Breast Ultrasound Volume Sweep Imaging

A New Horizon in Expanding Imaging Access for Breast Cancer Detection

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Objective—The majority of people in the world lack basic access to breast diagnostic imaging resulting in delay to diagnosis of breast cancer. In this study, we tested a volume sweep imaging (VSI) ultrasound protocol for evaluation of palpable breast lumps that can be performed by operators after minimal training without prior ultrasound experience as a means to increase accessibility to breast ultrasound.

Methods—Medical students without prior ultrasound experience were trained for less than 2 hours on the VSI breast ultrasound protocol. Patients presenting with palpable breast lumps for standard of care ultrasound examination were scanned by a trained medical student with the VSI protocol using a Butterfly iQ handheld ultrasound probe. Video clips of the VSI scan imaging were later interpreted by an attending breast imager. Results of VSI scan interpretation were compared to the same-day standard of care ultrasound examination.

Results—Medical students scanned 170 palpable lumps with the VSI protocol. There was 97% sensitivity and 100% specificity for a breast mass on VSI corresponding to 97.6% agreement with standard of care (Cohen's $\kappa = 0.95$, $P < .0001$). There was a detection rate of 100% for all cancer presenting as a sonographic mass. High agreement for mass characteristics between VSI and standard of care was observed, including 87% agreement on Breast Imaging-Reporting and Data System assessments (Cohen's $\kappa = 0.82$, $P < .0001$).

Conclusions—Breast ultrasound VSI for palpable lumps offers a promising means to increase access to diagnostic imaging in underserved areas. This approach could decrease delay to diagnosis for breast cancer, potentially improving morbidity and mortality.

Key Words—breast; breast cancer; global health; telemedicine; ultrasound

Breast cancer is the most common cancer in women, and its prevalence is increasing. In 2020, it was predicted there would be 1.7 million new cases of breast cancer with most cases and deaths occurring in low- and middle-income countries (LMICs).[1] Furthermore, it is estimated there has been a nearly 60% increase in both incidence and mortality of breast cancer in LMICs in the last 20 years.[2] In comparison, there has been a reported breast cancer mortality decrease of up to 40% in those with access to screening mammography.[3–5] Delay to diagnosis is harmful as prompt treatment is needed to optimize outcomes from breast cancer. While it is estimated more than 70% of patients in high-income countries are

diagnosed with breast cancer in stage 1 and 2, only 20–50% of patients will present with stage 1 and 2 disease in LMICs.[6] In a study conducted in Northern Peru, in a sample of 113 women, 105 self-diagnosed their cancer, and the mean total delay from symptom onset to initiation of treatment was 407 days.[7] Furthermore, although the majority of breast cancer deaths now are expected to occur in LMICs, only 5% of global spending on cancer is targeted to those countries.[8] Given the severity and urgency of this public health crisis, new solutions are needed to help improve access to care and decrease delays in diagnosis.

Diagnostic imaging is essential for accurate and timely diagnosis of breast pathology, but over half of the world's population has limited access to medical imaging.[9] Ultrasound is a portable and cost-effective imaging modality that is first-line evaluation for breast pathology with potential to improve access to medical imaging in LMICs.[10] However, ultrasound's deployment has been limited by a lack of trained sonographers who may require months to years of training.[11,12] Volume sweep imaging (VSI) offers one means to circumvent the need for a trained sonographer by employing a standardized imaging protocol that can be performed with 1 to 2 hours of training. In VSI, an inexperienced operator obtains video clips of the target region based only on external body landmarks. These video clips are then sent to an imaging professional for interpretation.

The goal of this study was to test the diagnostic accuracy of a VSI protocol for palpable breast lumps in relation to standard of care imaging. While there have been several studies of VSI for other indications and a few studies exploring the use of breast ultrasound in underserved areas, to our knowledge, there has been no previous study regarding the diagnostic accuracy of breast VSI.[13–20] Based on prior VSI studies and general knowledge of breast ultrasound, we hypothesized that breast VSI interpretations would show high agreement with same-day standard of care imaging interpretations.

Materials and Methods

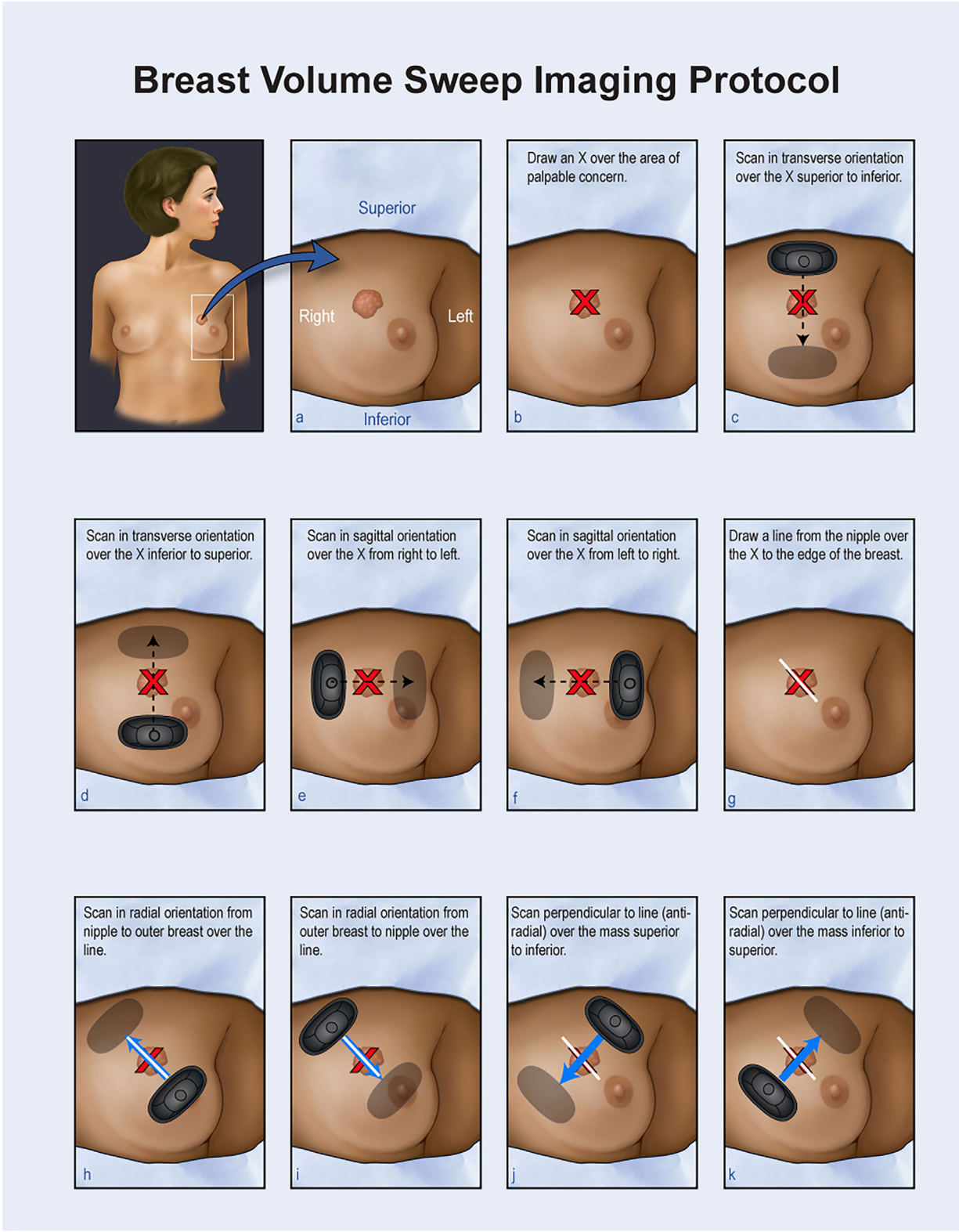
Breast VSI

VSI is an imaging technique in which the operator sweeps the ultrasound probe over the target region in relation to external body landmarks requiring no significant anatomic or medical knowledge. Sweeps are recorded as video clips which are then saved for later interpretation by a specialist. It must be emphasized that the operator does not interpret the images. Rather, operators, who may have no medical training, are encouraged to focus on their probe technique during the sweep. Individuals without prior ultrasound experience or medical background can learn VSI over the course of hours as opposed to months or years for traditional sonography.[21] VSI for lung, obstetrics, thyroid, and right upper quadrant scanning has been previously described and piloted successfully.[14–17,19]

