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Evaluating Estrogen Receptor Immunohistochemistry on Cell Blocks From Breast Cancer Patients in a Low-Resource Setting

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Abstract

- **Context.——**Breast cancer biomarker assessment is critical in determining treatment and prognosis. In Tanzania, immunohistochemistry (IHC) is limited to surgical specimens and core biopsies. However, performing IHC on fine-needle aspiration biopsy cell blocks would offer numerous advantages.

Objective.——To compare the performance between estrogen receptor (ER) IHC performed at Muhimbili National Hospital (MNH) in Tanzania and ER IHC performed at University of California, San Francisco (UCSF), to demonstrate feasibility of performing IHC using cell blocks in Tanzania.

Design.——Patients with breast masses were recruited prospectively from the fine-needle aspiration biopsy clinic at MNH. Estrogen receptor IHC results on cell blocks, performed at both MNH and UCSF, and corresponding tissue blocks, performed at MNH, were compared to determine concordance.

Results.——Eighty-six cell blocks were evaluated by ER IHC at MNH, with 41 of 86 (47.7%) positive and 45 of 86 (52.3%) negative. Among 65 UCSF and MNH cell block pairs, overall ER IHC concordance was 93.8% (61 of 65) and positive concordance was 93.5% (29 of 31) (κ= 0.88, P >.99). Among 43 paired UCSF cell blocks and MNH tissue blocks, overall ER IHC concordance was 88.3% (38 of 43) and positive concordance was 90.5% (19 of 21) (κ= 0.77, P >.99). We compared 62 MNH cell block and tissue block pairs. Overall ER IHC concordance was 90.3% and positive concordance was 87.9% (κ = 0.81, P = .69).

Conclusions.——Pairwise comparisons between ER IHC at MNH, on cell blocks and tissue blocks, with ER IHC at UCSF on cell blocks showed excellent concordance. We demonstrate that ER IHC on fine-needle aspiration biopsy specimens can be implemented in resource-constrained settings.

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Low- and middle-income countries face a growing burden of cancer with health care systems that are inadequately prepared to meet this public health challenge. Tanzania is home to an estimated 42 000 new cancer patients per year.[1] Breast cancer is the second-leading cause of cancer-related mortality among women in Tanzania, and most patients (63%–84%) present with advanced disease.[1–5] Estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor 2 (HER2) testing are critical for the classification of breast cancers, thus guiding clinicians in treatment decisions and determining prognosis. The National Comprehensive Cancer Network Harmonized Guidelines for Sub-Saharan Africa[6] and Tanzania's new National Cancer Treatment Guidelines[7] recommend determination of ER, PR, and HER2 status as part of the standard evaluation for newly diagnosed breast cancer cases.

Estrogen receptor expression has been identified in approximately one-third to one-half of breast carcinomas in Tanzania.[2–5,8] This reported prevalence of ER in Tanzania is low compared with the United States, where the prevalence is 72% to 85%.[9] Although this low rate of ER expression has been hypothesized as possibly due to unique disease biology of breast cancers in sub-Saharan Africa, it may also be due to technical issues affecting pathology quality, including insufficient human resources, inadequate education and training, and inadequate infrastructure and facilities, as well as insufficient quality management.[10] This emphasizes the need for epidemiologic studies that rely on high-quality pathology data.

Muhimbili National Hospital (MNH) is Tanzania's largest and premier referral hospital and only 1 of 2 public hospitals that perform routine immunohistochemistry (IHC). Currently, MNH can perform IHC, including ER, PR, and HER2, only on surgically resected specimens, including open biopsies and mastectomies, and core biopsies. Meanwhile, nearly all breast cancers presenting at MNH are locally advanced or metastatic and are initially diagnosed by fine-needle aspiration biopsy (FNAB), a rapid, minimally invasive, and relatively inexpensive diagnostic procedure. Moreover, in cases of breast cancer recurrence, FNAB is the procedure of choice to confirm the diagnosis at MNH. Because IHC is not yet performed on cell blocks in Tanzania, some patients undergo unnecessary nontherapeutic surgical resections to obtain tissue solely for biomarker testing. In Tanzania, core needle biopsies are prohibitively expensive for most patients and are performed in only a minority of cases. Surgical tissue is also subject to suboptimal tissue fixation in this setting, which can affect the accuracy of IHC results.[11,12] Several studies from other settings have previously established strong concordance of ER, PR, and HER2 expression between cell blocks and tissue blocks, but, to our knowledge, feasibility has never previously been evaluated in sub-Saharan Africa.[13–19]

This study aimed to demonstrate whether ER IHC can be performed on FNAB cell blocks at the MNH Central Pathology Laboratory and to determine the concordance of ER IHC performed at MNH and University of California, San Francisco (UCSF), on FNAB cell blocks collected and processed in Tanzania. In addition, we compare ER IHC results performed on FNAB cell blocks versus tissue blocks at MNH.

