# Comparison Of Clinical Assessment, Mammography And Ultrasound In Pre-Operative Estimation Of Primary Breast-Cancer Size: A Practical Approach

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**Abstract**

The stage of breast cancer and prognosis for the patient depend, in part, on the largest diameter of the primary tumour. The measurement modality is not specified in literature but the best estimate of tumour size is accepted to be the histopathological measurement, which is not available until after the initial surgery. Management is therefore planned using the size of the tumour at imaging/clinical palpation. We wished to determine which of the modalities provides the closet estimation of histopathological tumor size.

In our study, clinical palpation tended to overestimate tumour size and gave the largest standard deviation of the difference and ultrasound tends to underestimate tumor size. Although there is little difference between the precision of ultrasound and mammography in measuring tumour size, mammography is the most precise method for measuring primary breast tumor size. The wide 95% confidence intervals for any method of pre-operative tumor measurement should be considered when planning patient management.

## INTRODUCTION

The breast is the commonest site of cancer in women and carcinoma of the breast is second only to lung carcinoma as a cause of death from cancer among women. One out of eleven women or about 9% will develop it during her life time These facts emphasize the magnitude of the breast cancer problem and stress the importance of determining epidemiological factors responsible for its development and of trying to isolate any preventive measures that might reduce its incidence. But breast cancer appears to be due to a constellation of epidemiologic factors rather than to a single one, including genetic predisposition, carcinogen exposure and various adverse personal and demographic conditions; therefore, it would seem highly improbable that an epidemiological factor of overwhelming importance in breast cancer will be determined. Although there are some preventive measures that could be of importance, most of the etiologic factors in breast cancer are beyond the control of physicians and patients, so the best way to reduce the impact of carcinoma of the breast is early diagnosis, staging and treatment according to it, at the earliest moment possible. In general, prognosis of carcinoma of the breast seems to be based on the dynamic interplay between the anatomic extent of cancer when it is first diagnosed and its growth potential, i.e. aggressiveness or virulence, on one side versus the degree of immunocompetence of the host and appropriate early treatment on the other side. The treatment modality of carcinoma of the breast depends upon the stage at the time of presentation.

Hutten (1980) has emphasized the fact that one of the most significant discriminations in staging and in predicting survival in breast cancer is the presence or absence of axillary lymph node metastases. The size and configuration of ordinary clinically invasive cancer can be used as an indicator of the probability of axillary metastasis and survival, thus the stage of breast cancer and prognosis for the patient depends in part on the largest diameter of the primary tumour; however, size estimated on clinical judgement is subject to a considerable amount of error. The measurement modality is not specified in available literature but the best estimate of tumour size is accepted to be the histological measurement which is not available until after the initial

surgery. Management is, therefore, planned using the size of tumour at imaging/clinical palpation.

In our study we wished to determine which of the modalities (clinical palpation, mammography or ultrasound) provides the closest estimation of histological tumour size.

## PATIENTS AND METHOD

The study was carried out in the Department of General Surgery, M.G.M. Medical College and M.Y. Group of Hospitals, Indore (M.P.), and included all patients admitted as primary breast cancer from each unit of general surgery.

## PATIENT SELECTION CRITERIA AND METHOD

All patients presenting with a lump in the breast, proven by FNAC as primary breast cancer, over a 1½ year period (Jan 2006 to July 2007).

Patients were excluded when:

a) only in situ disease was present.
b) histological size was not measurable.
c) they had endocrine therapy only.
d) they had Chemotherapy only.
e) they had Neoadjuvant chemotherapy.
f) they had Multifocal tumours.
g) the tumour was not seen on mammography/ultrasound.
h) they had delayed surgery.

Study data was recorded prospectively.

## CLINICAL TUMOUR MEASUREMENT

All patients underwent thorough physical examination at the out-patient department of M.Y. Hospital and for those with a palpable breast mass a single estimate of the maximum diameter of the mass between 2 examining fingers was recorded.