The breast VSI protocol used in our study is only indicated for evaluation of palpable breast lesions. The first step in performing this protocol is to mark the palpable area with an "X." With the patient lying supine with their arm above their head, the marked palpable area is scanned with eight sweeps (Figure 1). Sweeps are conducted in the transverse, sagittal, radial, and anti-radial orientations to image the mass in different planes and increase redundancy. As each sweep images the same location, there are 8 separate attempts to acquire a diagnostic image of the palpable area greatly increasing the chance of obtaining at least one diagnostic view. This protocol takes minimal time to learn (approximately 1–2 hours). Patients are scanned with a breast preset, and operators do not change any probe settings from the preset. Again, the operator is not interpreting the image, and VSI is ideally performed focusing on the sweep over the target region, not the ultrasound screen. Each sweep is recorded as a cine clip that is later reviewed by an expert interpreter asynchronously. VSI image acquisition is completely independent of specialists. The exam is short in duration and can be performed within 5 minutes including setup. The breast and axilla outside the palpable abnormality is not imaged.

Although consideration has been given to the use of ultrasound as a primary screening modality in the absence of mammography, we are only proposing VSI for targeted evaluation of palpable lesions and not generalized scanning for screening at this time.[22,23] The use of ultrasound for palpable lesions is well established and is considered standard of care.[24–27] Even in high-income settings, the most common presenting symptom of breast cancer is a palpable lesion.[28] Additionally, a study of 1222

Figure 1. Breast volume sweep imaging (VSI) protocol. Poster illustrating how to perform the breast VSI protocol.



women with breast cancer found that 13% presented with a palpable mass even after having a mammography within the past year, often with aggressive cancer.[29] In areas without screening, the vast majority of breast cancers will present as a palpable lesion.[30] Breast VSI may also be useful for infectious conditions including suspected breast abscesses.[31,32]

Study Design

We piloted the breast VSI protocol in an academic setting after receiving institutional review board approval from the University of Rochester Research Subjects Review Board. Over the course of a single training session less than 2 hours, medical students with no prior ultrasound experience were trained how to perform the breast VSI protocol. Trainees were provided a poster and written instructions of the protocol (Figure 1). Training consisted of a brief didactic explanation of the protocol followed by hands on practice. Prior to the end of the training session, trainees performed 10 consecutive error-free scans.

Patients over 18 years of age, both male and female, presenting for routine standard of care ultrasound with a palpable mass were eligible to enroll in the study. All eligible subjects presenting to clinic during scan times were approached and informed about the study by a member of the clinical breast imaging team. If interested, the subject provided informed consent, and a medical student scanned the patient with the VSI protocol. The medical student scanning was blinded to the standard of care results and instructed not to look at the screen while scanning. Each subject enrolled in the study also completed their same-day standard of care ultrasound obtained by a professional sonographer specialized in breast imaging. Pathological confirmation of the mass findings was not a specific part of the study procedure but was noted when incidentally obtained. Benign pathology was biopsy/surgically proven or Breast Imaging-Reporting and Data System (BI-RADS) 1/2. Indeterminate pathology was BI-RADS 3 (not definitively benign or malignant). Finally, malignant pathology was biopsy/surgically proven.

The VSI scans were performed with the Buttefly iQ handheld ultrasound probe (Butterfly Network, Guilford) using the small organ preset (Figure 2). The iQ is a handheld ultrasound probe that connects to a tablet and operates at a frequency between 1 and 10 MHz. It was purchased for a cost of approximately $2000. The standard of care ultrasound was performed on a state-of-the-art Logiq e10 (General Electric, Boston) or Epiq 7G (Phillips, Amsterdam). At the time of writing, these machines are approximately 50 to 75 times more expensive than the iQ. The standard of care ultrasound settings vary between exams as set by the expert sonographers to optimize imaging acquisition. In general, standard of care exams is performed with a high-frequency linear transducer. The standard of care frequency ranged between 15 and 18 MHz.

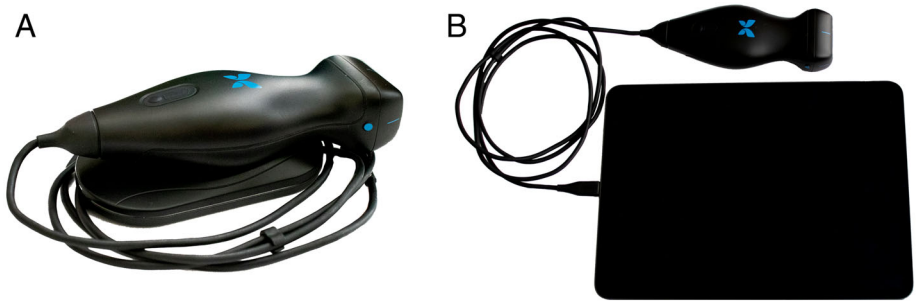
Sample Size Calculation

Sample size was calculated based on an estimated prevalence of all malignant lesions among those scanned with palpable masses, desired sensitivity and specificity, and an acceptable width of the 95% confidence interval, using the method described by Buderer.[33] Assuming $\alpha = 0.05$, prevalence = 25%, and a confidence interval width of 10%, 140 subjects would be required to observe 90% sensitivity and 46 would be required to observe 90% specificity. Taking the larger of these, a total of 140 subjects are required. Assuming 10% of images are nondiagnostic or indeterminate, this brings the final sample size to 154 subjects. As this sample size is based upon an estimated prevalence of malignancy, we recruited 160 subjects to improve power.

Readings

Both standard of care and VSI studies were interpreted in accordance with the BI-RADS Atlas.[34] BI-RADS was developed by the American College of Radiology and offers a standardized approach to interpreting and reporting breast imaging findings that is considered standard of care and regularly used in breast imaging practices.[35] In addition to the overall BI-RADS assessment, each study was also evaluated for the presence/absence of a mass, mass size (mm), mass orientation (parallel, antiparallel, or not visualized), mass shape (round, oval, irregular, or not visualized), mass margins (circumscribed, indistinct, microlobulated, angular, spiculated, or not visualized), mass echogenicity (anechoic, hypoechoic, isoechoic, complex echogenicity, or not visualized), and mass posterior acoustic features (none, enhancement, shadowing, combined, or not visualized) according to

Figure 2. Butterfly iQ. **A**, Photograph of the Butterfly iQ handheld ultrasound probe. **B**, Photograph of the Butterfly iQ connected to an Apple iPad.



the BI-RADS lexicon. Since the operators were scanning using the iQ's small organ preset, large masses over 3 to 4 cm are not completely included in the field of view. In these cases, the reader still performed their best size estimation. Readers picked a single best descriptor for each category with multiple choices.

