Radiology

Shear-Wave Elastography of Benign versus Malignant Musculoskeletal Soft-Tissue Masses: Comparison with Conventional US and MRI

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Conflicts of interest are listed at the end of this article.

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Purpose: To examine if shear-wave elastography (SWE) improves the accuracy of diagnosing soft-tissue masses as benign or malignant compared with US alone or in combination with MRI.

Materials and Methods: Two hundred six consecutive adult participants (mean age, 57.7 years; range, 18–91 years), including 89 men (median age, 56.0 years; range, 21–91 years) and 117 women (median age, 59.1 years; range, 18–88 years), who were referred for biopsy of a soft-tissue mass were prospectively recruited from December 2015 through March 2017. Participants underwent B-mode US, MRI, and SWE prior to biopsy. Three musculoskeletal radiologists independently reviewed US images alone, followed by US and MRI images together, and classified lesions as benign, probably benign, probably malignant, or malignant. For SWE, the area under the receiver operating characteristic (ROC) curve (AUC) was calculated for transverse shear-wave velocity (SWV). Multivariable logistic regression was used to investigate the association between SWE and malignancy alongside individual demographic and imaging variables.

Results: At histologic examination, 79 of 206 (38%) participants had malignant lesions. SWV showed good diagnostic accuracy for lesions classified as benign or probably benign by US alone (AUC = 0.87 [95% confidence interval {CI}: 0.79, 0.95]). SWV did not provide substantive diagnostic information for lesions classified as probably malignant or malignant, whether the classification was made with or without MRI. However, multivariable modeling indicated that diagnostic accuracy may vary by lesion position (interaction $P = .02$; superficial, odds ratio [OR] = 17.7 [95% CI: 1.50, 207], $P = .02$; deep/mixed, OR = 0.24 [95% CI: 0.07, 0.86], $P = .03$) and participant age (interaction $P = .01$; eg, age 43 years, OR = 0.72 [95% CI: 0.15, 3.5], $P = .69$; age 72 years, OR = 0.08 [95% CI: 0.02, 0.37], $P = .001$).

Conclusion: Shear-wave elastography can increase accuracy of soft-tissue lesion diagnosis in conjunction with US. However, a single cut-off may not be universally applicable with diagnostic accuracy that is affected by lesion position and patient age.

Online supplemental material is available for this article.

Soft-tissue masses are common and a frequent reason for performing musculoskeletal imaging. The primary aim of imaging in this setting is to obtain a provisional or definitive diagnosis of any underlying lesion. Where a mass is identified but characterization is not possible, the overarching question referring physicians have is whether the mass could be malignant (1). Despite the ubiquity of soft-tissue lesions, the majority are benign, with lipomas the most common subtype (2). In particular, soft-tissue sarcomas are uncommon, representing less than 1% of cancers (3). B-mode US may be used in more superficial lesions, given its low cost, ease of access, and high spatial resolution (4), with MRI usually performed to provide more definitive characterization and local staging.

Traditionally, a combination of patient demographic information, especially age, and imaging features are used to attempt to characterize lesions on the benign-malignant spectrum. Features such as large lesion size and greater depth, irregular margin, heterogeneity, and invasion of local structures, along with absence of definitely benign features (eg, purely cystic), are regarded as concerning (1,5,6).

Shear-wave elastography (SWE) is an emerging technique that uses US to provide quantitative data regarding the biomechanical properties of tissue. By measuring the velocity of propagation of shear waves produced by the transducer, the elasticity of tissues can be inferred (7). SWE has been used to aid lesion characterization in a variety of body sites, most commonly in the breast (8) and liver (9), but also in the prostate (10) and thyroid (11). Within the field of musculoskeletal imaging, SWE has mainly been used in evaluation of tendon disorders but has not yet found widespread clinical use (7). A small number of

Abbreviations

AUC = area under the ROC curve, CI = confidence interval, ICC = intraclass correlation coefficient, OR = odds ratio, ROC = receiver operating characteristic, SWE = shear-wave elastography, SWV = shear-wave velocity

Summary

Shear-wave elastography helps characterize musculoskeletal soft-tissue lesions as benign or malignant over evaluation with conventional US, but not when US is combined with MRI.

