for a 4 cm thickness of PMMA was used and the correct operation of the AEC was checked regularly.

	Centre 1	Centre 2
Number of women	160	200
Film type	Sterling Microvision C	Fuji UM-MA (HC)
Screen type	Sterling Microvision Detail	Fuji UM fine
X-ray system used	GE 600 TS Senix or Siemens Mammomat 2	Siemens Mammomat 3000 or 2
Processing Cycle	Sterling T6 + Sterling chemicals extended (34 °C)	Fuji FPM 3000 + Photosol chemicals extended (34 °C)

Table 1: Imaging systems.

Case selection

- Cases were selected between 1992 and 1998.
- Selection process was randomised.
- All the FNIC between the study dates were used from one of the centres. The cases from the second larger centre were evenly selected from the cases occurring between the specified dates.
- TPSC were also evenly selected from the cases occurring between the study dates.
- Matched normals were independently selected for the TPSC and FNIC. The matched normal was the next woman with a true negative mammogram that was screened on the same day as the woman in the cancer group.
- Normals were chosen to ensure that target film density, imaging system, location and the process of mammogram review were all as closely matched as possible.
- A total of 360 case files were assessed.

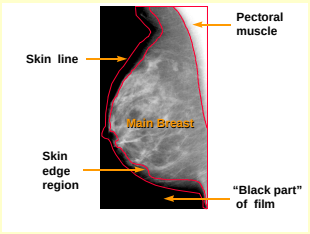

Figure 1: Mammogram image ROIs.

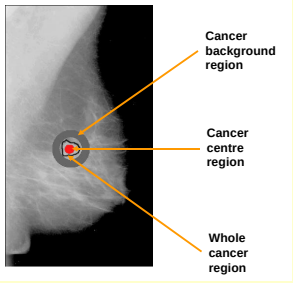

Figure 2: Cancer ROIs.

Digitisation and radiological review

- Mammograms were digitised using a Lumisys Lumiscan 150 HR laser scanner with a pixel size of 210 µm.
- The digitised mammograms were calibrated from image pixel values to optical density units.
- Two expert film readers viewed the mammograms.
- Screening mammograms were used to grade the breast composition as either fatty, mixed density or dense.
- Cancer locations and outlines on the screening mammograms were recorded on transparent overlays for each of the TPSC and FNIC.

Image analysis

- The three regions of interest (ROI) shown in Figure 1 were created for each mammogram.
- Three additional ROI were manually drawn for each cancer, as shown for one cancer location in Figure 2.
- All ROI were subject to image analysis, including measuring the area, maximum, minimum, and mean OD.
- To compare the cancer positions on the mammograms, all the cancer centres were marked on a "typical breast" image (an average sized right breast image selected from the study).
  - Each mammogram was warped to more closely match the typical breast.
  - The dimensions of each mammogram image were first linearly scaled to those of the typical breast image.
  - An affine warping technique was then used to map each breast outline to that of the typical breast.
  - Cancer centre locations on the modified mammogram images were recorded and plotted on the typical breast image.
  - Visual checks were made to ensure that the cancer centre was consistent with the original mammogram.

Results

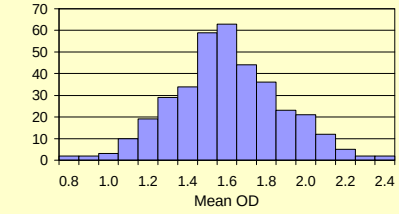

Figure 3: Histogram of mean OD in the main breast ROI.

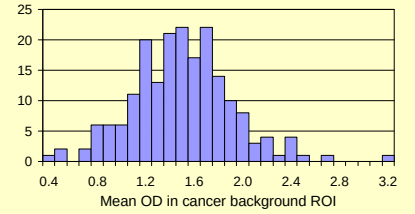

Figure 4: Histogram of mean OD in the cancer background ROI.

- Figure 3 shows the distribution of the mean OD in the main breast ROI of all the mammograms, with an overall mean ± SD of 1.60 ± 0.28.
- Mean OD data is subdivided by cancer group and breast type in Table 2 and for the normal groups in Table 3. The mean ODs for dense breasts in the cancer groups are equivalent and lower than for other breast types.
- The percentage of dense breasts in which FNIC were discovered is greater than in the TPSC. (χ^2 test generated a p value of 0.147.)
- For both normal groups the mean OD increases as tissue type changes from dense, to mixed density, to fatty.
- Table 2 also contains data on the local cancer contrast, where local cancer contrast = (mean OD in the whole cancer ROI) – (mean OD in the cancer background ROI). For both cancer groups the local cancer contrasts were significantly lower in dense breasts, than in mixed density or fatty breasts.
- In 88.8% of the mammograms the mean OD in the whole cancer ROI was less than in the main breast region.
- Figure 4 shows the distribution of the mean OD in the cancer background ROI for all the mammograms.
- For the two cancer groups (Tables 4 and 5) there are comparable total numbers of spiculate masses, but more poorly defined masses in the FNIC group than in the TPSC group (χ^2 test p value of 0.109, for all mass types).
- The local cancer contrasts for FNIC poorly defined masses are of the order of 0.1 OD lower than for TPSC.