MATERIALS AND METHODS

Study Setting and Design

This was a prospective study of patients presenting to the FNAB clinic at MNH with a palpable breast lump from May 1, 2018, to January 31, 2019. Muhimbili National Hospital, besides being a national referral hospital, is the public teaching hospital for the Muhimbili University of Health and Allied Sciences in Tanzania. All suspected cancer cases referred to MNH must be evaluated by the MNH Central Pathology Laboratory for pathologic confirmation prior to referral for treatment. Muhimbili National Hospital has a well-established FNAB clinic where more than 50 patients are seen weekly, with an average of 4 new breast cancer diagnoses per week. The study received approvals from the institutional review boards at the Muhimbili University of Health and Allied Sciences (DA.287/298/01.A/) and UCSF (17-22963).

Study Population

All patients aged 18 years or older who were referred to the MNH FNAB clinic with a palpable breast lump were invited to participate. Patients who were pregnant or lactating or who had a prior diagnosis of breast cancer or bilateral malignant masses were excluded. The aims of the study, risks and benefits of participation, and sampling procedure were explained by a clinical research coordinator and a pathology resident. Patients were provided with written informed consent in Swahili, the native language of Tanzania. Clinical data were collected using a data-collection sheet, including age, sex, mass location, clinical tumor size, and lymphadenopathy, in the FNAB clinic by a pathology resident.

Specimen Acquisition

Fine-needle aspiration biopsy of the breast masses was performed by a pathologist using a 23-gauge needle, and the aspirate was used to prepare 3 direct smears fixed in 95% ethanol. Smears were submitted for routine diagnosis as per MNH protocol. A lymph node was also sampled for routine diagnosis if lymphadenopathy was present. Rapid on-site evaluation was performed using toluidine blue stain to assess for sample adequacy and to identify cases that were either suspicious for malignancy or definitely malignant. Additional passes were not performed on patients with benign preliminary diagnoses, and these patients were excluded from analysis. In patients with suspicious or malignant masses as determined by rapid on-site evaluation, 1 or 2 dedicated FNAB passes were performed and the material was rinsed into a 50-mL conical tube containing 15 mL of 10% neutral buffered formalin and fixed for 6 to 72 hours, according to guidelines from the American Society of Clinical Oncology (ASCO) and the College of American Pathologists (CAP).[20,21] Before completion of the procedure, formalin vials were checked for the presence of visible tissue fragments.

Cell Block Preparation

After fixation, FNAB cell blocks were prepared using SeaPlaque agarose (Lonza). Samples were centrifuged at 1500 rpm for 5 minutes, and the supernatant fluid was discarded. In a 15-mL conical tube, 0.2 g of agarose powder and 3.5 mL of distilled water were microwaved at 900 watts for 2.5 minutes in a water bath and mixed well. When warm to the touch but

no longer hot, 2.5 mL of agarose was added to the pellet and mixed. Samples were again centrifuged for 1 minute at 1500 rpm. Pellets were chilled at 4°C to 6°C for 10 minutes and then removed from the tube. Two cross sections, each approximately 3 mm thick, were sliced from the tip of the pellet using a scalpel, wrapped in tissue paper, placed in a cassette, and processed as routine histology samples. Hematoxylineosin–stained slides from cell blocks were reviewed for adequate tumor cellularity, which was defined as the presence of at least 1 well-preserved cluster of 10 tumor cells. Cell blocks with insufficient neoplastic cells were excluded from analysis.

Tissue Block Preparation

Tissue blocks from surgical specimens were fixed in formalin, processed, and embedded in paraffin according to standard histologic techniques at MNH as previously described.[4] Hematoxylin-eosin slides from paired histologic specimens were reviewed. Samples with no invasive tumor were excluded from the analysis.

Immunohistochemistry

At MNH, ER IHC was performed using a rabbit monoclonal antibody EP1 against ERα (ready-to-use, Cat# IR084, RRID: AB_2617140, Dako Agilent) by manual morphometry as previously described.[4] Immunohistochemistry was then reviewed on paired MNH and UCSF FNAB cell blocks and tissue blocks from the same patient. In discrepant cases, IHC was repeated on both the cell block and tissue block.