Implications for Patient Care

- Shear-wave elastography can be used to add confidence to diagnosis of soft-tissue masses that appear benign or probably benign using conventional B-mode US.
- Shear-wave elastography does not improve the diagnostic performance for such lesions when MRI is combined with conventional US.
- The association between shear-wave velocity and malignancy may vary by lesion position and patient age.

studies have attempted to investigate the value of SWE in musculoskeletal masses (12–14); the largest of these studies found no additional benefit of SWE over conventional US-based classification (13). We hypothesized that malignant soft-tissue masses have altered elasticity that is significantly different from that of benign masses, which can be detected using SWE.

The aim of this study was to examine whether SWE evaluation, in addition to imaging-based assessor grading of conventional US images alone and in combination with MR images, helps characterize soft-tissue masses as benign or malignant.

Materials and Methods

Patient Population

The study was approved by the institutional ethics review board, and written informed consent was obtained from all participants. The study prospectively screened 220 consecutive patients suspected of having soft-tissue sarcoma who were referred for US-guided biopsy between December 2015 and March 2017 by a specialist sarcoma center. There were no exclusion criteria. Histologic evaluation using the biopsy result or surgical specimen (where available) was used as the reference standard, with the pathologic diagnosis confirmed after analysis by one of two specialist soft-tissue sarcoma pathologists. US and biopsy were performed by one of two musculoskeletal radiologists (H.G. and P.R., with 10 and 19 years of experience, respectively) using a 6–15-MHz linear transducer (LOGIQ-E9; General Electric Health Care, Milwaukee, Wis). All biopsies were performed percutaneously by using a minimum 16-gauge core needle to obtain at least three cores.

B-Mode US

The anonymized US and MR images were reviewed independently by three musculoskeletal radiologists (M.A., H.G., and P.R., with 3, 10, and 19 years of experience, respectively) who performed a visual assessment to categorize the lesions into one of four categories: benign, probably benign, probably malignant, or malignant based on qualitative assessment using published criteria (4).

An initial assessment of US images alone was made while radiologists were blinded to any prior MRI study findings and the shear-wave velocity (SWV) but were aware that all participants had undergone biopsy.

MRI Examination

A second assessment was independently performed based on a combination of anonymized US and MR images at least 3 weeks after the scoring with US alone. MRI examinations for 189 participants prior to biopsy were performed by using a 1.5-T system (Magnetom Avanto; Siemens Healthcare, Erlangen, Germany). T1-weighted and fat-suppressed T2-weighted images were obtained in two planes without intravenous contrast medium. The same assessment criteria were used (4) and readers were blinded to SWV.

For assessments based on US alone and US combined with MRI, analyses used the majority score (see statistical evaluation below) of the three independently obtained scores without discussion or further analysis by the radiologists.

US SWE

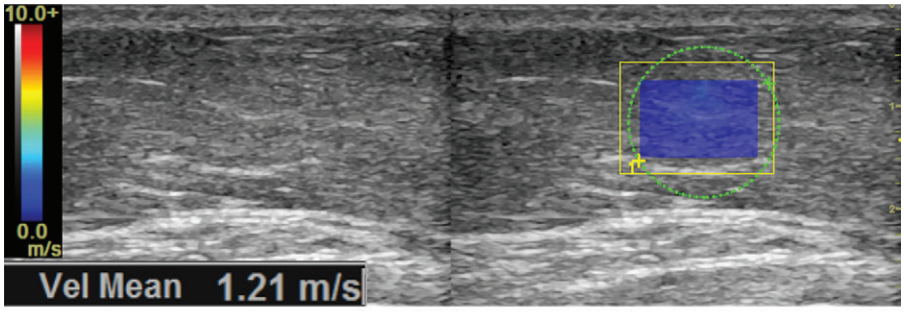
Before biopsy, two-dimensional SWE was performed by using a 9–4-MHz linear transducer (LOGIQ-E9; General Electric Health Care). This system has demonstrated substantial reliability in comparison to other SWE systems (15). The system reports SWE readings in SWV (meters/second) and Young modulus (kilopascals). Both units are proportional to elasticity and can be used as a surrogate for tissue stiffness.