Two breast imaging attendings served as blinded readers for the VSI ultrasounds. Each VSI study was interpreted by one blinded reader who did not interpret the standard of care exam. The readers offered a BI-RADS interpretation of the VSI exam as described above, the same way they would read any standard of care ultrasound. This interpretation was based off the best VSI sweep images available among all 8 sweeps. Overall image quality for the VSI scan was classified as "diagnostic" or "nondiagnostic." Additionally, the percent visualization of each mass on each sweep was recorded. Readers also selected the perceived sweep orientation that best imaged the palpable finding. Any other notes were documented with additional free text comments. For the purposes of assessment of the VSI scans, the reads were conducted mostly blinded with minimal offered information as clinical information can bias interpretation. The only clinical details disclosed related to the patient's sex and the presence of infectious symptoms as these fundamentally inform interpretation of breast ultrasound findings. In cases of disagreement between VSI and standard of care on the presence of a mass, two expert breast imagers reviewed the case to ascertain the source of the discrepancy.

Standard of care examinations were read per standard clinical practice by an attending breast radiologist unblinded to the clinical history after images were obtained by an experienced certified sonographer. However, comparison of BI-RADS assessments between VSI and standard of care is problematic as VSI only examines the palpable location, not the entire breast. In contrast, the BI-RADS assessment in the standard of care examination applies to the overall evaluation of the entire area imaged with the final score reflecting the most concerning finding. Similarly, we asked VSI readers to interpret the exams blinded from clinical information including prior exams aside from the patient's sex and signs of infection, but the clinical context often informs the final BI-RADS assessment in standard of care imaging. Therefore, in an effort to address these problems and provide a more valid comparison, in addition to the regular overall BI-RADS assessment that is assigned to every breast ultrasound study, an adjusted BI-RADS assessment was determined by the attending reading the standard of care examination based solely on the imaging findings at the palpable region. This is similar in concept to the idea of a "forced" BI-RADS assessment already described in the literature.[36,37] Readers were instructed to ignore any clinical knowledge outside the patient's sex and history of infectious symptoms (in accordance with the procedure for the VSI reads) when determining the adjusted assessment.

Statistical Analysis

Throughout, continuous variables are summarized as mean ± standard deviation, and categorical variables are summarized as proportion (95% confidence interval [CI]). Agreement on categorical measures between VSI and standard of care ultrasound was calculated using Cohen's kappa. Agreement on continuous measures was quantified using the intraclass correlation coefficient

(ICC) and Bland–Altman analysis. ICC was calculated using a two-way mixed effects model for absolute agreement. Bland–Altman bias was calculated as VSI—standard of care. For both ICC and Bland–Altman bias, *P* values were calculated for a one-sample *t*-test comparing to a theoretical mean of 0. Sensitivity and specificity were calculated for mass detection on VSI, using standard of care as the gold standard. For calculation of BI-RADS sensitivity and specificity, VSI BI-RADS was compared to standard of care adjusted BI-RADS after grouping of categories. We considered three scenarios: 1) BI-RADS 4/5 versus 1/2/3, 2) BI-RADS 3/4/5 versus 1/2, and 3) BI-RADS 4/5 versus 1/2. BI-RADS 4/5 versus 1/2/3 assessed accuracy for likely benign findings from findings requiring biopsy. BI-RADS 3/4/5 versus 1/2 assessed accuracy for findings requiring further management from findings requiring no further management. BI-RADS 4/5 versus 1/2 removed all probably benign cases from analysis. All statistical analysis was performed using MATLAB (R2019b, The Mathworks, Inc., Natick, MA), SPSS (v26, IBM Corporation, Armonk, NY), and GraphPad Prism (v6, GraphPad Software, Inc., San Diego, CA).

Results

Medical students without prior ultrasound experience enrolled 160 patients corresponding to 170 palpable lumps. Demographics are shown in Table 1 including pathology information for the masses. All exams were rated of diagnostic imaging quality. Example benign lesions are shown in Figures 3 and 4 with comparison to standard of care imaging. Example malignant lesions are shown in Figures 5 and 6 with comparison to standard of care imaging. Online supplemental Videos S1–S4 have been provided as exemplary sweeps corresponding to the cases in the figures. Excellent agreement was seen between VSI and standard of care (Table 2). Out of the 170 lumps, there were 4 disagreements on the presence of mass between VSI and standard of care imaging. This corresponded to 97.6% agreement (Cohen's $\kappa = 0.95$ [0.89–1.0], $P < .0001$) and a 96.6% sensitivity and 100% specificity for mass detection. There were 20 cases of cancer presenting as a palpable lump with a corresponding sonographic mass, which were all detected (100% agreement). The average largest mass diameter in standard of care was 23.1 ± 16.9 mm and 22.5 ± 15.6 mm in VSI (ICC = 0.98 [0.96–0.98], $P < .0001$). The Bland–Altman Bias for these measurements was −1.02 (−7.8 to 5.77, $P = .002$) suggesting that VSI slightly underestimated mass size compared to standard of care. There was 86.5% agreement on adjusted BI-RADS assessments between VSI and standard of care (Cohen's $\kappa = 0.82$ [0.75–0.89], $P < .0001$). There was 86.4% sensitivity and 96.8% specificity for BI-RADS 4/5 versus BI-RADS 1/2/3, 88.9% sensitivity and 99% specificity for BI-RADS 3/4/5 versus BI-RADS 1/2, and 95% sensitivity and 100% specificity for BI-RADS 4/5 versus BI-RADS 1/2.

Consensus analysis of discrepancies of VSI and standard of care ultrasound was performed. Of the 4 cases where there was disagreement between VSI or standard of care as to whether there was a mass or no mass, the mass could not be seen in retrospect on consensus review. Of the 4 cases, 2 of them involved likely clinically insignificant subcentimeter masses. One of these lesions was rated as BI-RADS 3 on standard of care (<2% chance of malignancy), and the other was rated as BI-RADS 2. The third case involved an isoechoic lesion in a reconstructed breast that was difficult to discern even on standard of care imaging. This was reported as BI-RADS 3 on standard of care. The last lesion was reported to be 17 cm from the nipple, likely not truly in the breast tissue. This lesion was reported as BI-RADS 2 without clinical significance. In no case did the expert breast imagers state a sonographic mass was present that was not seen on standard of care imaging.