Breast Type	FNIC Number	FNIC %	FNIC Mean OD in the main breast ROI	FNIC Local cancer contrast	TPSC Number	TPSC %	TPSC Mean OD in the main breast ROI	TPSC Local cancer contrast
Dense	22	23.9	1.42 ± 0.06	0.13 ± 0.02	14	15.4	1.35 ± 0.07	0.15 ± 0.03
Mixed	47	51.1	1.62 ± 0.04	0.29 ± 0.02	52	57.1	1.56 ± 0.03	0.30 ± 0.03
Fatty	23	25.0	1.64 ± 0.07	0.28 ± 0.03	25	27.5	1.81 ± 0.05	0.36 ± 0.04

Table 2: Mean OD data for FNIC and TPSC.

Breast Type	FNIC normals Number	FNIC normals %	FNIC normals Mean OD in the main breast ROI	TPSC normals Number	TPSC normals %	TPSC normals Mean OD in the main breast ROI
Dense	19	20.7	1.40 ± 0.05	17	18.7	1.47 ± 0.10
Mixed	51	55.4	1.64 ± 0.03	66	72.5	1.63 ± 0.03
Fatty	22	23.9	1.71 ± 0.05	8	8.8	1.75 ± 0.07

Table 3: Mean OD data for FNIC and TPSC normals.

Tables 4 & 5: Cancer OD data for FNIC (top right) and TPSC (bottom right).

FNIC Mass type	Total	Mean OD in cancer centre	Mean OD in whole cancer	Local cancer contrast
spiculate	39	1.09 ± 0.06	1.16 ± 0.06	0.30 ± 0.03
poorly defined	30	1.29 ± 0.08	1.34 ± 0.08	0.23 ± 0.02

TPSC Mass type	Total	Mean OD in cancer centre	Mean OD in whole cancer	Local cancer contrast
spiculate	42	1.09 ± 0.05	1.22 ± 0.04	0.35 ± 0.03
poorly defined	19	1.14 ± 0.09	1.23 ± 0.09	0.34 ± 0.04

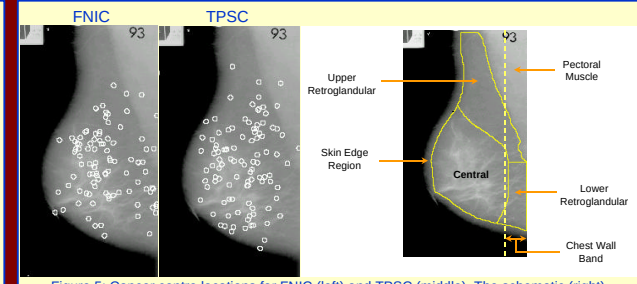

Figure 5: Cancer centre locations for FNIC (left) and TPSC (middle). The schematic (right) shows the ROIs used to assess the distribution of cancer locations.

Region Of Interest (ROI)	FNIC Frequency	FNIC %	TPSC Frequency	TPSC %
Pectoral muscle	4	4	3	3
Upper retroglandular	18	19	28	27
Lower retroglandular	10	10	0	0
Central	61	63	65	63
Skin Edge	4	4	7	7
Total	97	100	103	100
Chest wall band	21	22	10	10

Table 6: Cancer centre locations.

- Cancer centre locations for the FNIC (left) and the TPSC (middle) are shown in Figure 5 together with a schematic of the ROIs used to assess the distribution of cancer centres.
- Table 6 shows the main difference is in the lower retroglandular region of the images. 10 % of the FNIC occur in this region while no TPSC were found here (overall group difference had a p value of 0.011, χ^2 test).

Discussion

- Mean OD in the main breast ROI of the mammograms varied widely.
- Mean OD in the cancer background ROIs also varied over a wide range of optical densities, with the majority of cancers being located against mean background ODs between 1.1 and 2.0.
- FNIC were more common in dense breasts than TPSC.
- In both cancer groups the local cancer contrast was approximately a factor of two lower in the dense breasts than in other types of breast.
- A poorly defined mass is at increased risk of being a FNIC. Local cancer contrast of FNIC poorly defined masses were about 0.1 OD lower than for TPSC.
- There are similar numbers of cancer centres in the central and pectoral muscle ROIs. The greatest difference was in lower retroglandular ROI. Results suggest that there is an imbalance in cancer detection in mammograms and that more attention should be given close to the chest wall edge of the film, and particularly the lower retroglandular region, during routine screening.