Participants were placed in relaxed positions to ensure that no active (contraction) or passive (stretching) effects directly influenced the elasticity results. An SWE rectangular elasticity box was fixed at a size of 1.5 cm × 2 cm and a circular region of interest was used to cover and calculate elasticity within the most homogeneously solid and vascularized area (Fig 1a, 1b). Selected SWE maps were free from random inconsistent artifactual color patterns. Five repeated measurements in both craniocaudal and transverse planes were acquired by a board-qualified musculoskeletal radiologist (P.R., with > 19 years of experience, including > 3 years with SWE). In 100 participants, repeated SWE readings were independently acquired immediately after the first scan by a board-qualified sonographer (A.M.A., with 5 years of experience, including > 2 years with SWE) who was blinded to the first scan measurements and clinical information. Total scanning time ranged 5–10 minutes per reader.

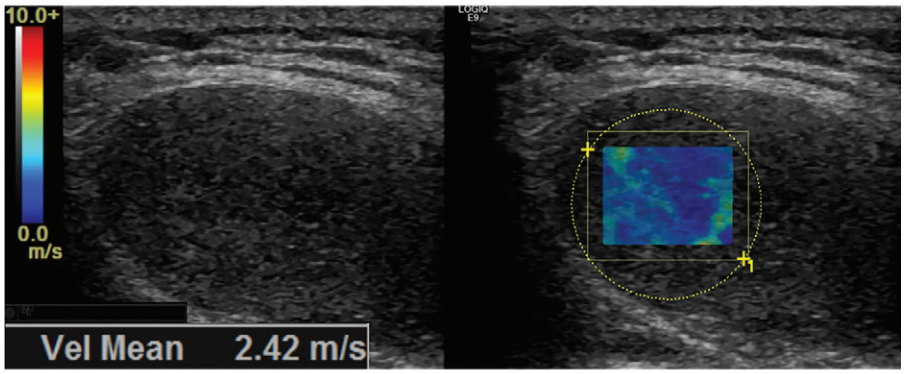
Statistical Analysis

Sample size required for a multivariable logistic regression model of malignancy was based on an estimated malignancy rate of 37% from a previous study at this center (13). With 13 independent variables, a minimum of 175 participants (65 with malignant lesions) were required to provide at least five events per variable, recommended in rules of thumb for logistic regression (16).

Multirater kappa (κ) and category-specific proportions of positive agreement were used to assess interradiologist agreement over lesion classification. Nonparametric areas under the receiver operating characteristic (ROC) curve (AUCs)



a.



b.

Figure 1: Shear-wave velocity (SWV) maps in **(a)** 46-year-old male participant with histologic diagnosis of lipoma and **(b)** 75-year-old female participant with histologic diagnosis of grade 3 spindle cell sarcoma. The SWV color bar is set at a scale from 0 to 10 m/sec.

Table 1: Bland-Altman Limits of Agreement and Intraclass Correlation Coefficients for Shear-Wave Measurements Made by Two Readers

	Geometric Mean			
Shear-Wave Measurement	Reader 1	Reader 2	Bias ± LOA	$ICC_{(2, 1)}$*
Craniocaudal velocity (m/sec)	2.10	2.04	0.06 ± 0.80	0.90 (0.85, 0.93)
Craniocaudal stiffness (kPa)	15.70	14.91	1.45 ± 15.60	0.89 (0.84, 0.92)
Transverse velocity (m/sec)	2.10	2.11	0.01 ± 0.80	0.93 (0.89, 0.95)
Transverse stiffness (kPa)	15.65	15.70	1.13 ± 16.22	0.92 (0.88, 0.94)

Note.—ICC = intraclass correlation coefficient, LOA = limits of agreement.
* Data in parentheses are 95% confidence interval.

were compared for classifications based on US alone versus US and MRI by using the Stata (Stata, College Station, Tex) roccomp command. Bland-Altman plots were used to compare SWE measurements by two different readers for 100 of the participants. Two-way mixed intraclass correlation coefficients (ICCs) were calculated for SWE measurements to evaluate the interobserver agreement. Lesion position was coded as deep intermuscular, deep intramuscular, subcutaneous, or mixed (deep intraintermuscular or deep subcutaneous).

