Infrared Imaging of the Breast:
Initial Reappraisal Using High-Resolution Digital
Technology in 100 Succesive Cases of Stage I and II Breast Cancer

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Abstract: There is a general consensus that earlier detection of breast cancer should result in improved survival. Current breast imaging relies primarily on mammography. Despite better equipment and regulation, variability in interpretation and tisuue density still affect acuragy. A number of adjuvant imaging techniques are currently being used, including doppler ultrasound and gadolinium-enhanced MRI, which can detect cancer-induced neovascularity. In order to assess the potential contribution of currently available high-resolution digital infrared technology capable of recognizing minute regional vascular flow related temperature variation, we retrospectively reviewed the relative ability of our preoperative clinical exam, mammography, and infrared imaging to detect 100 new cases of ductal carcinoma in situ, stage I and II breast cancer. While the false-negative rate of infrared imaging was 17%, at least one abnormal infrared sign was detected in the remaining 83 cases, including 10 of the 15 patients, a slightly younger cohort, who had nonspecific mammograms. The 85% sensitivity rate of mamography alone thus increased to 95% when combining both imaging modalities. Access to infrared information was also pertinent when confronted with the relatively frequent contributory but equivocal clinical exam (34%) and mammography (19%). The average size of those tumors undetected by mammography or infrared mamography was 1.66 cm and 1.28 cm, respectively, while the false-positive rate of infrared imaging in concurrent series of 100 successive benign open breast biopsies was 19%. Our initial experience would suggest that, when done concomitantly with clinical exam and mammography, high-resolution digital infrared imaging can provide additional safe, practical, and objective information. Further evaluation, preferably in controlled prospective multicenter trials, would provide valuable data.

Key words: breast, cancer, detection, imaging, infrared

Our first-line strategy for the detection of breast cancer still-depends essentially on clinical examination and mammography. Limitation of the former, with its reported sensitivity rate below 65% is well recognized (1), and even the proposed value of breast self-examination is now being contested (2). With the current emphasis on earlier detection, there is an increasing reliance on better imaging. Mamography is still recognized as our most reliable and cost-effective imaging modality (3). However, variable interpretation (4) and tissue density, now proposed as a risk factor in itself (5) and seen in both younger patients and those on hormone replacement (6), prompted us to reassess currently available infrared technology, spearheaded by recent military research and development, as a potential complementary imaging strategy. This modality is capable of of quantitating minute temperature variations and and qualifying abnormal vascular patterns, potentially reflecting the regional angiogenesis, neovascularization, and nitric oxide-induced regional vasodilation (7) frequently associated with tumor initiation and progression and

possibly early predictors of tumor growth rate (8,9). We thus acquired in July 1995 a new fully integrated infrared imaging station to compliment our mammography unit. To evaluate its reported ability to detect early tumor-induced metabolic changes (10), we limited our initial reappraisal to ductal carcinoma in situ (DCIS), stage I and II breast cancer patients.

PATIENTS AND METHODS

The charts of our first 128 patients who had their initial diagnosis of breast cancer as of August 1995 were reviewed to accumulate 100 successive cases who filled the following criteria: minimal evaluation included a clinical exam, mamography, and infrared imaging; definitive surgical management constituted the preliminary therapeutic modality and was carried out at one of our affiliated institutions, and the final staging consisted of either DCIS (n = 4), stage I (n = 42), or stage II (n = 54) invasive breast cancer. While 94% of these patients were referred to our Comprehensive Breast Center for the first time, 65% from family physicians and 29% from specialists, the remaining 6% had their diagnosis of breast cancer at a follow-up visit. Age at diagnosis ranged from 31 to 84 years with a mean of 53 years. The mean histologic tumor size was 2.5cm. Lymphatic, vascular, or neural invasion was noted in 28% and concomitant DCIS was present, along with the invasive component, in 64%. One third of the 89 patients who had axillary lymph node dissection had involved nodes and 38% of the tumors were histologic grade III. While most of these patients underwent standard four-view mammorgraphy, with additional views when indicated, at our accredited center using a GE DMR appartus, in 17 cases we relied on recent and adequate quality outside films. Mammograms were interpreted by our examining physician and radiologist, both having access to the clinical findings and, like the clinical exam, were considered suspicious if either noted findings indicative of carcinoma. The remainder were considered either contributory but equivocal or nonspecific. A nonspecific mammography required concordance with our examining physician, radiologist and the authors.