## ULTRASONOGRAPHIC TUMOUR MEASUREMENT

Diagnostic ultrasound was performed on all patients by the same radiologist in the department of radiodiagnosis of M.Y. Hospital. The same ultrasonography machine was used through the study. A probe frequency of 75, 10 or 13 MHz was selected for optimal visualization of tumour and in all cases where the tumour was identified the probe was rotated until the largest diameter was displayed and measured on the frozen image using the integral calipers. Tumour size and probe frequency was recorded at that time.

## MAMMOGRAPHIC TUMOUR MEASUREMENT

Mammograms were performed on the Siemens Mammomat unit of the radiodiagnosis department of M.Y. Hospital using Kodak Min-R 2000 films. They were subsequently assessed for the study by a single radiologist who was blinded to all other measurements. Routine oblique and craniocaudal projection plus any other available film was examined, excluding macroradiographs, i.e. films where the mass extends beyond the field of view. A single measurement of the largest tumour diameter on any projection was recorded. Spiculation and microcalcification surrounding a tumour mass were excluded from the measurement. The nature of the mammographic abnormality was also recorded (well-defined mass, poorly defined mass, disturbance of architecture, other).

## HISTOLOGIC TUMOUR MEASUREMENT

This was performed by one and the same histopathologist of the department of pathology of M.Y. Hospital, Indore. The operative specimen was sectioned along its longest plane and a single measurement of the tumour diameter was made using a plastic ruler. For tumours less than the width of a microscope slide, the measurement was refined using the vernier caliper on the microscope. If the tumour reached the margins of the specimen and residual tumour was identified on wider excision, the histological size was considered unmeasurable and the patient was excluded from the study. If no residual tumour was identified at wider excision, the histological measurement was considered reliable.

## STATISTICAL ANALYSIS

The difference between the preoperative size estimated by each modality and the histopathology was plotted against the average of the two estimates. The mean difference between preoperative and histopathological measurement, the standard deviation of the differences and the 95% limits of agreement (limits between which 95% of differences should lie) were calculated for each preoperative modality. The correlation between various measuring modalities and histopathology was calculated using the z-test.

## RESULTS

The mean of difference for clinical palpation was 0.8448, for ultrasonography 0.3038, and for mammography 0.10.

Standard deviation of difference for clinical palpation was 1.425, for ultrasonography 1.375, and for mammography 1.251

The mean size for clinical palpation was 5.09cm, for ultrasonography 3.96cm, for mammography 4.21cm, and for histopathology 4.24cm.

The standard deviation for clinical palpation was 1.87, for ultrasonography 1.81, for mammography 1.69, and for histopathology 1.60.

The 95% confidence limit for clinical palpation (mean size ±2 standard deviation) was 1.35-8.83cm, for ultrasonography 0.34-7.54 cm, for mammography 0.83-7.59 cm, and for histopathology 1.04-7.44cm.

The z-test value for clinical palpation was 3.05, for ultrasonography -0.507 and for mammography 0.423 depicting that there was significant statistical difference between clinical palpation, size and histopathological size, and although ultrasonography underestimated the size there was no significant difference in measurement of size by ultrasonography and histopathology. For mammography also, there was no significant difference in measurement of size by mammography and histopathology and it is most close to histopathology in measuring primary breast tumour size.