At UCSF, ER IHC was performed using a rabbit monoclonal antibody SP1 against ERα (concentrate, Cat# RRID: AB_149901, Thermo Fisher Scientific) by manual morphometry as previously described.[22] The protocol is clinically validated and already in use for routine clinical practice in a licensed and accredited anatomic pathology laboratory. The results from the UCSF ER IHC were used as the gold standard.

Estrogen receptor status was interpreted as positive when 1% or more of invasive tumor cells demonstrated any nuclear staining, based on ASCO/CAP scoring guidelines.[20] When present, normal breast tissue was used as a positive internal control in tissue block specimens. External controls were used in the absence of normal breast tissue and in all cell block specimens. All slides were independently interpreted and scored by the principal investigator and reviewed by 2 senior pathologists. In-person consensus review by all 3 pathologists was conducted in cases of disagreement.

Statistical Analysis

De-identified data were electronically transcribed from the data-collection sheets and stored in a secure Web-based REDCap database. Relationships between clinical variables and ER IHC results were assessed with Pearson χ^2 tests. Estrogen receptor IHC concordance was assessed using the McNemar test. Statistical significance was declared based on $P < .05$. Measure of agreement was determined using the Cohen κ coefficient. Performance characteristics, including sensitivity and specificity, were evaluated with 95% CIs. All the statistical analyses were performed using the statistical computing software SPSS (version 20, SPSS Inc).

RESULTS

A total of 87 patients were recruited from the FNAB clinic, but 1 patient with an insufficient cell block was excluded from the analysis (Figure 1). All 86 remaining patients were female, with a median age of 50.5 years (range, 25–84 years). Of these 86 patients, 51 (59.3%) presented with masses that were more than 5 cm in greatest diameter. Fifty-four patients (62.8%) had palpable axillary lymphadenopathy; all 54 were confirmed to have metastatic breast adenocarcinoma by FNAB (Table 1). The proportion of positive ER IHC on cell blocks performed locally at MNH was 41 of 86 (48%) and negative ER IHC was 45 of 86 (52%). Estrogen receptor positivity on cell blocks showed a statistically significant relationship with lower pathologic tumor grade (P <.001) (Table 2). There was no statistically significant relationship between ER positivity on cell blocks and age (P = .50), axillary lymph node metastasis (P = .91), tumor size (P = .74), or histologic subtype (P = .20) (Table 2).

Of the 86 study cases, 65 cell blocks were available for ER analysis at both MNH and UCSF. Twenty-nine cases were ER positive at MNH of 31 ER-positive cases at UCSF (93.5% concordance rate), whereas 32 cases were ER negative at MNH of 34 ER-negative cases at UCSF (94.1% concordance rate) (Table 3). The overall concordance rate of ER IHC performed on UCSF and MNH cell block pairs was 93.8% (61 of 65) (κ = 0.88) (Table 3). No statistically significant difference was observed between ER IHC results on the UCSF and MNH cell blocks (P.>.99) (Figure 2, A through D). The sensitivity and specificity of ER IHC of breast cancer on cell blocks was 93.5% (95% CI, 78.6%–99.2%) and 94.1% (95% CI, 80.3%–99.3%), respectively. Four pairs were discordant: 2 false-negative and 2 false-positive cases. Among the 2 false-positive cases, in which ER was noted to be positive at MNH but negative at UCSF, the cell blocks had low cellularity but were overall considered adequately cellular for analysis at both sites. One of these cases had normal duct-lobular elements, which served as a positive internal control. In the 2 false-negative cases where UCSF cell block IHC was positive and MNH cell block IHC was negative, the 2 MNH cell block sections were considered sufficient for ER testing, but, again, had low cellularity. These cases did not contain normal duct-lobular elements.

Of the 86 cases with FNAB cell blocks, we were able to access 62 tissue block specimens, which were obtained from open biopsies (n = 30), mastectomies (n = 24), and core needle biopsies (n = 9). The most frequent histologic subtype was invasive ductal carcinoma (55 of 62; 88.7%). A total of 43 available paired cases between UCSF cell blocks and MNH tissue blocks were analyzed with the following results: 19 MNH tissue blocks compared with 21 UCSF cell blocks were ER positive (90.5% concordance rate) and 19 MNH tissue blocks compared with 22 UCSF cell blocks were ER negative (86.4% concordance rate), resulting in 5 discordant pairs: 3 false-positive and 2 false-negative MNH tissue blocks (Table 4). Among the false-positive cases, 3 corresponding cell blocks were also assessed and considered sufficient for testing. As mentioned previously, 1 of these cell blocks had normal duct-lobular elements that served as a positive internal control for the negative IHC at UCSF. In the 2 cases in which UCSF ER IHC on cell blocks was positive but MNH ER IHC on tissue blocks was negative, 1 case was a mastectomy specimen with suboptimal fixation and morphologic evidence of poor cellular preservation. The remaining