The majority classification categories from the three readers' independently obtained scores for assessment of malignancy by US alone and by US and MRI combined were merged into the two categories, benign or probably benign and malignant or probably malignant, and the AUC was calculated for SWE within each merged category. We identified the point yielding 100% sensitivity (false-negative rate, 0) and the point that maximized the Youden index (sensitivity + specificity − 1; the probability of making an informed decision rather than a random guess). Penalized, or LASSO, binary logistic regression was used to determine the association with histologically confirmed malignancy for individual US findings and SWVs, adjusted for demographic variables, choosing optimal lambda from a grid of starting values. Interactions between SWV and other variables were retained in the model if significant at *P* less than .1. All analyses were conducted in Stata 14.1 (Stata, College Station, Tex).

Results

Of the 220 patients screened, 12 who did not or could not consent were not included in the study. Of the 208 patients who had lesions assessed, two were excluded from analysis: one had an error in all SWE measurements and the other was lost to follow-up, meaning that malignancy status could not be determined. All 206 participants underwent US and SWE, and 189 of 206 participants underwent MRI prior to biopsy (see Fig 2 for participant flowchart). The mean age of the 206 participants was 57.7 years (range, 18–91 years); for the 89 male participants, it was 56.0 years (range, 21–91 years), and for the 117 female participants, it was 59.1 years (range, 18–88 years). Pathology was considered the reference standard (diagnoses listed in Table E1 [online] and clinical and imaging characteristics presented in Table E2 [online]). Lipomas and liposarcomas were the most common benign and malignant lesions, respectively. Seventeen participants, five with benign lesions and 12 with malignant lesions, did not have an MRI performed for clinical reasons, such as a small or superficial mass or claustrophobia.

MRI and US Reader Agreement for Lesion Classification

Agreement of MRI and US for lesion classification was assessed in 189 participants with MR images available. By using US features alone to classify lesions, proportions of positive agreement (ie, the probability that a lesion classified into a category by one reader would be classified into the same category by another) were 41%, 80%, 67%, and 64% for benign, probably benign, probably malignant, and malignant categories, respectively (69% overall; multirater κ, 0.55 [95% confidence inter-

val {CI}: 0.48, 0.62]). By using US and MRI features combined to classify lesions, the proportions of positive agreement were 25%, 87%, 74%, and 78%, respectively (77% overall; κ, 0.67 [95% CI: 0.61, 0.73]). When readers used both US and MRI features to classify lesions, the agreement between readers improved (bootstrapped difference in κ, 0.12 [95% CI: 0.03, 0.20]; P = .01).

Agreement over SWE Measurements

Intraclass correlations for all four measures (SWV and stiffness measured in craniocaudal and transverse planes) were very high, with negligible mean differences (Table 1). However, Bland-Altman limits of agreement were wide compared with the average measurement (Table 1, Fig 3). For SWV, 95% of repeat measurements were expected to lie within −0.74 and +0.86 m/sec of each other, when the mean measurement was approximately 2 m/sec. In concurrence with recent findings in a study of reliability of muscle SWE (15), overall agreement was better for SWV than for stiffness (kPa). Due to high correlation (r = 0.82) between the two planes, only the most reliable measurements (transverse SWV) were used in further analysis.

Does SWV Add Information Beyond Lesion Assessment with US Alone and US with MRI?

Majority classification by the three radiologists showed diagnostic accuracy (AUC) of 0.82 (95% CI: 0.75, 0.89) when based on US alone, and this improved to 0.94 (95% CI: 0.90, 0.97) when based on US combined with MRI ($\chi^2_{(1)}$ = 11.7; $P < .001$). Sensitivity and specificity, using each classification category in turn as the cut-point for malignancy, are provided in Table 2. If we were to consider it safe to discharge patients with lesions graded benign by US alone, as is current practice, this would give a negative predictive value of 76%, indicating that some malignant lesions may be missed during US-only first-line screening, revealing a potential role for SWE.