Consensus analysis also was performed for differences in mass size, mass characteristics, and adjusted BI-RADS assessments. In general, the disagreements between VSI and standard of care on mass characteristics and measurements were often thought to be related to the known significant inter-reader reliability that occurs in assessing mass characteristics.[38,39] The image quality of the iQ was generally noted to be of lower resolution than standard of care imaging, but this was not thought to have significantly affected the agreement between VSI and standard of care in most cases. When masses were measured over 5 mm in difference between VSI and standard of care, it was always related to a mass size greater than 4.5 cm ($n = 8$) on standard of care. The field of view on the

Table 1. Study Demographics

Measure	Category	Summary
Age (years)	-	42 ± 15.4
Sex	Female	91.8% (86.6–95.4%)
	Male	8.24% (4.58–13.4%)
Race	African American	18.8% (13.2–25.5%)
	Asian American	2.35% (0.645–5.91%)
	Hispanic	7.06% (3.7–12%)
	White	70.6% (63.1–77.3%)
	American Indian/ Alaskan Native	0.588% (0.0149–3.23%)
	Other	0.588% (0.0149–3.23%)
BMI (kg/m^2)	-	29.7 ± 7.89
Breast scanned	Left	54.7% (46.9–62.3%)
	Right	45.3% (37.7–53.1%)
Quadrant scanned	Upper outer	51.8% (44–59.5%)
	Lower outer	11.8% (7.34–17.6%)
	Upper inner	17.1% (11.7–23.6%)
	Lower inner	9.41% (5.48–14.8%)
	Retroareolar	9.41% (5.48–14.8%)
Palpable lump?	Yes	100% (97.9–100%)
Pain?	Yes	51.8% (44–59.5%)
Discharge?	Yes	8.24% (4.58–13.4%)
Fever?	Yes	2.35% (0.645–5.91%)
Trauma?	Yes	2.94% (0.962–6.73%)
Number of lumps	-	1.14 ± 0.399
Pathology	Benign	75.9% (68.7–82.1%)
	Malignant	12.9% (8.29–18.9%)
	Indeterminate	11.2% (6.86–16.9%)
Pathology proven?	Yes	25.9% (19.5–33.1%)
	No	53.5% (45.7–61.2%)
	No pathology	20.6% (14.8–27.5%)

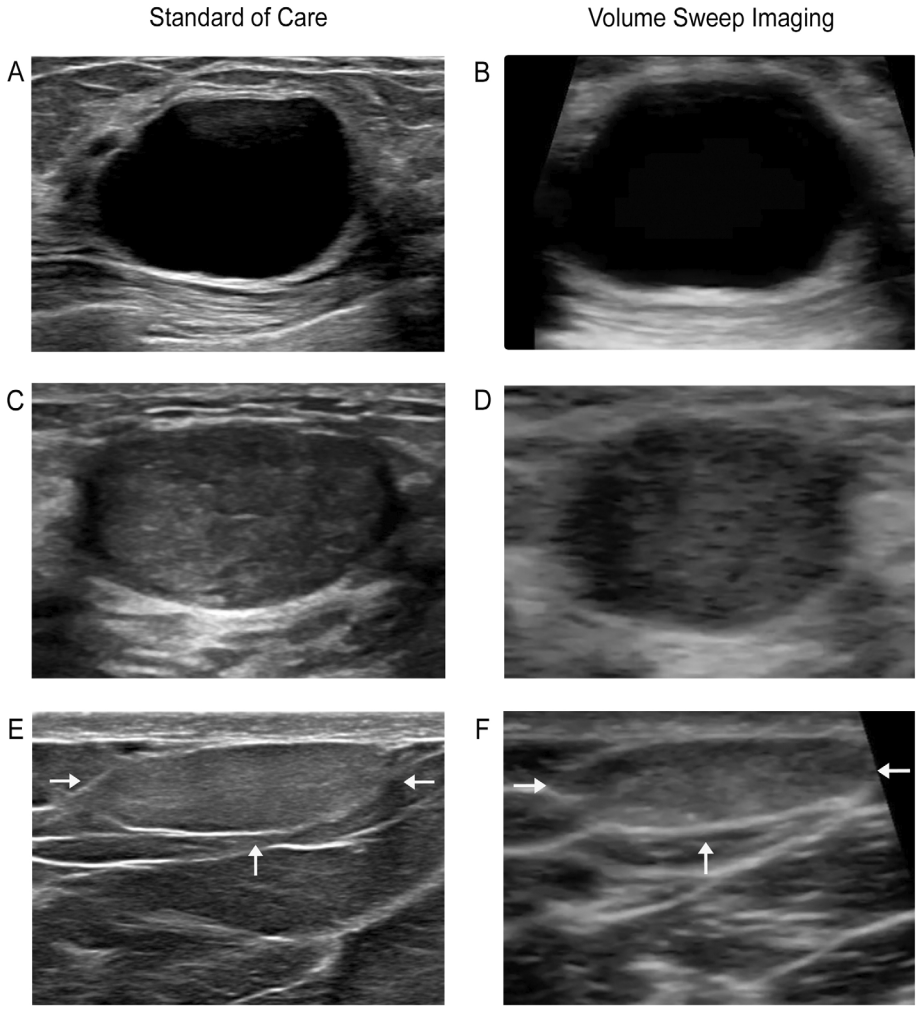
Continuous variables are summarized as mean ± standard deviation. Categorical variables are summarized as proportion (95% confidence interval).

iQ is limited, and the operators do not adjust imaging to facilitate accurate measurements in these cases which explains the discrepancies which are not likely clinically significant. In general, there was limited evaluation for large masses (>5 cm) compared to standard of care. However, these cases are generally clinically obvious and would not be necessarily indicated for routine examination with VSI. The mass sizes in our sample ranged from 4 to 120 mm. Subcentimeter lesions ($n = 15$) were often likely incidental to the palpable abnormality or superficial in nature. The smallest palpable cancer was measured at 14 mm on standard of care imaging.

There were 23 disagreements between VSI and standard of care on the adjusted BI-RADS assessments. Many of these disagreements were thought again to be related to the known inter-reader reliability in breast imaging.[38–40] The most frequent disagreement was between BI-RADS 3 and 4 ($n = 8$). On consensus analysis, these cases were borderline between the categories and management of 6-month follow-up versus immediate biopsy would likely both be reasonable in accordance with different management styles and patient preference. Most of the disagreements were often thought to be of minimal clinical significance (BI-RADS 1 versus BI-RADS 2 [$n = 2$], BI-RADS 1 versus BI-RADS 3 [$n = 2$], BI-RADS 2 versus BI-RADS 3 [$n = 5$], and BIRADS 4 versus BI-RADS 5 [$n = 4$]). Of importance, there were $n = 2$ cases of disagreement of BI-RADS 4 on standard of care and BI-RADS 1 on VSI. These were two cases of pathologically proven ductal carcinoma in situ (DCIS) diagnosed on mammography due to microcalcifications. On standard of care ultrasound, sonographers were able to identify heterogenous tissue with the benefit of the mammogram but no discrete sonographic mass. On VSI, in retrospect individuals were able to identify heterogenous tissue, but the consensus was that this would not be possible to identify blinded.

Analysis of individual VSI clips is shown in Table 3. There was no significant difference in mass presence on a sweep ($P = .40$) or percent mass visualization in any sweep ($P = .30$) when comparing all the sweeps. Clip lengths were generally under 10 seconds per sweep. The average total sweep time was 72 ± 15.3 seconds. The average file size of all clips combined was 16.9 ± 4.99 MB Readers stated they preferred having all 8 sweeps to maximize the amount of information available. Of all exams, when asked to select their most preferred sweep set, readers selected sweeps 1 to 2 (transverse) 16.6% of the time, sweeps 3 to 4 (sagittal) 16.6% of the time, sweeps 5 to 6 (radial) 17.8% of the time, and sweeps 7 to 8 (anti-radial) 11.8% of the time. No preference was selected in 37.3% of cases. Most of the time, when one sweep was considered better than another it was related to improved percent mass visualization. Technical issues such as missing sweeps were rare ($n = 4$) and seen in 2.4% of exams related to operator error or iQ technical difficulties. In all cases, technical errors were related to a minority of sweeps, and the exam was still diagnostic quality overall.