Our integrated infrared station consisted of a scanning mirror optical system containing a mercury-cadmium-telleride detector (Bales Scientific, CA) with a spatial resolution of 600 optical lines, a central processing unit providing multitasking capabilities, and a high-resolution color monitor capable of displaying 1024 X 768 resolution points and up to 110 colors or shades of gray per image. Infrared imaging took place in a draft-free, thermally controlled room, maintained at between 18°C and 20°C , after a 5 minute equilibration period during which the patient sat disrobed with her hands locked over her head. We requested that the patients refrain from alcohol, coffee, smoking, exercise, deoderant, and lotions 3 hours prior to testing. Four images, consisting of an anterior, an undersurface, and two lateral views, were generated simultaneously on the video screen by the examining physician, who would digitally adjust them to minimize noise and enhance detection of more subtle abnormalities prior to exact on-screen computerized temperature reading and infrared grading. Images were then stored on retrievable laser discs. Our grading scale relies on pertinent clinical information, comparing infrared images of both breasts and current with previous images (unavailable during this first series). An abnormal infrared image required the presence of atleast one abnormal sign (Table 1).

TABLE 1. Ville Marie Infrared (IR) Grading Scale
Abnormal signs
1. Significant vascular assymetry.* 2. Vascular anarchy consisting of unusual tortuous or serpignious vessels that form clusters, loops, abnormal arborization, or aberrant patterns. 3. A 1°C focal increase in temperature (change in T) when

compared to the contralateral site and when associated with the area of clinical abnormality.
4. A 2°C focal change in T versus the contralateral site.*
5. A 3°C focal change in T versus the rest of the ipsilateral breast when not present on the contralateral site.*
6. Global breast change in T of 1.5°C versus the contralateral breast.*

Infrared Scale

IR1 = Absence of any vascular pattern to mild vascular symmetry.
IR2 = Significant but symmetrical vascular pattern to moderate vascular asymmtry, particularly if stable.
IR3 = One abnormal sign.
IR4 = Two abnormal signs.
IR5 = Three abnormal signs.

* Unless stable on serial imaging or due to known non-cancer causes (e.g., abcess or recent benign surgery).

To assess the false-positive rate of infrared imaging, we reviewed, using similar criteria, our last 100 consecutive patients who underwent an open breast biopsy that produced a benign histology. We used our Carefile Data Analysis Programme to evaluate the detection rate of variable combinations of clinical exam, mammography, and infrared imaging.

RESULTS

Sixty-one percent of this series presented with a suspicious palpable abnormality, while the remainder had either an equivocal (34%) or a nonspecific clinical exam (5%). Similarly, mammography was considered suspicious for cancer in 66%, while 19% were contributory but equivocal and 15% were considered nonspecific. Infrared imaging revealed minor variations (IR-1 or IR-2) in 17% of our patients, while the remaining 83% had at least one (34%), two (37%), or three (12%) abnormal infrared signs. Of the 39 patients with either a nonpspecific or equivocal clinical exam, 31 had at least one abnormal infrared sign, with this modality providing a more pertinent indication of a potential abnormlity in 14 percent of these patients who, in addition, had either an equivocal or nonspecific mammography. Among teh 15 cancer patients with a nonspecific mammography, 10 (mean age of 48; 5 years younger than the full sample) had an abnormal infrared image, which consistuted a particularly important indicator in 6 of these patients who also had only equivocal clinical findings (Table 2).
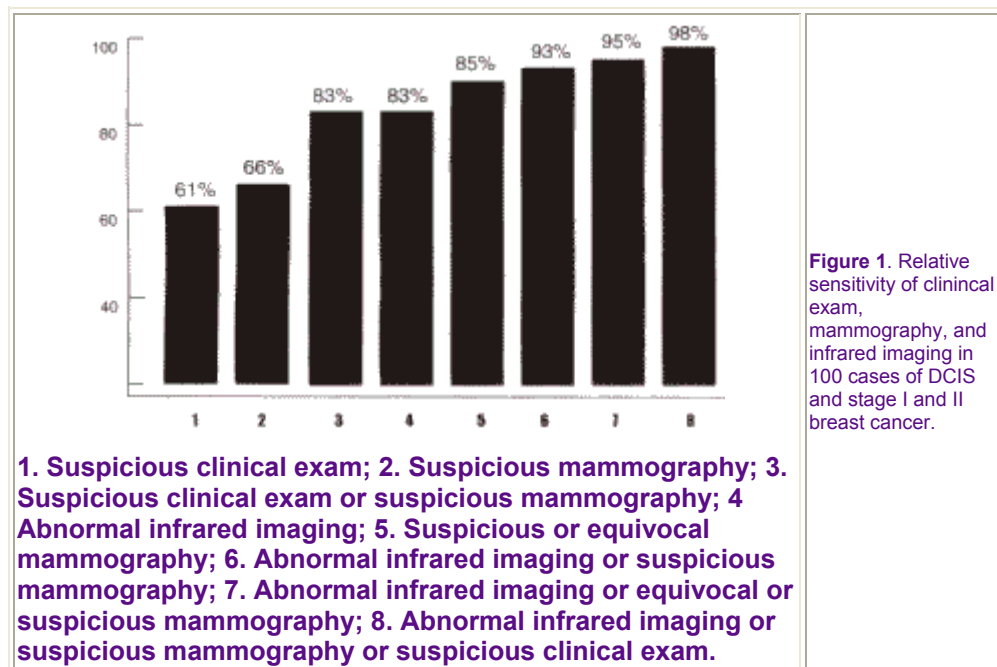
TABLE 2. Description of 15 Cases Who Had Nonspecific Mammograms