SWV grouped by imaging classification category and confirmed histologic status are presented in Figure E1 (online). The use of SWV alone for all lesions, with lower values assumed to indicate malignancy, did not demonstrate diagnostic accuracy better than chance (AUC = 0.53 [95% CI: 0.44, 0.61]). However, of the 116 lesions classified as benign or probably benign by US alone, 14 were malignant at histologic examination. For this group, the AUC was 0.87 (95% CI: 0.79, 0.95) (Fig E1a [online]; Fig 4a). In lesions classified as benign or probably benign by US alone, at transverse SWV of 2.02 m/sec or less, sensitivity was 100% (14 of 14 [95% CI: 78%, 100%]), specificity was 62% (63 of 102 [95% CI: 52%, 71%]), positive predictive value was 26% (14 of 53 [95% CI: 16%, 40%]), and negative predictive value was 100% (63 of 63 [95% CI: 94%, 100%]); 66% of all lesions were correctly classified. At velocity of 1.78 m/sec or less, where the Youden index was maximized, the sensitivity was 93% (13 of 14 [95% CI: 69%, 99%]), specificity was 72%

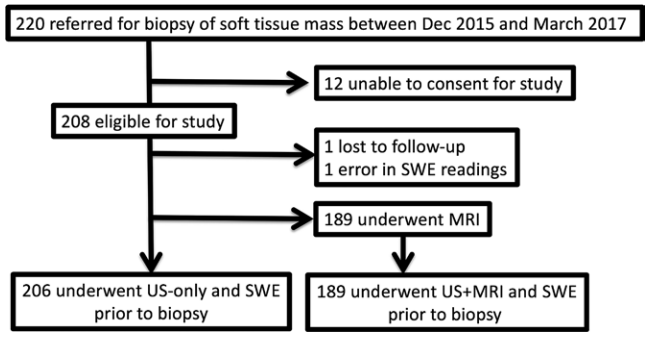


Figure 2: Flowchart of participants in the study. *SWE* = shear-wave elastography.

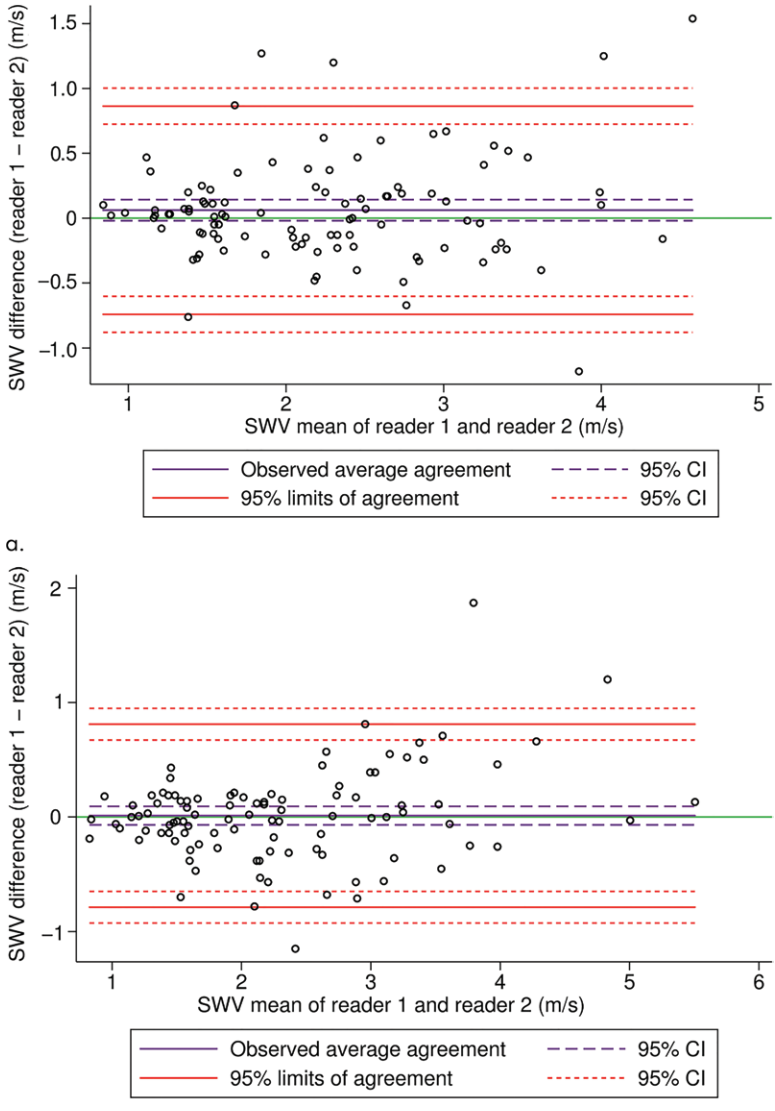


Figure 3: Bland-Altman plots of shear-wave velocity (*SWV*) measurements by two readers in the **(a)** craniocaudal and **(b)** transverse planes. CI = confidence interval.