Figure 3. Benign breast lumps on standard of care ultrasound and volume sweep imaging (VSI). Benign anechoic cyst with posterior acoustic enhancement seen on standard of care ultrasound (**A**) and VSI (**B**). Hypoechoic well-circumscribed oval fibroadenoma seen on standard of care ultrasound (**C**) and VSI (**D**). Isoechoic or hyperechoic lipoma (arrows) in the superficial breast tissue on standard of care ultrasound (**E**) and VSI (**F**). Online supplemental Video S1 shows a VSI cine clip of the fibroadenoma seen in (**C**) and (**D**).



Discussion

In this study, we have shown that individuals without prior ultrasound experience were able to obtain diagnostic imaging of palpable breast lesions after minimal training with a handheld ultrasound probe. These results suggest clinically significant palpable lesions would be reasonably expected to be effectively imaged using breast VSI. Furthermore, there was high agreement between VSI and standard of care on mass size, mass features, and adjusted BI-RADS assessments suggesting that this approach has potential to distinguish between benign, indeterminate, and malignant entities. While simply identifying the presence or absence of a mass is a potentially life-saving outcome, the ability to effectively characterize lesions offers even more potential value to patients.

The VSI protocol has several uses in clinical practice with the main goal of decreasing delay to diagnosis for malignant entities. Critically, we found 100% accuracy in identifying palpable cancer presenting as a sonographic mass with VSI. Since the delay to diagnosis (sometimes on the scale of months) is a critical factor in treating cancer, deployment of this approach

Figure 4. Other benign breast lumps on standard of care ultrasound and volume sweep imaging (VSI). Hypoechoic collection in the superficial soft tissues of the breast consistent with abscess in a patient with history of infectious symptoms on standard of care ultrasound (**A**) and VSI (**B**). Complex echogenicity suspicious mass biopsied as benign on standard of care ultrasound (**C**) and VSI (**D**). Online supplemental Video S2 shows a VSI cine clip of the complex mass seen in (**C**) and (**D**).

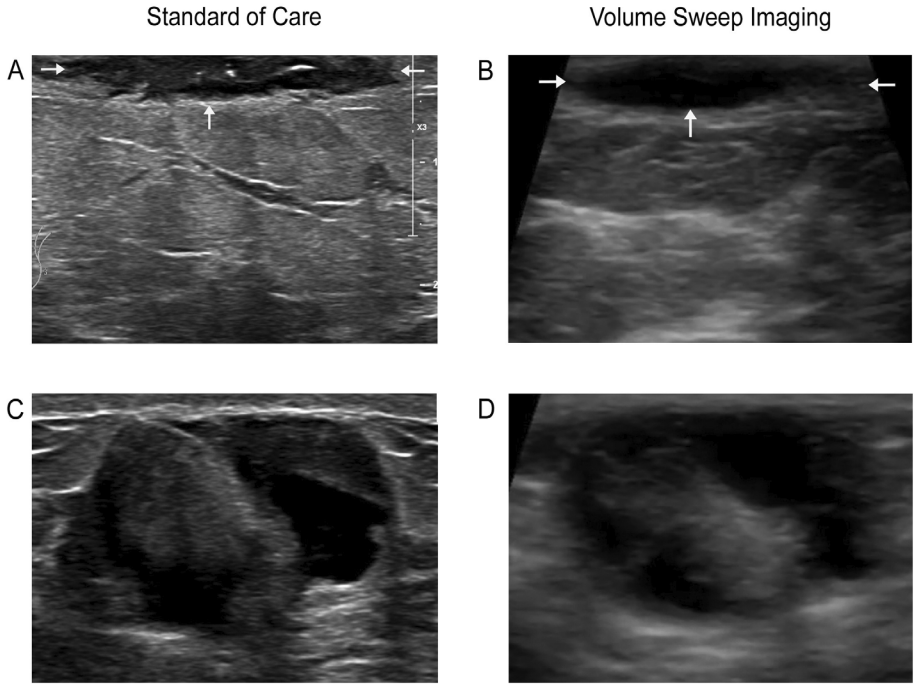


Figure 5. Cancer on standard of care ultrasound and volume sweep imaging (VSI). Complex hypoechoic microlobulated mass on standard of care ultrasound (**A**) and VSI (**B**). Irregularly shaped suspicious mass on standard of care (**C**) and VSI (**D**). Both cases correspond to pathologically proven invasive ductal carcinoma. Online supplemental Video S3 shows a VSI cine clip of the cancer seen in (**A**) and (**B**).

