

Accuracy of Screening Methods for the Diagnosis of Breast Disease

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Summary: Clinical examination, thermography, and 70-mm. mammography were performed in 891 patients—414 presented to hospital with symptoms of breast disease and 477 were asymptomatic. Comparison of the diagnostic accuracy of these methods showed that neither thermography nor 70-mm. mammography has a useful place as an isolated screening procedure for breast cancer. In fact, we consider such a policy dangerous.

Introduction

Recently there has been increasing interest in the development of mass screening techniques for the early diagnosis of carcinoma of the breast. The most significant study from New York has been designed to compare the mortality from breast cancer in women in whom regular annual screening has been carried out by clinical examination and mammography with the mortality of those who are receiving normal medical care (Strax *et al.*, 1967, 1968, 1969; Venet *et al.*, 1969). Though the final evaluation of this study must await assessment of mortality, it is already apparent that those cases of breast cancer which have been discovered in the screened group have a lower incidence of lymphatic involvement than those arising in the control population. It is also clear that *both* methods of examination are required for satisfactory screening and that clinical examination or mammography *alone* detected only about half of the total number of cancers discovered.

Mammography, as ordinarily performed, uses large film and the radiographic image is the same size as the patient's breast. It is time-consuming and expensive. Alternative simpler diagnostic methods which might be suitable for screening are therefore being studied. Two such methods, thermography and 70-mm. mammography (Strax and Oppenheim, 1968; Gravelle, 1969), are the subject of this report, in which their diagnostic value has been compared with that of routine clinical examination in 891 patients with or without symptomatic breast disease.

Methods

Of the 891 patients included in the diagnostic survey, 414 (aged 16-78 years) had come to hospital with symptoms of breast disease and 477 (aged 18-78 years) had no such symptoms and were attending hospital for some unrelated reason, usually gynaecological. The survey included clinical examination, thermography, and 70-mm. mammography.

Each patient was briefly interviewed for relevant history. The breasts were then clinically examined by one observer (either I.G.F. or H.J.S.). Thermography was then performed by technicians using an AGA Thermovision apparatus. After the removal of clothes above the waist, the patient sat with hands

on hips in the thermography room for 15 minutes. This was to allow cooling of the breasts and axillae to the temperature of the room, which was maintained between 18 and 21°C. The hands were raised above the head and the breasts were scanned individually with the infrared camera. Frontal and oblique views of both breasts were taken and the thermographic image obtained on the oscilloscope screen was recorded on 35-mm. panchromatic film. Then 70-mm. mammography was carried out on an Odelca photofluorographic unit. This unit produces a 70-mm. photograph of the fluorographic image of the breast. Two standard views (craniocaudal and mediolateral) were taken of both breasts. As the fine-focus x-ray tube and an Odelca camera unit were mounted on a motorized stand, the position of the tube could be rapidly changed while the patient remained stationary in the erect position. In this way complete radiographic examination of both breasts could be carried out in five minutes. It took about 40 minutes to survey each patient by all three methods.

The results of each form of investigation were separately and independently reported. For thermography and 70-mm. mammography independent reports were received from three radiologists, each of whom examined the thermography and mammography films separately without knowledge of the patient or her complaints. As all films were processed in batches there was no opportunity for repeat examination should the films be unsatisfactory.

The patients with symptomatic disease had also been examined by a consultant surgeon. Further, all patients with symptomatic breast disease and most of those in the control series had full-size mammography, an examination which forms part of our routine assessment of patients with breast complaints.

The value of clinical examination, thermography, and 70-mm. mammography was compared by the percentage of correct diagnosis in each group of subjects.

Results

Symptomatic patients

Of the 414 women in this group 214 had histologically proved benign or malignant breast disease. A further eight women with advanced cancer did not have histological confirmation of their disease, but as the diagnosis was not in doubt they have been included with the malignant group. Seventy-seven patients had cancer and 145 had proved benign disease. The remaining 192 patients in the symptomatic group had not had a biopsy performed and were considered by the clinician responsible for their care to have either benign diffuse disease not requiring biopsy (152 patients) or normal breasts (40 patients). This assumption was made on the findings of clinical and mammographic examinations and on the results of follow-up for not less than 12 months.

The diagnostic accuracies of clinical examination as recorded by one observer and of thermography and 70-mm. mammography as recorded by three observers in the confirmed cases are shown in Table I. Thermography and 70-mm. mammography are obviously relatively inaccurate compared with clinical examination in both benign and malignant conditions. There was considerable observer error between

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the three radiologists. This has been further defined in Table II, in which the accuracy of diagnosis in malignant disease has been calculated when all three radiologists agreed with the diagnosis and when at least one report of the three radiologists was correct.