surgical specimens showed satisfactory morphology and ER IHC staining in normal ducts and lobules. The cause of discrepancy in the 3 false-positive incisional biopsies and the 1 false-negative case was unclear, and the cases remained discrepant after repeating IHC on both the cell blocks and tissue blocks. The overall concordance rate of ER IHC performed on UCSF cell block and MNH tissue block pairs was 88.3% (38 of 43; $\kappa = 0.77$) (Table 4). No statistically significant difference was observed between ER IHC on the cell blocks and tissue blocks ($P > .99$). The sensitivity and specificity of ER IHC of breast cancer on cell blocks were 90.5% (95% CI, 69.6%–98.8%) and 86.4% (95% CI, 65.1%–97.1%), respectively.

In addition, the study analyzed a total of 62 MNH tissue block and MNH cell block pairs with the following results: 29 cell blocks compared with 33 tissue blocks were ER positive (87.9% concordance rate) and 27 cell blocks compared with 29 tissue blocks were ER negative (93.1% concordance rate). The overall concordance rate of ER IHC performed on cell blocks and tissue block pairs was 90.3% ($\kappa = 0.81$) (Table 5). No statistically significant difference was observed between ER IHC on MNH cell blocks and MNH tissue blocks ($P = .69$) (Table 5; Figure 2, E and F). The sensitivity and specificity of ER IHC on cell blocks were 87.9% (95% CI, 71.8%–96.6%) and 93.1% (95% CI, 77.2%–99.2%), respectively. Six pairs were discordant among this pairwise comparison: 4 false-negative and 2 false-positive, using the MNH tissue blocks to represent the current standard of clinical care. All of the 4 false-negative cases were considered sufficient for testing but were scantly cellular. In 1 of the 2 false-positive cases where the ER IHC in the cell block was positive but in the tissue block was negative, again, the previously mentioned mastectomy specimen with suboptimal fixation likely affected the ER IHC results in the tissue block. The cause of discrepancy in the second case was unclear, and the case remained discrepant after IHC was repeated on both the cell block and the tissue block, but the discrepancy could partly be due to differences in antibodies used between MNH and UCSF.

Overall, there was strong concordance between the ER IHC performed on cell blocks at both sites and between ER IHC performed on cell blocks and tissue block samples in Tanzania.

DISCUSSION

In the current study, we investigated the performance of ER IHC on FNAB cell blocks from breast carcinomas in a low-resource setting. To our knowledge, this study is the largest series to evaluate the diagnostic accuracy of ER IHC performed on FNAB formalin-fixed cell block samples in sub-Saharan Africa and the first of its kind in Tanzania. Approximately half of the breast cancers evaluated were ER positive, which is similar to previous studies from Tanzania, where ER positivity ranged from 33% to 48%.[2–5,8] Of note, a review of breast cancer in sub-Saharan Africa showed a highly variable rate of ER positivity that ranged between 36% and 79%, but these data are limited by the lack of cancer registries and high-quality pathology laboratories.[23] Therefore, epidemiologic studies that use high-quality pathology techniques and interpretation are imperative to better understand the characteristics of breast cancer in this region. The study showed ER expression on cell blocks was significantly associated with lower pathologic tumor grade. All grade 1 tumors, based on the modified Bloom-Richardson score,[24] were ER positive, whereas more

than two-thirds of grade 3 tumors were ER negative, implying an inversely proportional relationship. No association was observed between ER expression on cell blocks and age, tumor size, lymph node involvement, or histologic subtype.

Overall, there was excellent concordance among the 3 pairwise comparisons of ER IHC results. The study revealed overall concordance rates of 93.8% (MNH versus UCSF cell blocks), 88.3% (MNH tissue blocks versus UCSF cell blocks), and 90.3% (MNH cell blocks versus MNH tissue blocks), and is consistent with the literature, where overall concordance rates ranged from 82% to 99%.[14,18,25] The majority of discrepancies among false-positive and false-negative cases may be attributable to intratumoral heterogeneity or limited FNAB sampling, as well as the use of different antibody clones from different manufacturers. This notion raises the question of whether specimen adequacy criteria should be established for cell blocks when evaluating for predictive biomarkers. In one case in which the cell block was positive by ER IHC performed at both MNH and UCSF and the tissue block was negative, the paired histologic specimen demonstrated evidence of suboptimal fixation, including poorly preserved cellular detail and architecture of the tumor and adjacent normal ductal structures, which likely affected ER IHC expression of the tissue specimen.