Table 2: Classification Success for Majority Classification of Three Readers Classifying Lesions with US Alone or US and MRI Combined (in 189 Participants with Both US and MRI Available)

Majority Classification	Benign (n = 122)*	Malignant (n = 67)*	Sensitivity (%)†	Specificity (%)†	Positive Predictive Value (%)†	Negative Predictive Value (%)†
US alone						
Benign	13 (11)	4 (6)	100 (95, 100)	0 (0, 3)	35 (29, 42)	Not applicable
Probably benign	85 (70)	9 (13)	94 (86, 98)	11 (6, 17)	37 (30, 44)	76 (53, 90)
Probably malignant	21 (17)	26 (39)	81 (70, 88)	80 (72, 86)	69 (58, 78)	88 (81, 93)
Malignant	3 (2)	28 (42)	42 (31, 54)	98 (93, 99)	90 (75, 97)	75 (68, 81)
US and MRI combined						
Benign	7 (6)	1 (1)	100 (95, 100)	0 (0, 3)	35 (29, 42)	Not applicable
Probably benign	89 (73)	0 (0)	99 (92, 100)	6 (3, 11)	36 (30, 44)	88 (53, 98)
Probably malignant	23 (19)	24 (36)	99 (92, 100)	79 (71, 85)	72 (62, 80)	99 (94, 100)
Malignant	3 (2)	42 (63)	63 (51, 73)	98 (93, 99)	93 (82, 98)	83 (76, 88)

* Data in parentheses are percentages.

† Data in parentheses are 95% confidence interval. Calculated using each category as the cut-off for malignancy, that is, using the benign category as the cut-off is equivalent to assuming all lesions are malignant.

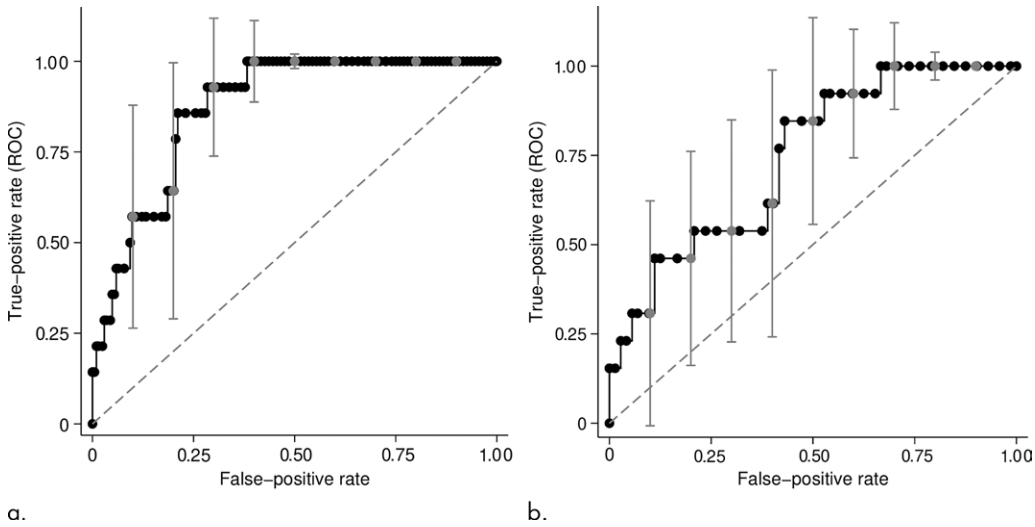


Figure 4: Receiver operating characteristic (ROC) curve for transverse shear-wave velocity predicting malignancy in lesions classified as benign or probably benign using US alone in **(a)** all lesions (area under the ROC curve [AUC] = 0.87 [95% confidence interval {CI}: 0.79, 0.95]) and **(b)** lipomatous lesions only (AUC = 0.74 [95% CI: 0.59, 0.89]).

