Is Breast transillumination a viable option for breast cancer screening in limited resource settings?

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Abstract

Background: Mammography is an established screening tool for breast cancer in high-income countries but may not be feasible for most resource poor nations. Alternative modalities are needed to mitigate the impact of the increasing incidence and mortality due to breast cancer. This may require the development of new technologies or reevaluation of old technologies applicable to resource limited settings.

Objective: To determine the sensitivity and specificity of breast transillumination as compared to mammography and to describe features of benign and malignant breast lesions as seen with breast transillumination.

Methods: A single group descriptive analytical study was conducted over a six month period (2011) in the breast unit of Mulago National hospital. Eligible participants were consecutively sampled. Participants underwent Clinical Breast Examination (CBE), breast transillumination (BT), mammography (MG) and histopathological analysis of identified breast lumps. Sensitivity, specificity and predictive values were calculated. Features of the masses detected by transillumination were then described.

Results: The number of participants recruited was 201 (mean age 42 years, range 30-80 years). The average palpable lump size was 3.8 cm (range 0.5 to 10 cm). BT had a sensitivity of 63.2% (PPV 86.8%) and a specificity of 89.5% (NPV 61.2%) with mammography as the reference standard. Also, 73.3% of breast lumps with irregular margins and 88.5% with dense opacity at transillumination turn out to be malignant at histopathology examination.

Conclusion: The Breast transillumination technique had a moderate sensitivity of 63.2%. This warrants a large scale population-based evaluation of BT as a screening tool. This technique may not substitute mammography but to be considered an option where mammography access is limited.

Introduction

Breast cancer accounts for about one third of all cancers diagnosed globally with both incidence and mortality reported to be increasing in sub-Saharan Africa. In Uganda breast cancer is the third most commonly diagnosed cancer after Kaposi's sarcoma and cancer of the cervix (1). The majority (77%) of women present in late stages (III & IV) with low 5-year survival (of 39%). In the past, resource allocation for health was skewed towards infectious diseases such as HIV/AIDS and malaria. Currently however, a rapidly growing burden of non-communicable diseases (NCDs) is demanding similar attention.

Screening reduces mortality due to breast cancer. Mammography has been shown to reduce breast cancer mortality by up to 25-30 % in women over 50 years old (2-4). Access to mammography is limited in developing countries. There are currently only a handful of mammography machines in Uganda which are not equitably distributed and some charge a fee thus precluding access for most women (5). Women below the age of 30 years are ineligible for mammography yet a sizeable portion of them are at risk and therefore need some form of screening. Alternative screening modalities should therefore be explored either by re-evaluation of old techniques or invention of new ones (6,7).

Culter first described the use of breast transillumination some 80 years ago (8). Advent of x-rays and mammography led to its abandon. There is justification for its revaluation with a view to determining its utility in areas where there is no mammography. The Breast light is a commercially available modification of earlier prototypes used for breast transillumination. It is comparatively much cheaper than mammography, easy to use and has minimal running costs.

The primary aim of this study therefore was to determine the sensitivity, specificity and predictive values of breast transillumination compared to mammography in a hospital setting.

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Methods

A descriptive study was conducted from January to June 2011 in the breast unit of Mulago Hospital, one of three national referral hospitals but the only public hospital with comprehensive breast care services in the country. Mulago has a bed capacity of 1500 and is the teaching Hospital for Makerere University College of Health Sciences. The outpatient Breast Clinic runs once a week and in the past three years over 600 incident cases of breast cancer were registered there.

All women aged 30 years or more who attended the breast clinic were prospectively included. Pregnant or lactating women and those with ulcerated breast lesions were excluded because of radiation risks in pregnancy and high breast density during lactation which interferes with mammography interpretation respectively. The sample size was determined using the formula for sample size for a descriptive study of a dichotomous variable (6, 7), alpha was 0.05 for 95% confidence interval, a sensitivity of BT of 67% was used. Consecutive sampling was done.

Procedure

CBE was performed to determine the presence or absence of a breast lump prior to transillumination. At transillumination, the number, size, site, density of opacity and regularity of margins of detected lumps were noted. Opacity was measured against a three point scale devised for this study as translucent, opaque or densely opaque. A lump with more than three quarters of its margin being even was considered regular, less than ¾ was considered irregular.