In addition, the MNH pathology laboratory protocol for ER IHC has undergone only limited validation and does not currently adhere to ASCO/CAP specimen handling guidelines, which may explain the lack of staining in the tissue specimens for which the corresponding cell blocks showed positive results. Of note, according to ASCO/CAP guidelines, cell block specimens are an acceptable sample type for ER testing and do not require additional validation.[20] Moreover, given the risk of inconsistent formalin fixation and prolonged ischemic times with tissue samples in many low-resource settings, FNAB samples may yield more reliable testing.

Increasing capacity for ER testing in particular would have high clinical impact, and would render a larger proportion of patients eligible for life-prolonging hormonal therapy that is inexpensive and widely available. Studies have shown that adjuvant endocrine therapy reduces the risk of recurrence and cancer-related mortality in patients with resected ER-positive breast cancer and also provides improved disease-free survival in women with metastatic disease.[26–28] Furthermore, this current study also serves as a guide for the evaluation and validation of PR and HER2 IHC in cell blocks from breast cancer specimens not only at MNH and in Tanzania, but also in other regions with similar resource constraints.

In Tanzania, there is an urgent need to develop high-quality pathology services that are reliable, accurate, and resource appropriate. Cytopathology is able to deliver rapid accurate diagnoses with minimal equipment and less laboratory infrastructure compared with histopathology, but its utility is limited by the skill of the operator and it requires specialized training.[29,30] Adopting routine formalin-fixed cell blocks at MNH would enhance the hospital’s diagnostic capacity by allowing IHC to be performed on FNAB material and would reduce the need for open biopsies to render definitive diagnoses on various tumor types, and is thus more cost-effective to health care providers and both less traumatic and more economical to patients who have to pay for the biopsy procedure and subsequent laboratory investigations. However, successful implementation of comprehensive

cytopathology services will require significant capacity-building efforts, including dedicated training as well as laboratory quality assurance and standardization.[30–32] Studies have shown that various training models in cytopathology are effective, including fellowships, Web-based modules, and intensive workshops at our institution.[29,33–35] However, the lack of systematic evaluation and standardization of the dozens of available cell block preparation methods limits the expansion of the use of the same in low-resource settings.[36–39] Strengthening the capacity of diagnostic cytopathology services by coupling them with ancillary tests such as cell blocks and IHC would also improve cancer care in Tanzania by shortening time and reducing the cost needed to achieve a definitive diagnosis.

Limitations of this study include the inability to control the quality of the tissue block samples, which were processed and tested using routine workflow and protocols. Therefore, cell blocks were transferred to UCSF for confirmatory testing and used as the gold standard. Because of different public procurement regulations and more limited resource availability in Tanzania, and the decision to use the well-established and preexisting clinical protocol at UCSF, testing was performed using 2 different antibody clones. Although tumor cells from ductal carcinoma in situ cannot be distinguished from the invasive component in FNAB specimens, all of the patients in this study presented with a palpable mass, and the majority of breast cancer patients in Tanzania present with locally advanced or metastatic breast carcinoma. In future clinical practice, sampling a lymph node involved by metastatic tumor would ensure that the invasive component is being tested. In addition, cell blocks are typically not collected for breast carcinoma at MNH, and the cell block processing method currently in place uses Bouin fixative, which does not adhere to ASCO/CAP processing guidelines for breast biomarkers, and, using current IHC protocols, leads to complete tissue lifting and loss after antigen retrieval for IHC. A new cell block processing method using 10% neutral well-buffered formalin was introduced for the current project, with which the study technician progressively became more proficient over time. Thus, the current study investigators expect to include the formalin-based cell block processing method in the routine diagnostic algorithm in the near future.