**Figure 1**

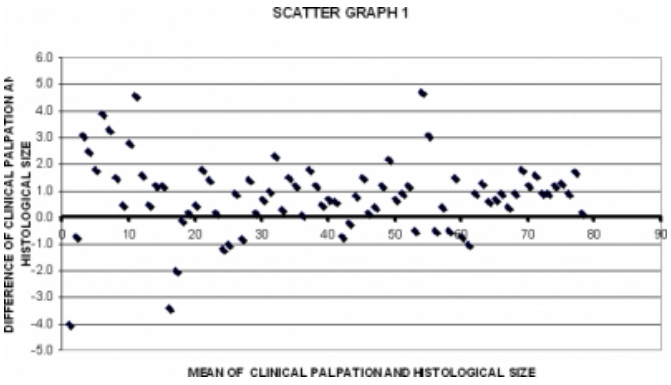



**Figure 2**

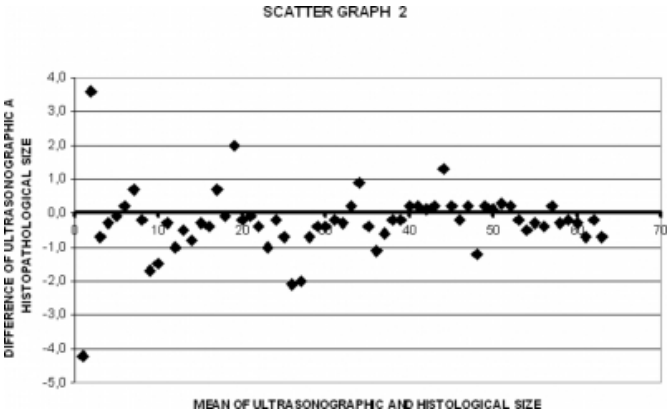
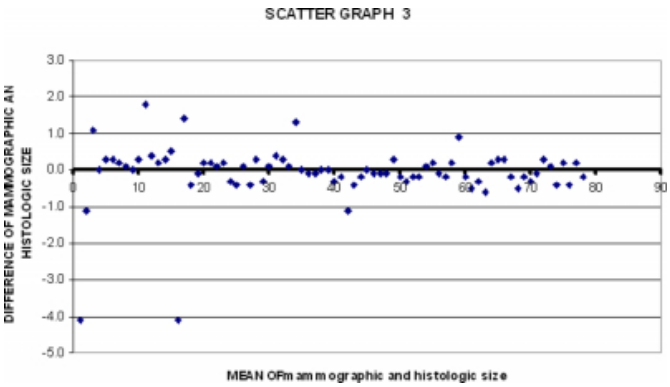



**Figure 3**




The scatter graphs in figures 1, 2 and 3 demonstrate the differences between preoperative and histological tumour measurement plotted against the mean of the two measurements, for palpation, mammography and ultrasound. The spread of results for palpation was wide, with a positive bias (tendency to overestimate size). For mammographic measurment, the spread of results was narrower and there was no bias (spread evenly around zero). Ultrasound showed a slight negative bias (tendency to underestimate size). The spread of results was similar to mammography. For all modalities, the size of the difference depended upon the size of the tumour being measured, with larger tumours yielding larger differences.

## DISCUSSION

We have identified seven studies from the literature that addressed the same research question as this study ([6,7,8,9,10,11,27]). Five concluded that ultrasound provided the most precise pre-operative indication of histological tumour size. Only one study concluded in favour of mammographic measurement. Sample sizes ranged from 31 to 207, five were prospective studies, two retrospective ones. Our results,

using a different statistical method, indicate that ultrasound does show a slight negative bias but both modalities exhibit a similar variability of differences. Both imaging modalities are more precise than clinical palpation and mammography is most precise one.

Our results support the findings of other studies, that clinical assessment overestimates tumor size ([6,8,11,27]). This is due to the inclusion of skin and healthy breast tissue between the examining fingers. Dixon et al. proposed a method of correcting clinical tumor measurement by subtracting the thickness of these tissues ([12]).

We made no assessment of inter-observer variability for palpation. A study by the Yorkshire breast cancer group showed poor inter-observer reproducibility for clinical assessment of tumor size ([13]). Agreement within 1 cm was seen in just over 50% of patients. Thomlinson has demonstrated a far more acceptable inter-observer variability by measuring palpable tumors using engineer's calipers ([14]). This method was used in five of the studies with which we are comparing our results. We chose not to use calipers because we felt that it would make the examination process more unpleasant for the patient and it does not reflect routine practice.