- Translucent – most light comes through (Red/pink)
- Opaque – some light comes through (Gray)
- Densely opaque – no light comes through (Black)

In a dark room, the Breast light (model BL 801 manufactured by PWB health, G82 3PW, UK) was used by a single observer to examine the woman's breasts in seated position with the arms raised to hold the back of the head. A water based gel lubricant was applied to both breasts to ease the examination for the user and make it more comfortable for the participant. The light was switched on and applied firmly to the skin on the inferior aspect of the breast beginning with the right, thereby giving a craniocaudal view. The Breast light was moved to either side up to the edge of the breast. The light was then moved forward and upwards over the breast to ensure that all parts of the breast were transilluminated. The Breast light was finally moved superolaterally along the milk line towards the axilla to examine the axillary tail. At all times the investigator observed the transmission of light through the breast at a point directly opposite the light bulb of the Breast light. The same was repeated on the left breast. The participant was cleaned and allowed to dress.

Mammography was performed on all participants and read as normal (BI-RADS 1) or abnormal (BI-RADS 2-5) by a total of four consultant radiologists at different times. Participants who had a clinically palpable abnormality and consented underwent a core needle biopsy. Histopathological analysis was performed by an experienced team of pathologists. Findings were recorded in a structured data collection tool.

The investigators performing the breast transillumination, mammography and histological examination were blinded to findings of any of the other tests.

Data management and analysis

Raw data were entered using Epidata Version 3.1 software, and then exported to Epidata Analysis v.2.2.1.171 for analysis. Sensitivity, specificity and predictive values were calculated for transillumination technique. Features of malignant and benign lumps at transillumination were described.

Ethical clearance was secured from the Ethics and research Committee. Informed consent was obtained from all participants.

Results

A total of 201 participants were recruited, 10 (5%) of whom were asymptomatic. The average palpable lump size was 3.8 cm (range 0.5 to 10 cm). The smallest lump detected by CBE, BT and MG was 0.5 cm. Participants were aged 30- 80 years with an average of 42 years.

Overall, mammography detected more abnormalities than the other two techniques (Fig 1-2). Mammography performed best for lumps less than 2 cm where it detected 7.5 times as many lumps as BT but for lumps 2-5 cm, MG detected only 1.08 times more lumps than transillumination. BT picked up more than CBE for all lumps < 5cm.

Transillumination was negative in 14 (14.4%) of participants with abnormal CBE and 46 (36.8%) with abnormal mammography. The average lump size was 2.1 cm for CBE and 1.5 cm for mammography (Table 1). 50% of these were located in the deep in breast tissue close to the

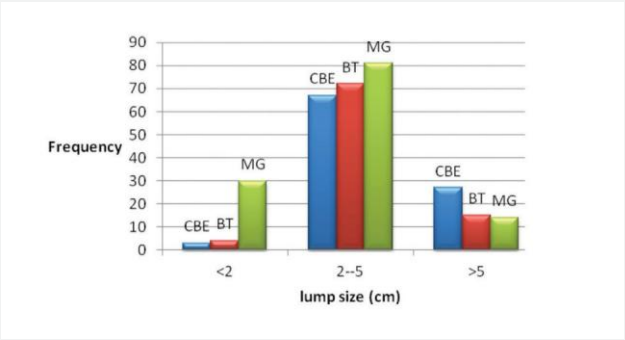

Figure 1: distribution of lump sizes by technique of detection CBE=Clinical Breast Examination, BT= Breast Transillumination, MG= mammography

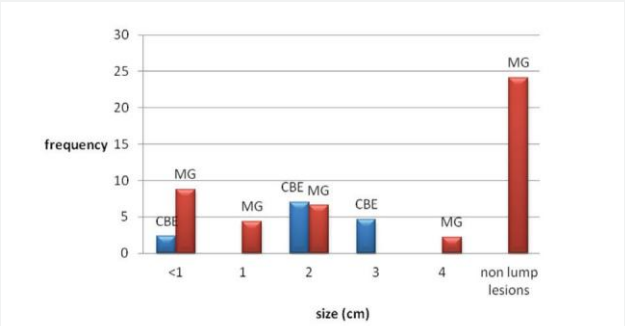

Figure 2: Distribution of the false negative picked up by CBE and MG

Breast Transillumination	Mammography				Total	
	Abnormal		Normal			
	No.	%	No	%	No.	%
Positive	79	63.2	8	10.5	87	90.8
Negative	46	36.8	68	89.5	114	59.6
Total	125	37.8	76	62.2	201	