In summary, the validation of ER IHC of breast cancer on cell blocks at MNH showed high concordance between cases performed on the same cell block material with a Clinical Laboratory Improvement Amendments of 1988–accredited laboratory and with tissue blocks from corresponding surgical specimens, which is the current clinical protocol at MNH. Thus, ER IHC on cell blocks is feasible and can be adopted in a low-resource setting. The ability to perform ER IHC on cell blocks might improve the turnaround times for ER IHC results and help patients with breast cancer access hormonal therapy without necessitating surgery. Further, analyzing ER by IHC on cell blocks preserves resources and reduces costs by avoiding surgery for the sole purpose of ER evaluation, and this renders the whole process more economical to heath care providers and health insurers as well as patients. The results of this study are expected to have high clinical impact and will significantly build laboratory capacity at MNH and subsequently facilitate the expansion of cytopathology services in the country.

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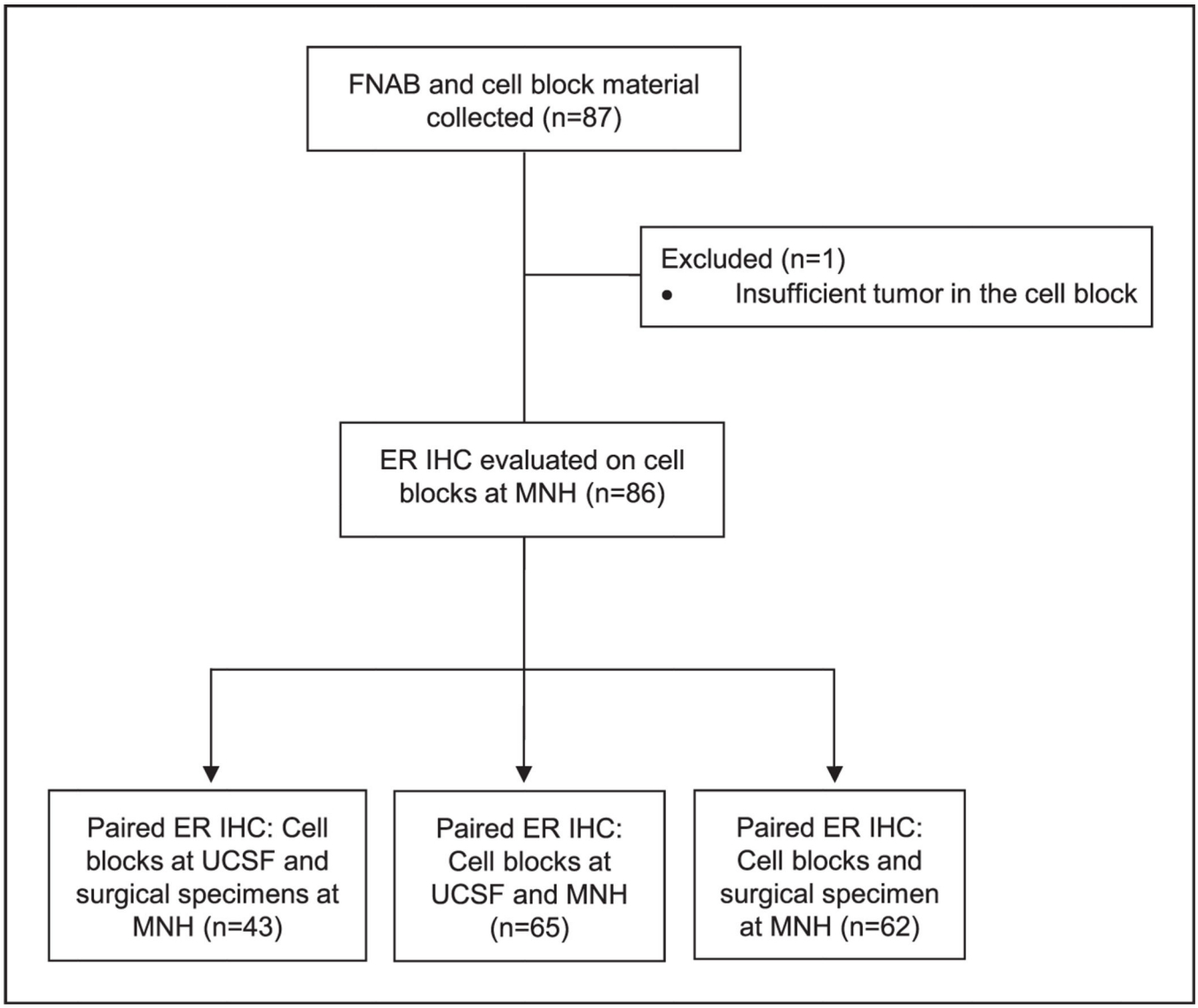

Figure 1.