Age	Clinical exam	Infrared grade	Mammography	Histological size of	Grade

				tumor (cm)	
65	+ -	4	-	2	2
50	+ -	3	-	1.2	3
32	+	4	-	3	1
45	+ -	--	-	2.5	1
42	+ -	3	-	2	3
43	+	3	-	2.9	2
66	+ -	--	-	0.7	1
53	+	--	-	1	1
38	+ -	3	-	2.8	2
53	+	--	-	0.8	3
45	+	3	-	1.4	3
66	+ -	3	-	1.5	1
48	+	--	-	DCIS	--
46	+	3	-	1.7	3
53	+ -	4	-	0.7	2

+ = suspicious; + - = equivocal; - - = nonspecific.

While 61% of our series presented with a suspicious clinical exam, the additional information provided by the 66 suspicious mammograms resulted in an 83% detection rate. The combination of the same suspicious mammograms and abnormal infrared imaging increased the sensitivity to 93%, with a further increase to 98% when suspicious clinical exams were also considered (Fig.1).

Figure 1. Relative sensitivity of clinincal exam, mammography, and infrared imaging in 100 cases of DCIS and stage I and II breast cancer.

1. Suspicious clinical exam; 2. Suspicious mammography; 3. Suspicious clinical exam or suspicious mammography; 4 Abnormal infrared imaging; 5. Suspicious or equivocal mammography; 6. Abnormal infrared imaging or suspicious mammography; 7. Abnormal infrared imaging or equivocal or suspicious mammography; 8. Abnormal infrared imaging or suspicious mammography or suspicious clinical exam.

Of the four patients with DCIS, three had abnormal mamography consisting of either mocrocalcifications or asymmetrical density and three had an associated clinical finding, including the one with a nonspecific mammography. Comedo-type DCIS was noted in both cases with abnormal infrared imaging and noncomedo type was found in the remaining two.

The mean histologically measured tumor size for those cases with a nonspecific mammography was 1.66 cm, while those undetected by infrared imaging was 1.28 cm. In our concurrent series of 100 consecutive eligible patients who had an open biopsy that produced benign histology, 19% had an abnormal infrared image, while 30% of these same cases had an abnormal preoperative mammography that was the only indication for surgery in 16 cases.

DISCUSSION

The 83% sensitivity of infrared imaging in this series is higher than the 70% rate for similar stage I and II patients reported from the Royal Marsden Hospital two decades earlier (11). Although our results might reflect an increased index of suspicion associated with a reffered population, this factor should apply equally to both clinical exam and mammography, maintaining the validity of our evaluation. Additional factors could include our standard protocol, our physicians' prior experience with infrared imaging, their involvement in both image production and interpretation, as well as their access to much improved image acquisition and precision (Figs. 2 and 3).
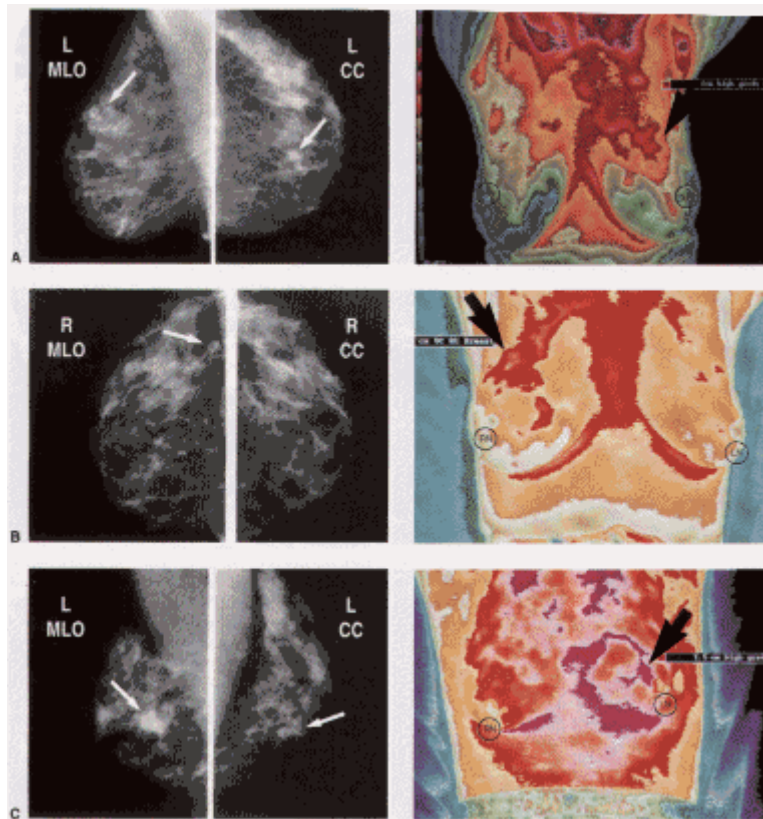