BT had a sensitivity of 63.2% (95% CI 54.5 -71.1) with a positive predictive value of 90.8% (95% CI 82.9 – 95.3). The specificity of 89.5% (95% CI 80.6 – 94.6) with a negative predictive value of 59.6% (95% CI 50.5-68.2%)

Table 1: Comparison of Breast transillumination to mammography

Transillumination	Histology				Total No.
characteristic	Malignant		Benign		
	No	%	No.	%	
Irregular	11	(73.3)	4	(26.7)	15
Regular	23	(56.1)	18	(43.9)	41
Opaque	11	(36.7)	19	(63.3)	30
Densely opaque	23	(88.5)	3	(11.5)	26
Diffusely opaque	3	(75.0)	1	(25.0)	4

Table 2: Comparison of transillumination characteristics to Histology

chest wall. Non-lump lesions included mammographic abnormalities not described as lumps e.g. focal area of increased density, calcifications, or tramline calcifications. These accounted for 52.4% of the mammograms.

Histology was done on a total of 60 lumps, 61.7% of which were malignant, the rest were benign. Of the lumps with irregular margins, 73.3% were histologically confirmed to be malignant as were 88.5% of those that appeared densely opaque (Table 2).

Discussion

The challenges that face cancer control efforts in sub Saharan Africa are numerous and complex; the majority of women who need screening are young (therefore not eligible for the standard mammography screening), national screening programs are non existent and public awareness is low. Resource allocation is skewed to infectious disease such as HIV/AIDS and malaria. Exploring the possibility of using BT as a screening modality is an attempt to contribute to Breast cancer control initiatives in sub Saharan Africa. Breast transillumination is not meant to be a substitute to x-ray screening but a stop gap measure in the absence of x-ray screening or other more appropriate screening tools to vulnerable populations. We also anticipate that in popularizing its use, awareness might be raised and access to screening enhanced.

Sensitivity and Specificity

This study found that BT in comparison to mammography had a moderate sensitivity of 63.2%, a specificity of 89.5%, and positive predictive value of 90.8%. BT detected 85.6% of palpable lumps and was able to detect lumps as small as 0.5 cm in widest diameter. Irregular margins and dense opacity at transillumination were found to be highly suggestive of malignancy. Although there were concerns by the investigators as to the applicability of transillumination in populations with the black skin as previous studies were conducted in predominantly white populations of the USA and UK (7-12), it worked well in this study. Mammography proved superior to BT in several ways: higher overall proportion of abnormalities in the study population, (62.2% vs. 45.3%), higher true positive test of abnormalities among CBE positive participants, (91.8% vs. 85.6%) and greater abnormalities in

CBE negative participants, (34.6% vs. 7.7%). However, BT showed some strength as well. We were able to detect lumps as small as 0.5cm with breast transillumination and most of the lumps detected with CBE negative participants were less than 2 cm in their widest diameter possibly demonstrating its potential for early detection of breast lumps. These findings demonstrate that breast transillumination is a promising tool, further evaluation of which is justifiable. This is particularly important given the high rate of presentation with advanced disease in our environment. The most important feature of a screening tool in a resource limited setting is sensitivity (13) to detect as many truly positive cases as possible since few opportunities exist for patients to undergo screening. The specificity of 89.5% means that the majority of normal patients will have negative transillumination (i.e. few false positives). This is important since false alarms are costly and may reduce confidence of the end users.

Coupled with a NPV of 59.6%, this minimizes the chances of a participant with disease having a negative test. Currently, transillumination detects benign and breast cancer alike. Approaches to such a distinction are evaluated in this paper. Whereas it is common practice in the developed world to monitor mammographically benign disease, in our setting a definitive diagnosis is often sought and appropriate treatment offered. This is because of high loss to follow up of many patients. Therefore, detection of benign disease should not raise similar concerns as in the developed world.

Transillumination had sensitivities of 67-95% in various other studies with histology as the reference standard (7). Although it may not be easy to directly compare sensitivities of transillumination and mammography because they were each calculated using different reference standards, it may still be possible to make some meaningful inferences. The reported sensitivity of mammography is 63%-95% (5,14). The fact that the sensitivity of transillumination at 63.2% fits within the reported sensitivity range of mammography makes it comparable in its use as a technique for detection of breast lumps.