Sample collection and estrogen immunohistochemistry testing. Abbreviations: ER, estrogen receptor; FNAB, fine-needle aspiration biopsy; IHC, immunohistochemistry; MNH, Muhimbili National Hospital; UCSF, University of California, San Francisco.

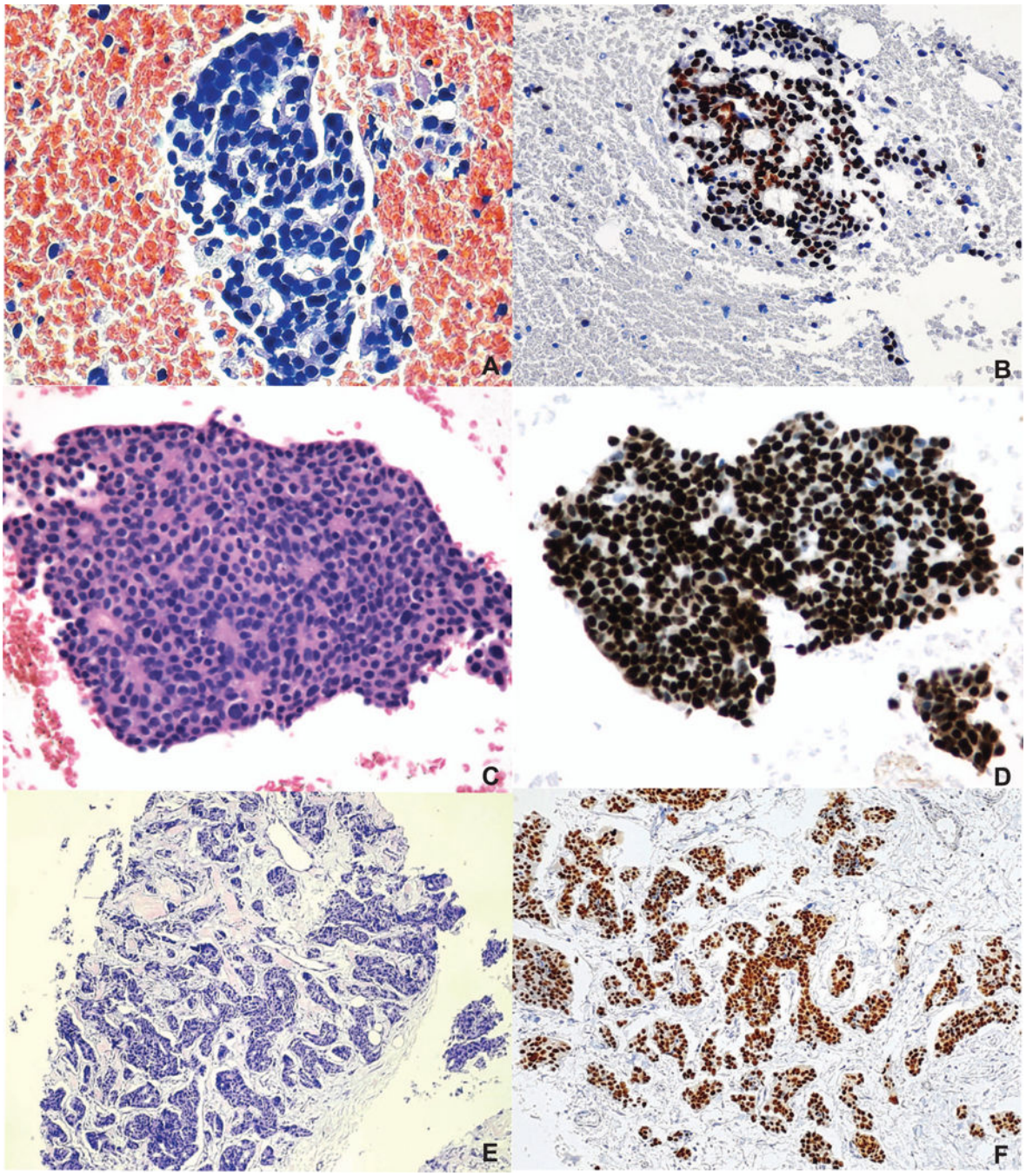

Figure 2.