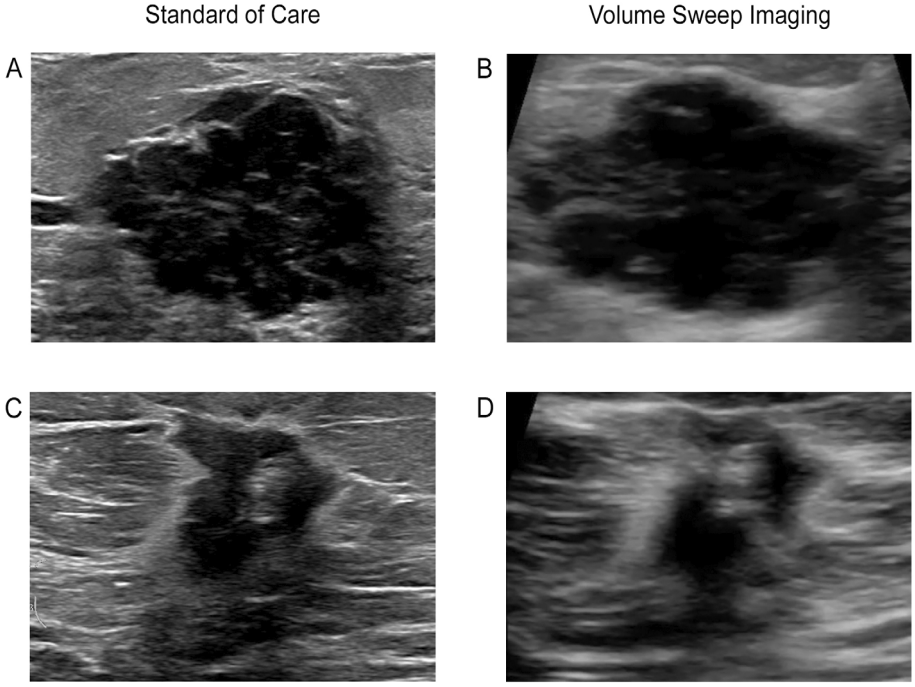
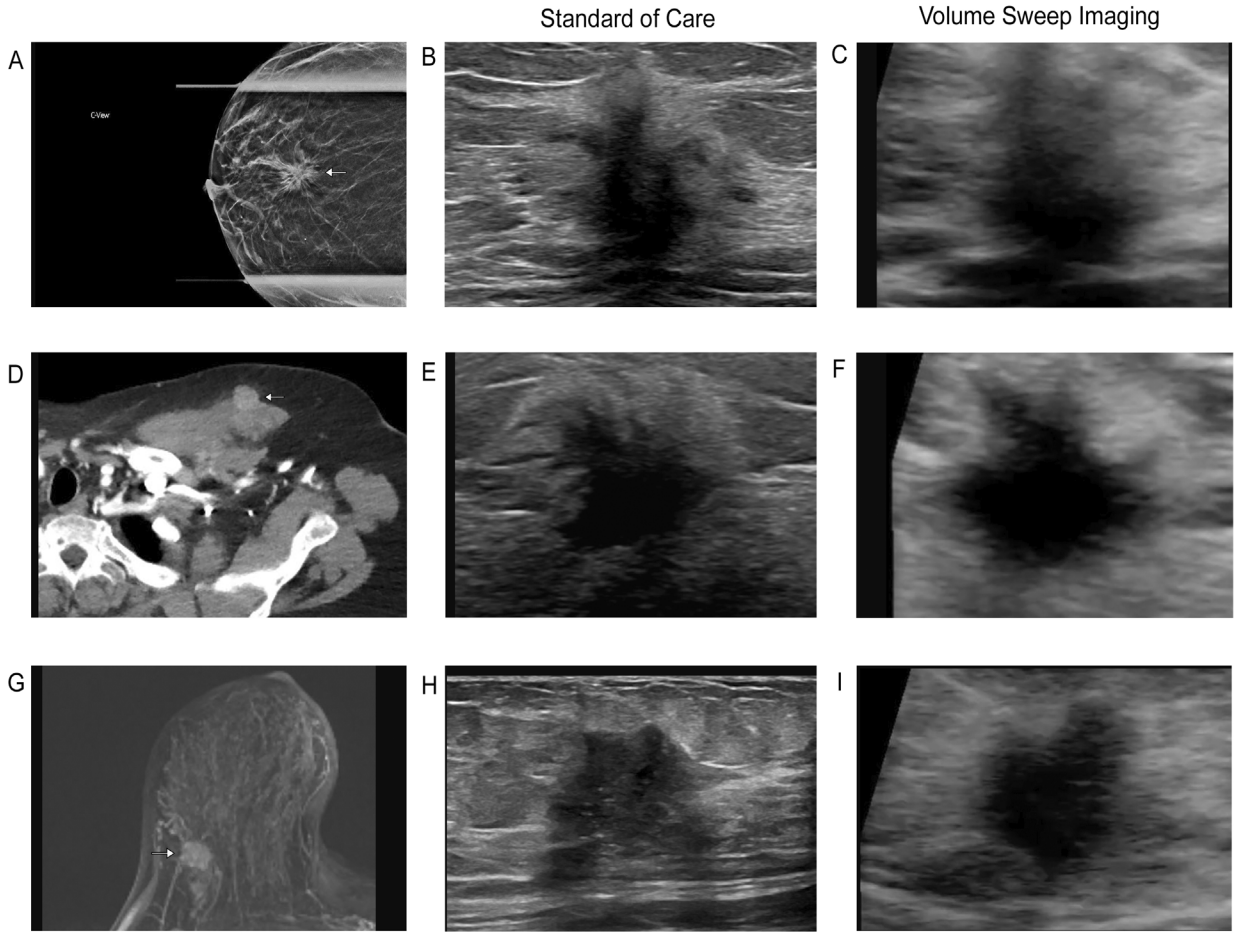


Figure 6. Cancer on standard of care imaging and volume sweep imaging (VSI). **A**, Spiculated mass on mammographic spot view (arrow). Corresponding hypoechoic mass with posterior shadowing on standard of care ultrasound (**B**) and VSI (**C**). Findings represent pathologically proven invasive lobular carcinoma. **D**, Hyperattenuating mass on CT scan in a patient with a reconstructed left breast invading the chest wall musculature (arrow). Corresponding hypoechoic spiculated mass on standard of care ultrasound (**E**) and VSI (**F**). Findings represent pathologically proven recurrent invasive ductal carcinoma. **G**, Enhancing mass on breast MRI maximum-intensity projection (arrow). Corresponding hypoechoic mass with indistinct margins on standard of care ultrasound (**H**) and VSI (**I**). Findings represent pathologically proven DCIS. Online supplemental Video S4 shows a VSI cine clip of the cancer seen in (**D**), (**E**), and (**F**).



would have potential in improving outcomes as it could substantially decrease the delay to diagnosis.[7,41] It could also reassure in patients with benign etiologies or completely negative findings which constituted a large percentage of our sample as described above. In another study of 935 palpable lumps, 39.3% were BI-RADS 1 (negative for any sonographic finding) and 8.2% malignant.[42] The epidemiological information regarding the lumps in our study has separate value as an outcome in and of itself but should be verified and compared to rural settings.

VSI protocols have been previously combined with an asynchronous telemedicine platform capable of sending imaging acquisitions over low bandwidth in the absence of a specialist. VSI for lung, obstetrics, right upper quadrant, and thyroid has been successfully piloted in the United States and Peru.[14,15,17,19] This system for palpable breast abnormalities is shown in Figure 7. It removes the need for an experienced sonographer and an available specialist allowing deployment to rural areas. Thus, we propose integration of teleultrasound

Table 2. Agreement Between VSI and Standard of Care

		Summary		Agreement	
Metric		**VSI**	**Standard of Care**	**% Agreement**	**Cohen's Kappa**
Mass visualized?	Yes	67.6% (60.1–74.6%)	70% (62.5–76.8%)	97.6%	0.95 (0.89–1, $P < .0001$)
Mass orientation	Parallel	82.6% (74.4–89%)	86.6% (79.1–92.1%)	93%	0.75 (0.58–0.92, $P < .0001$)
	Antiparallel	11.3% (6.16–18.6%)	13.4% (7.88–20.9%)		
	Not visualized	6.09% (2.48–12.1%)	0% (0–3.05%)		
Mass shape	Round	16.5% (10.3–24.6%)	17.6% (11.3–25.7%)	90.4%	0.85 (0.76–0.93, $P < .0001$)
	Oval	43.5% (34.3–53%)	39.5% (30.7–48.9%)		
	Irregular	39.1% (30.2–48.7%)	42.9% (33.8–52.3%)		
	Not visualized	0.87% (0.022–4.75%)	0% (0–3.05%)		
Mass margins	Circumscribed	65.2% (55.8–73.9%)	65.5% (56.3–74%)	85.2%	0.73 (0.61–0.85, $P < .0001$)
	Indistinct	15.7% (9.55–23.6%)	16.8% (10.6–24.8%)		
	Microlobulated	4.35% (1.43–9.85%)	7.56% (3.52–13.9%)		
	Angular	4.35% (1.43–9.85%)	4.2% (1.38–9.53%)		
	Spiculated	7.83% (3.64–14.3%)	5.88% (2.4–11.7%)		
	Not visualized	2.61% (0.541–7.43%)	0% (0–3.05%)		
Mass echogenicity	Anechoic	20.9% (13.9–29.4%)	21.8% (14.8–30.4%)	93%	0.88 (0.8–0.96, $P < .0001$)
	Hypoechoic	59.1% (49.6–68.2%)	58% (48.6–67%)		
	Isoechoic	2.61% (0.541–7.43%)	1.68% (0.204–5.94%)		
	Hyperechoic	3.48% (0.956–8.67%)	4.2% (1.38–9.53%)		
	Complex	13.9% (8.17–21.6%)	14.3% (8.55–21.9%)		
Mass posterior acoustic features	None	60.9% (51.3–69.8%)	66.4% (57.2–74.8%)	91.3%	0.83 (0.74–0.93, $P < .0001$)
	Enhancement	27.8% (19.9–37%)	26.1% (18.4–34.9%)		
	Shadowing	6.96% (3.05–13.2%)	7.56% (3.52–13.9%)		
	Not visualized	4.35% (1.43–9.85%)	0% (0–3.05%)		
BIRADS (adjusted)	1	27.1% (20.5–34.4%)	23.5% (17.4–30.6%)	86.5%	0.82 (0.75–0.89, $P < .0001$)
	2	34.7% (27.6–42.4%)	34.1% (27–41.8%)		
	3	13.5% (8.77–19.6%)	16.5% (11.2–22.9%)		
	4	20% (14.3–26.8%)	18.8% (13.2–25.5%)		
	5	4.71% (2.05–9.06%)	7.06% (3.7–12%)		

Summary values are percentage (95% confidence interval). Percent agreement is overall agreement between VSI and SOC. Cohen's kappa is presented as kappa (95% CI, *P* value), where *P* value is comparing to a theoretical kappa of 0. Anything marked not visualized was excluded from analysis.

with breast VSI to effectively deploy breast VSI to communities.