(73 of 102 [95% CI: 62%, 79%], positive predictive value was 31% (13 of 42 [95% CI: 19%, 46%]), and negative predictive value was 99% (73 of 74 [95% CI: 93%, 100%]). Restricting the lipomatous lesions (n = 49; 13 malignant) to the largest subgroup of masses, SWV still showed evidence of diagnostic ability (AUC = 0.74 [95% CI: 0.59, 0.89]) (Fig E1b [online]; Fig 4b). The ROC curve for the final model prediction is presented in Figure E2 (online).

For lesions classified as probably malignant or malignant by US alone (n = 90; 65 malignant), SWV alone did not demonstrate any diagnostic benefit (AUC = 0.50 [95% CI: 0.37, 0.63]) (Fig E1a [online]). None of the lipomatous lesions in this subgroup were found to be benign (Fig E1b [online]).

Using classification by US and MRI combined, none of the lesions classified as probably benign and only one lesion classified as benign was malignant, limiting the additional benefit SWE could offer. Among lesions classified as probably malignant or malignant by US and MRI combined (n = 92; 66 malignant), there was no evidence that SWV offered additional diagnostic information (AUC = 0.58 [95% CI: 0.46, 0.71]) (Fig E1c [online]). This remained the case when restricted to lipomatous lesions (n = 28; eight malignant; AUC = 0.64 [95% CI: 0.43, 0.86]) (Fig E1d [online]).

Does Association between SWV and Malignancy Differ according to Individual Demographic and US Variables?

Odds of malignancy associated with demographic, US, and SWE variables are presented in Table 3. Statistically significant interactions were identified between SWV and both age (P = .01) and lesion position (overall P = .02). LASSO removed the interaction for deep and mixed-position lesions, but a large interaction effect remained for subcutaneous lesions. SWVs observed in different positions are presented in Figure E3 (online). Estimates from the final multivariable model in Table 3 showed that subcutaneous lesions with higher SWVs were more likely to be malignant (odds ratio [OR] = 17.66 [95% CI: 1.50, 207.47]; P = .02) (Fig 5a). However, for lesions that were deep intermuscular, deep intramuscular, or in a mix of positions, the direction of association was reversed (OR = 0.24

Table 3: Binary Logistic Regression of Histologically Confirmed Malignancy on Demographic Characteristics, Individual B Mode Variables, and Shear-Wave Velocity