Six published studies have agreed with our finding that ultrasound tends to underestimate tumor size; none found that it overestimated the size ([6,7,10,15,16]). The most important source of error in ultrasonic measurement of tumor size is likely to be in identifying the tumor margins. Blunt et al. investigated the agreement between ultrasound and histological size ([17]). In the group where ultrasound overestimated the size of the invasive tumor, they found that the tumor tended to be surrounded by a region of DCIS or a desmoplastic response; both of these would increase the size of the ultrasonic abnormality. The tumors where ultrasound underestimated the size were often histologically diffuse or multifocal. Nishimura et al. found that ultrasound tended to underestimate the width of the tumor to a greater degree than the depth ([15]).

No validation measurements to assess inter-observer variability for ultrasonic tumor measurement were made for logistical reasons. We were also unable to identify any such assessment from the literature. This remains an area that needs further investigation.

Our study found that mammographic measurement tended to neither under- or overestimate tumor size. Five other studies from the literature found that mammography underestimated size ([6,7,10,11,16]). Three studies found that mammography overestimated size ([8,18,19]). There was also poor agreement on the nature of the mammographic abnormality. This indicates the highly subjective nature of these mammographic observations, a finding supported by Simpson et al. ([20])

Three potential sources of error are suggested. Firstly, there is difficulty in defining accurate margins of the mammographic abnormality. Our finding that there is a significant tendency to underestimate tumor size when the mammographic abnormality is classified as a disturbance of breast architecture supports this. The second source of error is radiographic magnification. Pain et al. used tumor model studies to demonstrate a 10% magnification for a 1cm tumor 5cm away from the film ([6]). Sphiris and Flannagan have both proposed correction factors to compensate for magnification ([18,19]). Our results do not indicate an overall tendency to overestimate tumor size on mammograms. Thirdly, it is possible that none of the standard mammographic projections demonstrated the largest tumor diameter.

Histological tumor measurement has been assumed to be the gold standard in this and all other studies. However, as with all other biological measurements, inaccuracies can be identified. The NHS breast screening programme quality assurance scheme circulates standard slides of breast cancer to be assessed by pathologists. For most of the slides assessed there was over 90% agreement on tumor size within +/- 3mm. In the worst case, only 68% of pathologists agreed within +/- 3mm and there was a range of reported diameters between 4 and 32mm ([21]). Possible sources of histological measurement inaccuracy include tumor shrinkage during fixation and sectioning of the tumor at an angle to its largest diameter. Difficulty in defining tumor margins may also lead to error, particularly for larger tumors when only macroscopic measurement is possible.

Three studies have compared tumor size assessment using ultrasound, mammography and MRI. Two have shown that MRI produced the most reliable measurement with no difference between the accuracy of mammography and ultrasound ([16,22]). Wei-tse Yang et al. found that ultrasound and MRI were equally reliable, and both were better than mammography ([23]). Two other studies have found MRI to be more precise than mammography ([24,25]). Whilst these results show promise for the future, MRI is not yet routinely available for the investigation of women with breast cancer.

In a review article, Davis and McCarty indicated the precision of MRI in measuring the volume of a tumor ([26]). This is of value in assessing response to primary systemic therapy, when a small error in measuring each dimension can translate to a large error in the tumor volume.

## CONCLUSION

We have found that both mammography and ultrasound are more reliable in the pre-operative estimation of breast cancer size than palpation. There is little difference in the accuracy of the two imaging modalities, although ultrasound does tend to underestimate the size. Several features of the imaging process have been investigated. Only the nature of the mammographic abnormality, a highly subjective observation, has been shown to influence the accuracy of measurement. We believe that both mammographic and ultrasonic tumor measurements should be used when planning management. When these two vary widely, repeat measurement by a second radiologist may be helpful. For any pre-operative tumor measurement, the wide 95% limits of agreement with the histological measurement must be considered.

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