Diagnosing and treating breast cancer in the developing world poses many challenges due to a variety of systemic and cultural factors.[43] The main determinants of breast cancer outcome are early detection, accurate diagnosis, and access to optimal treatment. In LMICs, there are multifaceted and interrelated obstacles to each of these critical areas.[2,44]

Lack of health infrastructure and resources pose major impediments.[45,46] Some women may be aware of a palpable finding but have no easy access to treatment or be ignorant of its significance. The lack of screening and resources means that patients are diagnosed with advanced disease the majority of the time.[1,6,47] In addition, in many cases, social stigma related to cancer results in delays in diagnosis and lack of funding/advocacy toward cancer related interventions.[48,49] A VSI protocol for palpable breast abnormalities helps to address many of these obstacles (Table 4).

There is much interest in new cost-effective strategies for breast imaging in LMICs.[2,50–52] Any intervention must be feasible within the economic constraints of the targeted country.[53,54] Traditional screening mammography, while effective in high-resource settings, may not be immediately feasible in many rural areas. In fact, evidence suggests that mammography has been unsustainable and possibly ineffective in some settings in LMICs.[55,56] Breast VSI for palpable masses may offer an opportunity for earlier detection, improved diagnosis, and increasing education as it is low-cost and presumably more easily integrated into healthcare delivery than many alternative approaches.[2,30,57,58] As a complex public

Table 3. VSI Sweep Data. Table presents details regarding mass visualization on the different sweeps. Sweep numbers correspond to the ordering on the protocol poster. Sweeps 1 and 2 are in the transverse orientation, sweeps 3 and 4 are in the sagittal orientation, sweeps 5 and 6 are in the radial orientation, and sweeps 7 and 8 are in the anti-radial orientation. If no mass was visualized in the examination, this was not included in the analysis

Sweep Number	Mass Present on Sweep	% of the Mass Visualized	Clip Length (s)
1	95.6% (90–98.5%)	82.1 ± 27.8	9.51 ± 2.63
2	94.7% (88.9–98%)	78.3 ± 30.6	9.34 ± 2.31
3	95.6% (90.1–98.6%)	81.5 ± 28.2	9.04 ± 2.48
4	94.7% (88.9–98%)	83.8 ± 27.1	9.45 ± 2.94
5	99.1% (95.2–100%)	85.5 ± 21.8	8.44 ± 2.35
6	98.2% (93.8–99.8%)	86.7 ± 21.9	8.5 ± 2.42
7	98.2% (93.8–99.8%)	85.3 ± 23.4	8.76 ± 2.47
8	95.6% (90.1–98.6%)	82.9 ± 25.7	9.32 ± 2.82
P value*	.40	.30	<.0001

*Results of chi-squared test for present, and ordinary one-way ANOVA for visualization and clip length.

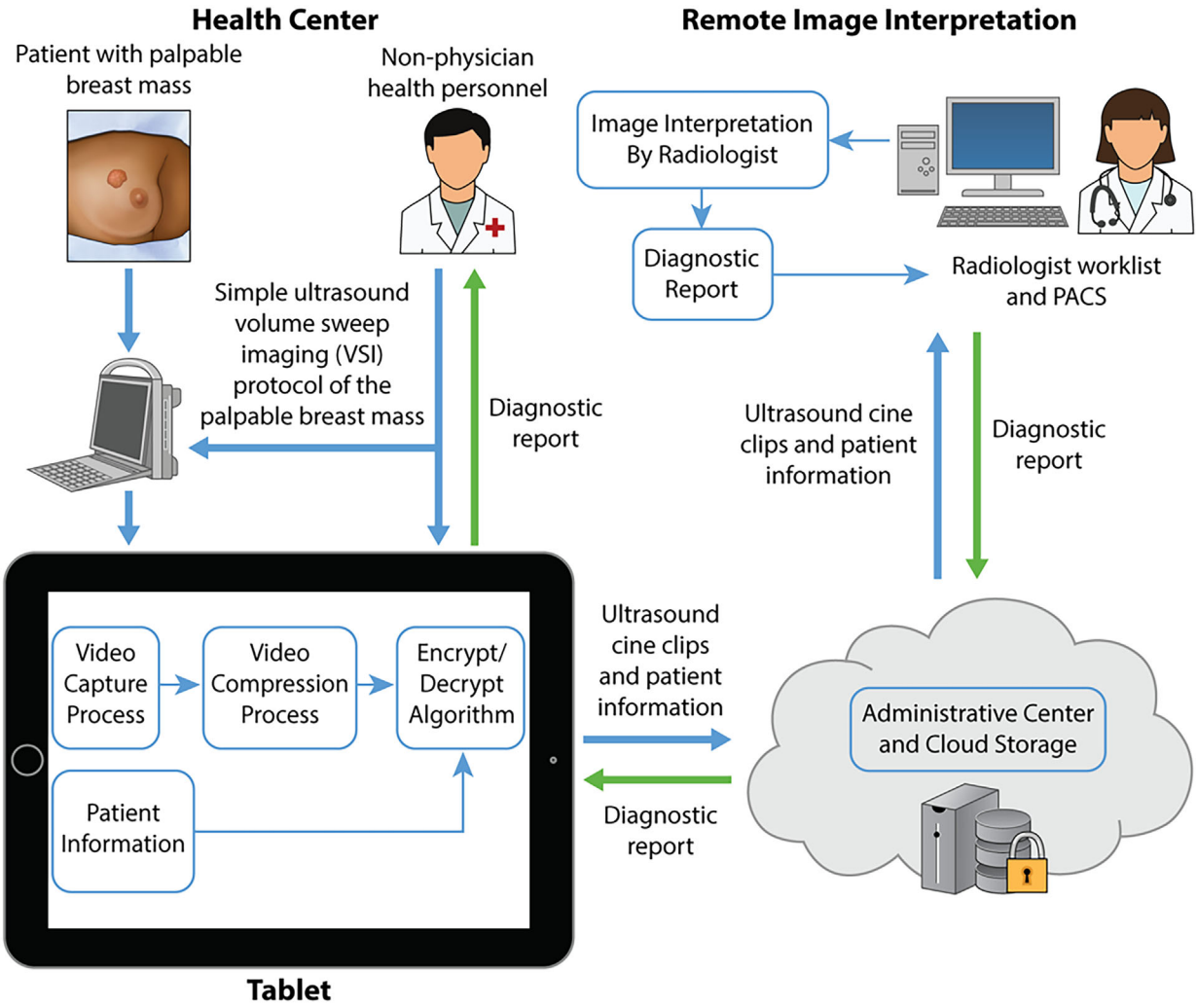
policy issue, any interventions to address breast cancer must be carefully weighed.[59] Future studies examining the public health aspects to this system would be necessary to elucidate how best to deploy this potentially life-saving technology.