Figure 2. Ipsilateral preoperative mediolateral oblique (MLO) and craniocaudad (CC) mammograms (Mammo) and anterior view infrared (IR) images showing corresponding abnormalities. (A) Age: 41. Clinical: 2 cm area of firm breast tissue in upper central area of left breast. Mammo: corresponding cluster of microcalcifications and increased focal tissue density (arrows). IR: significant proximal upper

central regional vascular asymetry (arrow) (IR-3). FNAC: malignant cells. Histology: 1 cm grade 3 IDCA; 1 of 11 positive ALN. (B) Age:45. Clinical: bilateral nodularities. Mammo: discreet opacity seen on right MLO view (arrow). IR: significant upper central vascularity asymetry and focal 1.5°C increase in T (arrow) (IR-4). Ultrasound guided excision. Histology: upper central .7 cm grade 2 IDCA; DCIS; 13 negative ALN. (C) Age:34. Clinical: 2 cm lump medial to left areola. Mammo: corresponding opacity (arrows). IR:significant corresponding vascular asymetry and focal 2°C increase in T (arrow) (IR-5). FNAC: malignant cells. Histology: 1.5 cm grade 3 IDCA: 20 negative ALN.

C = centigrade; delta T = increase in T; FNAC = fine needle aspiration cytology; IDCA = infiltrating ductal carcinoma; DCIS = ductal carcinoma-in-situ; ALN = axillary lymph node(s); RN = right nipple; LN = left nipple (on IR images); see table 1 for IR grading.
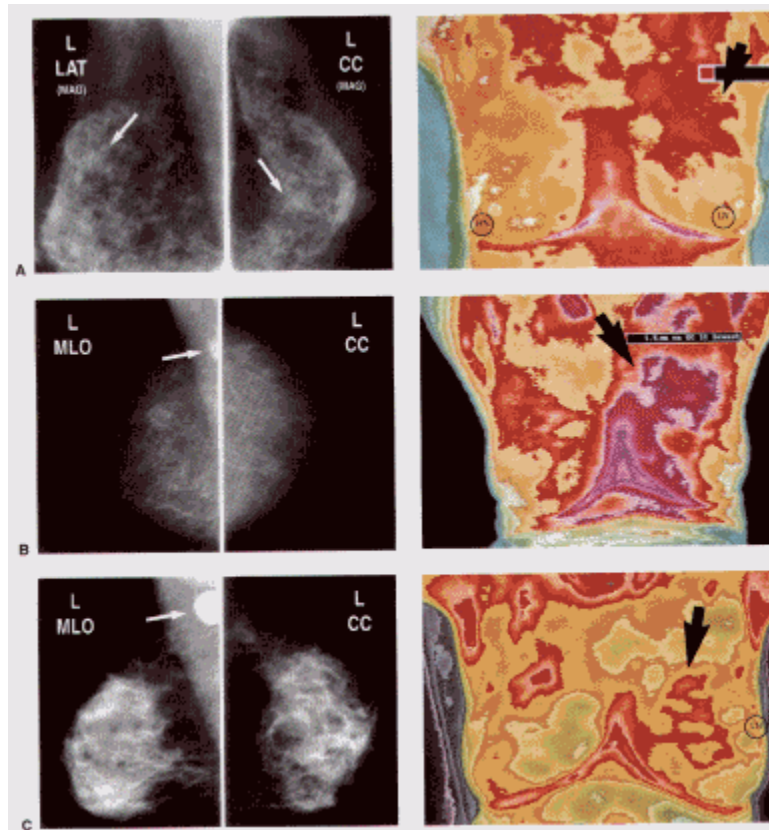