False negatives

An in depth analysis was done of the missed lumps that accounted for 36.8% of the false negative cases rate. The average size was 1.5 cm (range 0.5- 4cm) and 61.2 % of them were in breasts of density BI-RADS 2, but because lumps of similar sizes were found in other breast of similar density and size, size and breast density are unlikely explanations Nearly half of these lumps were located deep in the breast tissue and close to but not attached to the chest wall. Previous studies (8,15) showed that lumps deep in breast tissue, close to the chest wall do not transilluminate satisfactorily as was seen in this study. Many of these lumps were small and were in thin/flat (small volume) breasts. Such lumps did not transilluminate well in our study as was the case for Cutler (5). Transilluminated light may diffract around these lumps giving false negative appearances, but such a phenomenon may not occur with the much higher energy x-rays used in mammography. Another possible explanation for false negatives is that some mammographic diagnostic criteria such as calcifications are not detectable by transillumination. Although calcifications should not transilluminate, their small sizes possibly allow diffraction of light around them and therefore are not visualized. As was reported by Sickles (9), this remains a limiting factor for the use of breast transillumination, and represents a challenge for an improved transillumination device.

Diagnostic Value

This study also set out to evaluate the diagnostic potential of breast transillumination. The inability to distinguish benign from malignant disease was earlier brought out as a major weakness of the breast transillumination technique (9,15). In a previous study, tumour vascularity was investigated as a possible distinguishing feature between benign and malignant tumours but there was no significant difference. We once again attempted to determine with different tumour characteristics if a benign – malignant distinction could be made. We based on regularity of margins and degree of opacity measured against a predetermined standard. It was found that 73.3 % of lumps with irregular margins and 88.5 % of those with dense opacity were malignant. This correlates well with Ohlsson's findings in which malignant tumors were described as dark with irregular margins (10). Reproducibility of these distinctive characteristics may be need further validation.

Low cost screening

With a high burden of breast cancer disease and the majority of patients presenting with advanced disease (1,16-17), it is essential that the population at risk accesses screening tools that not only exhibit high sensitivity and

specificity but are affordable and can be used for all age groups as well as being culturally acceptable . In addition it should be easy to use for both the health worker and the patient.

Screening mammography remains the standard of care and its benefits in improving survival through early detection are well documented (2-4). However such benefits may not be achievable in these resource poor settings due to the inhibitory resource requirements related to mammography and the ineligibility of nearly half of women who are in dire need of such screening services. One may therefore wish to consider breast Ultrasonography but it is also not without limitations (5,18).

In the absence of these two modalities what can be offered to the woman concerned about her breast health is the premise for re-evaluation of breast transillumination, a once promising imaging technique that was overtaken by advances in investigative science.

A Breast light costs about US$ 150 and has minimal maintenance costs. It runs on dry cells easily available in rural areas where most of our patients stay. The transillumination devices could be individually or communally owned thus further lowering costs and increasing accessibility. Indeed even individual women can be trained and empowered to examine their own breasts.

Study limitations

Limitations of the study included the fact that it was conducted in a hospital setting and was not restricted to asymptomatic patients which may limit its external validity as a screening tool. However, none of the previous studies (7-12) on transillumination were restricted to asymptomatic participants either. To our knowledge, this is the first study of its kind in a black African population, and the cost of a population based study limited this initial study to the hospital setting. In addition, the greater number of patients with positive findings in the hospital made it suitable for the first study. And now that this study has given us insight into the capabilities of BT in comparison to mammography, a larger study in an asymptomatic population may be justified.

BT was conducted by a single observer without significant prior experience in its use. This may have an effect on accuracy of interpretation of the findings, but perhaps the use of BT to determine presence or absence of a lump should not require specialized training and prior experience. This suggests that BT can be performed by various cadres of health care providers. Although no measure of variability was done, the use of more than one experienced mammography interpreter possibly reduced such variability. A total of four consultant level radiologists who routinely read mammography did the reporting on mammography in this study.

Also, since no measure of intra or inter observer variability was done, no strong inferences can be made on the reliability of transillumination technique.

Conclusion

Breast transillumination has moderate sensitivity and high specificity for detecting breast lumps. Breast transillumination should be considered for a large scale population based evaluation as a screening tool for breast cancer in resource limited settings, though it is not intended to substitute x-ray screening where it is available.

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