In general, our readers were impressed with the image quality of the Butterfly iQ, especially considering its price (50–75 times cheaper) relative to the high-end machines. This is partially due to the breast being a superficial structure amenable to examination with high-frequency ultrasound resulting in high resolution images. That being said, there are inherent limitations that come from having a person scanning without looking at the image or adjusting the image settings. Our expert breast imagers concluded that the image quality was often suboptimal in comparison to standard of care imaging but in all cases still diagnostic for the purpose of gross evaluation. The agreement between VSI and standard of care suggests that the image quality of iQ relative to the high-end machines was not a substantial problem in our study, but further testing is needed to confirm this. Although our primary goal was the comparison of VSI with the iQ to standard of care, this study allowed us a general opportunity to assess the use of a hand-held ultrasound for evaluation of breast lumps. Of interest to the general medical community is that our findings suggest that the iQ could be effectively used for at least initial assessment of breast lesions by experts. In addition, the iQ could prove to be useful in ultrasound-guided biopsy in low-resource settings.

A potential limitation of VSI for palpable cancer relates to DCIS and other cancer which may present as a palpable lump without a clearly defined sonographic mass. In this study, we had two cases of DCIS which presented as a palpable lump without a clearly defined sonographic mass visualized on VSI or standard of care ultrasound. Microcalcifications were seen on mammogram in both cases which is how the diagnosis was made. This highlights the important point that VSI breast ultrasound is not a replacement for mammography or high-resolution ultrasound. A persistent unexplained palpable lump, especially in a patient over 40, should be evaluated with mammography as soon as possible (although in some settings this will not be possible). As malignancy presenting as a palpable lump with definite sonographic correlate is less common, the diagnostic accuracy of VSI for malignancy in palpable lumps should still remain overall high. Furthermore, ultimately the alternative to a breast VSI exam in many cases would likely be no imaging at all. Nonetheless, patients and clinicians should be aware of the limitations and that the results of this test are not perfect. In addition, VSI would not be able to stage cancers or provide information about other parts of the breast. Nonetheless, a positive VSI scan would presumably prompt patients to obtain the necessary medical evaluation for any concerning lesion.

An important goal of this study as a pilot of breast VSI was to test the utility of individual sweeps in the protocol. While literature supports the use of radial and anti-radial scanning, these may be difficult for some lay people to perform relative to simple transverse and sagittal scans (sweeps 1–4). In addition, there was a

Figure 7. Proposed model for integration of breast volume sweep imaging (VSI) and teleultrasound. This figure shows integration of VSI for breast lumps with an established asynchronous teleultrasound system. The tablet guides users to perform the VSI protocol and input patient clinical history. Imaging and patient data is sent to a cloud over low internet bandwidth. A specialist asynchronously receives the imaging and produces a diagnostic report. Blue arrows represent data input and green arrows represent the flow of the diagnostic report back to the tablet and health center. This system has been used for lung, obstetric, right upper quadrant, and thyroid indications in Peru.



possibility that the second redundant sweep in each set was unnecessary. Our conclusions in regards to the above are that all 8 sweeps demonstrated utility providing extra information with minimal drawbacks. We would recommend that any future modifications of the protocol continue to use redundancy and radial/anti-radial scanning. In addition, it may be helpful to add a question in the clinical history regarding the perceived size of the patient's breast lump. This could be phrased in terms of asking the patient to select the size of the lump relative to common objects like a pea, grape, golf ball, or tennis ball. It would help the interpreting physician to have an idea of the size of the abnormality they are looking to identify.

Future studies of breast VSI should be performed in clinical settings in LMICs where they would be most effectively deployed. This study was conducted at a high-resource setting in the United States for logistical reasons including convenience, availability of personnel, and availability of standard of care

Table 4. Obstacles to Improving Breast Cancer Outcomes in Low- and Middle- Income Countries and How Deployment of Breast VSI May Close the Divide

Obstacle	Description of the Problem	Impact of Breast VSI Deployment
Poor health infrastructure	Health establishments are unable to provide services necessary to ensure optimal outcomes. Delays in diagnosis are common.	A low-cost means of evaluating palpable breast masses will improve existing health infrastructure. Delays to diagnosis will decrease.
Lack of breast cancer awareness	Lack of education leads to a lack of awareness regarding breast cancer and its health impact.	A widely available way to analyze palpable breast masses will increase awareness of breast cancer. Breast VSI offers a chance to educate patients similar to clinical breast exams.
Lack of breast cancer screening	Mammography is not widely available.	Breast VSI would potentially decrease delays in diagnosis. As breast cancer awareness and advocacy increases, more funds will be available to improve primary screening programs.
Lack of morbidity and mortality data	Much remains unknown about breast cancer In LMICs.	Breast VSI imaging could be used to better study breast cancer trends in LMICs.
Social barriers	Cultural taboos regarding cancer lead to delays in diagnosis. Many view cancer with stigma and are afraid of disclosing their diagnosis. Lack of socioeconomic status makes access to care difficult.	Widespread breast VSI screening would decrease stigma. Its low-cost nature would decrease barriers to care and delay to diagnosis.

ultrasound performed by a breast specialist. Our medical student scanners had no prior ultrasound experience and several precautions were taken to minimize any bias in VSI scans. Given that our medical students did not look at the screen while scanning and learned the protocol in less than 2 hours, it would be expected that these findings would generalize even further to individuals with no medical experience. There is also a plethora of supporting evidence that VSI is learned by individuals without ultrasound experience with relative ease mitigating this limitation.[14,15,17,21] Nonetheless, another angle for future studies would be to verify our findings generalize to individuals with no medical background.

Similarly, this study was conducted with two expert readers of breast ultrasound both with over 20 years of experience. The excellent agreement we saw between VSI and standard of care should be verified in readers who might not have this degree of breast imaging experience. Although it would have been ideal, the adjusted BI-RADS assessments in this study were unable to be calculated by a blinded reader due to logistical considerations introducing possible bias against agreement with VSI. This same argument could be made for any of the standard of care variables which were also not analyzed by a blinded interpreter. Given the advantage and bias conferred by knowledge of the clinical history, it is possible that greater agreement between VSI and standard of care might be realized if the standard of care interpreter was completely blinded to the clinical history. While efforts were made to make the adjusted BI-RADS as objective as possible, a future study could blind both standard of care and VSI interpreters. For the purposes of this pilot study to preliminarily assess breast VSI and the iQ, the observed high agreement in all categories suggests this is a minimal limitation.

In summary, we have shown that after 2 hours of training, operators without prior ultrasound experience were able to obtain diagnostic imaging of palpable breast lesions with high agreement with standard of care related to mass presence, mass size, and BI-RADS assessments. Furthermore, these images were obtained using a handheld ultrasound probe that costs approximately $2000. Thus, for a small investment, communities could be equipped with an acceptable quality and potentially life-saving means to evaluate palpable breast abnormalities. As breast cancer rates and mortality continue to increase worldwide, this could represent a simple cost-effective means to improve outcomes and bring

potentially life-saving imaging where it is needed most in the world.

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