TABLE I.—Accuracy of Methods of Examination in 77 Patients with Cancer of Breast and in 145 Patients with Histologically Proved Benign Disease of Breast. A, B, and C Refer to the Three Radiologists

Method of Examination	Accuracy of Diagnosis, % Correct	
	Malignant Disease (77 Patients)	Benign Disease (145 Patients)
Clinical	81.8	81.4
Thermography	A 53.2	15.2
	B 51.9	11.7
	C 41.6	38.6
70-mm. mammography	A 48.1	49.7
	B 61.0	58.3
	C 39.0	47.6

TABLE II.—Observer Error in Diagnosis in Patients (77) with Malignant Disease of Breast by Three Radiologists

	Thermography	70-mm. Mammography
All three radiologists correct	29.9%	31.2%
All three radiologists wrong	32.5%	28.6%
At least one radiologist correct	67.5%	71.4%

The incidence of false-positive and false-negative reports with each method of investigation has been calculated for patients with histologically proved benign and malignant disease in the symptomatic group (Table III). There is a strikingly high incidence of false-negative diagnoses of cancer in patients with malignant disease. The false-positive rate in patients with benign disease is less pronounced.

TABLE III.—False-positive Rates (i.e., % Suspected Malignant) in 145 Patients with Histologically Proved Benign Disease and False-negative Rates (i.e., % Suspected Benign) in 77 Patients with Malignant Disease. A, B, and C Refer to the Three Radiologists

Method of Examination	Benign Breast Disease (145 Patients) % Suspected Malignant	Malignant Breast Disease (77 Patients) % Suspected Benign
Clinical	18.6	18.2
Thermography	A 16.6	46.8
	B 14.5	48.1
	C 13.1	58.4
70-mm. Mammography	A 11.7	51.9
	B 3.4	39.0
	C 6.9	61.0

While the survey was carried out to determine specifically the value of each of the methods in the diagnosis of malignant disease, their accuracy in combination has also been considered in the 77 patients with cancer. The diagnostic accuracy of clinical examination alone, clinical examination plus thermography, clinical examination plus 70-mm. mammography, and all three methods combined are noted in Table IV. In this table a report of suspected malignancy by any one of the three radiologists was included as positive for that patient, and represents the best possible accuracy.

TABLE IV.—Diagnostic Accuracy of Clinical Examination Alone and Combined with Thermography and 70-mm. Mammography in 77 Patients with Cancer of Breast

Method of Examination	Correct Diagnosis in Malignant Disease. (77 Patients)	
	No.	%
Clinical	63	81.8
Clinical + thermography	69	89.6
Clinical + 70-mm. mammography	70	90.9
Clinical + thermography + 70-mm. mammography	73	94.8

The addition of thermography and 70-mm. mammography to clinical examination enhanced the accuracy of the diagnosis of malignancy. Thus one radiologist of the three (but not the same radiologist each time) correctly diagnosed cancer by thermography in six patients and by 70-mm. mammography in seven in whom the correct diagnosis was not made clinically. With the use of both methods to complement clinical examination, 10 patients with a clinical diagnosis of benign disease were suspected of having cancer. However, all these patients had a clearly palpable discrete lump in the breast and consequently would have been submitted to biopsy.

One of the reasons for the low accuracy of 70-mm. mammography in this survey was the high incidence of unsatisfactory films reported by each observer. The number of thermograms and 70-mm. mammograms in the symptomatic group considered not entirely satisfactory technically by each observer but still reportable is shown in Table V: almost half of the 70-mm. mammograms were of inferior quality (average 45.7%) whereas 79% of thermograms were accepted as satisfactory. A similar proportion of 70-mm. mammograms in the asymptomatic group were reported as imperfect, and these poor quality films did not diminish in proportion as the survey proceeded.

TABLE V.—Thermograms and 70-mm. Mammograms Reported as Unsatisfactory by each Radiologist (A, B, and C) in the Symptomatic Patients (414)

Method of Examination	A	B	C
Thermography	25.6%	20.3%	16.2%
70-mm. mammography	51.5%	42.3%	43.2%

Asymptomatic patients

The results of surveying the 477 patients without symptoms of breast disease by clinical examination, thermography, and 70-mm. mammography are shown in Table VI. Clinical examination did not show any lesions which caused suspicion of malignant disease. Both thermography and 70-mm. mammography, however, detected suspicious lesions. When the findings of at least one observer for each patient were considered, 11.7% of the 477 patients were thought to have a malignant lesion on thermography and 2.5 on 70-mm. mammography. The comparable figures for suspect benign disease are also shown in Table VI. More patients were suspected of having benign disease according to all three methods of examination.