A and B, Histologic section and estrogen receptor (ER) immunohistochemistry (IHC) performed on cell block at Muhimbili National Hospital (MNH) from a patient with invasive ductal carcinoma. The IHC shows clusters of tumor cells with strong and diffuse nuclear staining. C and D, Histologic section and ER IHC performed on the same cell block at University of California, San Francisco. The IHC shows clusters of tumor cells with strong and diffuse nuclear staining. E and F, Histologic section and ER IHC from the corresponding mastectomy specimen performed at MNH. The section reveals infiltrating glands with an

associated desmoplastic reaction; IHC demonstrates strong and diffuse nuclear staining (hematoxylineosin, original magnifications ×400 [A and C] and 3200 [E]; ER IHC, original magnifications 3400 [B and D] and ×200 [F]).

Table 1.

Clinicopathologic Characteristics of Study Population (N = 86)

Characteristic	No. (%)
Tumor laterality	
Left	40 (46.5)
Right	46 (53.5)
Clinical tumor size, cm	
T1 (≤2)	2 (2.3)
T2 (>2 to ≤5)	33 (38.4)
T3 (>5)	51 (59.3)
Axillary lymphadenopathy	
Palpable	54 (62.8)
Nonpalpable	32 (37.2)
Axillary lymph node metastasis	
Present	54 (62.8)
Absent	32 (37.2)

Abbreviation: T, Tumor size per AJCC 8th edition.[40]

Table 2.

Relationships Between Estrogen Receptor (ER) Status and Age and Tumor Characteristics

	ER Status, No. (%)			
	Positive (n = 41)	**Negative (n = 45)**	**Total (N = 86)**	***P* Value**
Age group, y				
<35	6 (50.0)	6 (50.0)	**12** (100)	.50
35–55	20 (54.1)	17 (45.9)	**37** (100)	
>55	15 (40.5)	22 (59.5)	**37** (100)	
Axillary lymph node metastasis				
Present	26 (48.1)	28 (51.8)	**54** (100)	.91
Absent	15 (46.9)	17 (53.1)	**32** (100)	
Tumor size, cm				
≤2	1 (50.0)	1 (50.0)	**2** (100)	.74
>2 to ≤5	14 (42.4)	19 (57.6)	**33** (100)	
>5	26 (51.0)	25 (49.0)	**51** (100)	
Tumor grade[a]				
1	11 (100)	0 (0)	**11** (100)	.001
2	6 (50.0)	6 (50.0)	**12** (100)	
3	14 (35.9)	25 (64.1)	**39** (100)	
No available tissue biopsy	10 (41.7)	14 (58.3)	**24** (100)	
Histologic subtype				
Invasive ductal carcinoma	28 (50.9)	27 (49.1)	**55** (100)	.22
Invasive lobular carcinoma	2 (100)	0 (0.0)	**2** (100)	
Papillary carcinoma	0 (0.0)	1 (100)	**1** (100)	
Medullary carcinoma	0 (0.0)	1 (100)	**1** (100)	
Mucinous carcinoma	1 (100)	0 (0.0)	**1** (100)	
Carcinoma, NOS	0 (0.0)	2 (100)	**2** (100)	
No available tissue biopsy	10 (41.7)	14 (58.3)	**24** (100)	

Abbreviation: NOS, not otherwise specified.

[a]Modified Bloom-Richardson grading system.[24]

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Table 3.

Comparison of Estrogen Receptor Immunohistochemistry Results in Muhimbili National Hospital (MNH) Cell Blocks (CB) Versus University of California, San Francisco (UCSF) CB

	MNH CB			
	Positive, No. (%)	**Negative, No. (%)**	**Concordance, %**	***P* Value**
UCSF CB				
Positive, No. (%)	29 (93.5)	2 (6.5)	93.5	>.99
Negative, No. (%)	2 (5.9)	32 (94.1)	94.1	

Table 4.

Comparison of Estrogen Receptor Immunohistochemistry Results in Muhimbili National Hospital (MNH) Tissue Blocks (TB) versus University of California, San Francisco (UCSF) Cell Blocks (CB)

	MNH TB			
	Positive, No. (%)	**Negative, No. (%)**	**Concordance**	***P* Value**
UCSF CB				
Positive, No. (%)	19 (90.5)	2 (9.5)	90.5	>.99
Negative, No. (%)	3 (13.6)	19 (86.4)	86.4	

Table 5.

Comparison of Estrogen Receptor Immunohistochemistry Results in Muhimbili National Hospital (MNH) Cell Blocks (CB) Versus MNH Tissue Blocks (TB)

	MNH CB			
	Positive, No. (%)	**Negative, No. (%)**	**Concordance, %**	***P* Value**
MNH TB				
Positive, No. (%)	29 (87.9)	4 (12.1)	87.9	.69
Negative, No. (%)	2 (6.9)	27 (93.1)	93.1	