Figure 3. Ipsilateral preoperative lateral (L), mediolateral oblique (MLO) and craniocaudad (CC) mammograms (Mammo) and anterior view infrared (IR) images showing corresponding abnormalities. (A) Age: 56. Clinical: nodular process in upper central area of left breast. Mammo (magnification views): recent increase in previously stable cluster of microcalcifications (arrow). IR: corresponding significant vascular asymmetry and 1.5° increase in T (arrow) (IR-4). FNAC: malignant cells. Histology: 2.1 cm grade 2 IDCA; DCIS; 2 of 20 positive ALN. (B) Age: 61. Clinical: 2 cm lump high in midportion of left breast. Mammo: opacity visible on MLO view only (arrow), previously reported as an ALN. (C) Age: 42. Clinical suspicious left axillary lymph node with bilateral firm breast tissue, particularly in left subareolar area. Mammo: heterogenously dense breast tissue with suspicious ALN (arrow). IR: significant medial vascular asymmetry and anarchy (arrow) (IR-4). FNAC: malignant cells. Histology: 1.8 cm sub areolar grade 3 IDCA; DCIS; 4 of 12 positive ALN.

C = centigrade; delta T = increase in T; FNAC = fine needle aspiration cytology; IDCA = infiltrating ductal carcinoma; DCIS = ductal carcinoma-in-situ; ALN = axillary lymph node(s); RN = right nipple; LN = left nipple (on IR images); see table 1 for IR grading.

While most previous infrared cameras had eight-bit (one part in 256) resolution. Current cameras are capable of one part in 4,096, providing enough dynamic range to capture all images with a 0.05°C discrimination without the need for range switching. With the advancement of video display and enhanced gray and colors, multiple high-resolution views can be compared simultaneously on the same monitor. Faster computers now allow image processing functions such as image subtraction and digital filtering techniques for image enhancement. New algorithms provide soft tissue imaging by characterizing dynamic heat flow patterns. These and other innovations have made vast improvments in the medical infrared technology available today.

The detection rate in a series where half the tumors were under 2 cm would suggest that tumor-induced thermal patterns detected by currently available infrared technology are more dependent on early vascular and metabolic changes, possibly induced by regional nitric oxide diffusion and ferritin interaction, than strictly on tumor size (7). This agrees with the concept that angiogenesis mat precede and morphological changes (8).

Although both initial clinical exam and mammography are crucial in signaling the need for further investigation, equivocal and nonspecific findings can still result in a cimbined delayed detection rate of 10% (3). When eliminating the dubious contribution of our 34 equivocal clinical exams and 19 equivocal mamograms, often disconcerting to both the physician and patient, the alternative information provided by infrared imaging increased the index of concern of the remaining suspicious mammograms by 27% and the combination of suspicious clinical exams or suspicious mammograms by 15% (Fig.1). An imaging-only strategy, consisting of both suspicious and equivocal mammography and abnormal infrared imaging also detected 95% of these tumors, without the input of the clinical exam. Infrared's most tangible contribution in this series was in two-thirds of those patients, a slightly younger cohort, with nonspecific mammograms but with abnormal infrared findings.

While 17% of these tumors were undetected by infrared imaging, either due to insufficient production or detection of metabolic or vascular changes, the 19% false-positive rate in histologocally proven benign conditions, in part a reflection of our current grading system, suggests sufficient specificity for this modality to be used in an adjuvant setting.

Our initial reappraisal would also suggest that infrared imaging, based more on process than structural changes and requiring neither contact, compression, radiation nor venous access, can provide pertinent and practical complimentary information to both clinical exam and mammography, our current primary basic detection modalities. Multicenter controlled prospective trials consisting of sequential introduction of mammography, using the American College of Radiology Breast Imaging Reporting and Data System (12), and currently available infrared imaging would further define the validity and reproducibility of our current infrared protocol and better assess this modality's potential, along with other currently available technoligies, to promote the earlier detection of breast cancer.

CONCLUSION

In our limited series, quality controlled abnormal infrared imaging heightened our index of suspicion in cases where clinical or mammographic findings were equivocal or nonspecific and signaled the need for further investigation rather than observation. While additional refinement of our protocol using more dynamic features and improved computerized image evaluation should enhance its objective potential, we currently limit the role of infrared imaging to that of a closely controlled compliment to clinical exam and high quailty mammography. Our initial data should not

be extrapolated to either formal screening or noncontrolled diagnostic environments without appropriate evaluation, preferably in prospective controlled multicenter trials.

Acknowledgments

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