TABLE VI.—Lesions Suspected in 477 Patients without Symptoms of Breast Disease. A, B, and C Refer to the Three Radiologists, and Combined Results Indicate Total Percentage when at Least One of the Three Radiologists Identified a Lesion

Method of Examination	Lesions Suspected	
	Malignant (%)	Benign (%)
Clinical	0	9.4
Thermography	A 4.4	9.0
	B 8.8	6.1
	C 0.4	32.1
Combined results	11.7	37.5
70-mm. mammography	A 2.1	15.9
	B 0	16.8
	C 0.4	32.1
Combined results	2.5	41.7

Again, there was considerable disagreement between the three radiologists concerned in reporting the thermograms and the 70-mm. mammograms. Though at least one observer noted malignant disease on thermography in 56 women, in only nine was there agreement between two observers and in only two between all three. In none of the 70-mm. mammograms reported as malignant did two or all three of the radiologists agree on a diagnosis.

The combined results of all three methods of investigation suggest that 67 women in the asymptomatic group had malig-

nant disease of the breast and 307 had benign disease. These women with suspected malignancy were offered further investigation. If lesions were confirmed, the surgical opinion of a consultant was sought.

At the time of writing, 12 months after the end of the survey, biopsy had been carried out in 13 patients, in all of them proving benign. Eleven further patients in whom a repeat thermogram was again suspicious of malignancy were still under surveillance.

Discussion

The results of this survey indicate that the diagnostic accuracy of thermography and 70-mm. mammography does not approach that of clinical examination in patients with symptomatic breast disease. Thus, while one clinician correctly diagnosed malignant disease in 82% of women with breast complaints, the best possible accuracy, as represented by the highest individual accuracy when three radiologists independently surveyed the films, was only 53% for thermography and 61% for 70-mm. mammography. Even when one correct report from any of the three radiologists was considered, the accuracy was only 68% for thermography and 71% for 70-mm. mammography. Therefore neither thermography nor 70-mm. mammography is suitable for use as an isolated procedure in the diagnosis of breast disease. Nor can either method of examination be used in isolation as a screening procedure. Indeed, we consider it dangerous to use each method alone, as it would give the patient false security.

Furthermore, there is considerable observer error between radiologists using these two methods: thus all three radiologists agreed with the diagnosis in less than one-third of cases. A single radiologist reporting either thermogram or 70-mm. mammogram films is likely to be inaccurate in a significant proportion of cases. The inaccuracy of 70-mm. mammography is partly explained by the technical difficulty of getting films of satisfactory quality though possibly with

improved technique it may be of more value. The use of these methods as complements to clinical examination improved the diagnostic rate, but in all the patients in whom this occurred a palpable lump was present.

The incidence of false-positive reports as assessed in patients with benign disease and asymptomatic women is high. This has led to a considerable expenditure of time and money for the further investigation of suspect patients. As the number of asymptomatic women studied was relatively small and many were young, it is not surprising that no cancers have come to light in this group.

There is a current tendency to promote screening programmes for breast cancer with a single method of examination. Many such programmes have been set up and are generally uncontrolled. The reports of the New York group indicate that neither clinical examination nor mammography alone is an adequate method of screening, and our survey indicates clearly that thermography and 70-mm. mammography have no place as isolated screening procedures.

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Secretory IgA in Urinary Tract Infections

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Summary: Secretory IgA, measured by radial immunodiffusion, was compared in the urine of children with chronic and recurrent non-obstructive urinary tract infections with that in normal children. IgA, IgG, and IgM were also measured. Absent and low levels of IgA(s) were found in both groups; however, the mean levels of IgA(s) were significantly higher in the infected group compared with normals—3.3 to 0.78 mg./24 hours, respectively. Secretory IgA was found to be locally produced in the bladder. It is suggested that IgA(s) levels reflect an antibody response to infection.

Introduction

In some body secretions such as tears, saliva, and those of the gastrointestinal tract, secretory IgA (IgA(s)) is the predominant immunoglobulin (Chodirker and Tomasi, 1963; Tomasi and Zigelbaum, 1963). This IgA is chemically and immunologically distinct from serum IgA (Pollak *et al.*, 1968),

and its role in the local immune defence system of the respiratory, and gastrointestinal tracts has been shown by finding in those secretions naturally occurring antibodies of the IgA class to viruses and bacteria and by the viral neutralizing activity of human nasal secretions after poliovirus and influenza infections (Rossen *et al.*, 1966; Bellanti *et al.*, 1967; Bellanti, 1968; Tourville *et al.*, 1968).

The recent finding of IgA(s) in normal human urine (Bienenstock and Tomasi, 1968) and the suggestion that urinary IgA may participate in local immune defence mechanisms led us to study the role of IgA(s) in non-obstructive chronic and recurrent urinary tract infections in children.

Patients and Methods

The study included 29 patients (10 normal children, 17 with urinary tract infection (one a newborn), and two with ileal bladders). All patients with urinary tract infections had either chronic or recurrent (three or more) infections without evidence of significant anatomical or functional abnormalities as defined by intravenous pyelogram, cystourethrogram, cystoscopy, and creatinine clearance.

Specimens.—Twenty-four-hour urine samples were

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