Independent Variable	Confirmed Lesion Status		Odds Ratio					
	Benign* (n = 127)	Malignant* (n = 79)	Univariable†	*P* Value	Multivariable without SWV†	*P* Value	Multivariable with SWV†	*P* Value
Mean age (y) at imaging	53.3 ± 17.5	64.8 ± 17.5	1.04 (1.02, 1.06)	<.001	1.05 (1.02, 1.08)	<.001	1.06 (1.03, 1.09)	<.001
No. of female participants	61 (48)	26 (35)	0.59 (0.33, 1.06)	.08	0.81 (0.37, 1.78)	.60	0.61 (0.25, 1.47)	.27
Lesion volume (cm^3), geometric mean	30.1	94.7	1.44 (1.21, 1.71)	<.001	1.55 (1.21, 2.00)	.001	1.66 (1.24, 2.21)	.001
Heterogeneity present	87 (69)	58 (73)	1.27 (0.68, 2.37)	.45	0.52 (0.18, 1.53)	.24	0.59 (0.17, 2.02)	.40
Necrosis present	22 (17)	32 (41)	3.25 (1.71, 6.18)	<.001	2.74 (1.10, 6.82)	.03	3.43 (1.24, 9.43)	.02
Echotexture								
Hyper	22 (17)	6 (8)	Reference		Reference		Reference	
Mixed	50 (39)	25 (32)	1.83 (0.65, 5.10)	.24	0.88 (0.21, 3.69)	.86	0.89 (0.16, 4.91)	.89
Hypo	55 (43)	48 (61)	3.20 (1.20, 8.55)	.02	2.73 (0.69, 10.80)	.15	5.44 (1.01, 29.23)	.05
Doppler								
Absent	70 (55)	17 (22)	Reference		Reference		Reference	
Linear	27 (21)	6 (8)	0.92 (0.33, 2.57)	.87	1.00 (0.99, 1.01)	>.99	1.00 (0.99, 1.01)	>.99
Disorganized	30 (24)	56 (71)	7.69 (3.85, 15.34)	<.001	11.59 (4.60, 29.16)	.001	16.53 (5.74, 47.64)	<.001
Position								
Deep intermuscular	37 (29)	14 (18)	Reference		Reference		Reference	
Deep intramuscular	53 (42)	32 (41)	1.60 (0.75, 3.40)	.22	1.00 (0.99, 1.01)	>.99	1.35 (0.47, 3.88)	.57
Subcutaneous	36 (28)	22 (28)	1.62 (0.72, 3.64)	.24	1.04 (0.43, 2.55)	.93	1.05 (0.29, 3.87)	.94
Mixed	1 (<1)	11 (14)	29.07 (3.43, 246.47)	.002	2.74 (0.38, 19.51)	.31	6.14 (0.65, 57.63)	.11
SWV (m/sec), geometric mean	2.31	2.23	0.82 (0.42, 1.57)	.54	…	…	0.24 (0.07, 0.86)	.03
SWV × age	…	…	…	…	…	…	0.93 (0.87, 0.98)	.01
SWV ×								
Deep intramuscular	…	…	…	…	…	…	1.00 (0.98, 1.02)	>.99
Subcutaneous	…	…	…	…	…	…	74.68 (5.17, 1078.62)	.002
Mixed	…	…	…	…	…	…	1.00 (0.95, 1.05)	>.99

Note.—SWV = shear-wave velocity in the transverse plane.

* Data for mean age are mean ± standard deviation. Data in parentheses are percentages.

† Data in parentheses are 95% confidence interval.

[95% CI: 0.07, 0.86]; *P* = .03) (Fig 5b, 5c). Age also modified the association between SWV and malignancy; for example, in deep lesions there was no association in younger participants (estimated at age 43 years, OR = 0.72 [95% CI: 0.15, 3.55], *P* = .69) but the association increased in strength with age (at age 59 years, OR = 0.21 [95% CI: 0.06, 0.78], *P* = .02; at age 72 years , OR = 0.08 [95% CI: 0.02, 0.37], *P* = .001) (Fig 5b). For participants with lesions that spread across multiple locations, the pattern with respect to age and SWV was the same as for deep lesions, although the risk of malignancy was higher (Fig 5c).

Discussion

Our results show that while SWV alone was not diagnostic of malignancy, it improved the diagnostic ability of imaging-based classification using US alone when lesions were initially believed

to be benign or probably benign. No additional benefit of SWE was seen when assessment based on US alone was indicative of a possible or definite malignancy. In clinical practice when a lesion is considered potentially malignant, further evaluation (MRI and/or biopsy) is usually considered mandatory. Hybrid techniques combining visual inspection and quantitative methods such as SWE may provide additional confidence that a lesion is benign, and more invasive measures such as biopsy can be avoided as has been reported in breast radiology (8,17–19). SWE could be useful in avoiding unnecessary interventions, medical costs, and distress for patients.

A critical factor for an imaging biomarker, especially a quantitative one, is its reproducibility. We found near-perfect interreader reliability (> 0.89), similar to findings of other investigators (20–22). Despite this, the limits of agreement were wide; for velocity, 95% of measurements were expected to lie within −0.74 and +0.86 m/sec of each other, when the mean measurement was approximately 2 m/sec. This could be potentially improved by acquiring additional SWE measurements per lesion.

Our results do not support an additional benefit of SWE when used in conjunction with both US and MRI. This is in contrast to studies in breast lesions where SWE and MRI combined outperformed MRI alone (23). It seems that SWE is potentially another variable that cannot be specific for malignancy in soft-tissue tumors. As shown in Table 3, age, increasing lesion size, lesion necrosis, and disorganized lesion Doppler flow were significantly linked to malignant lesions, but these features can all still be associated with benign soft-tissue pathology.

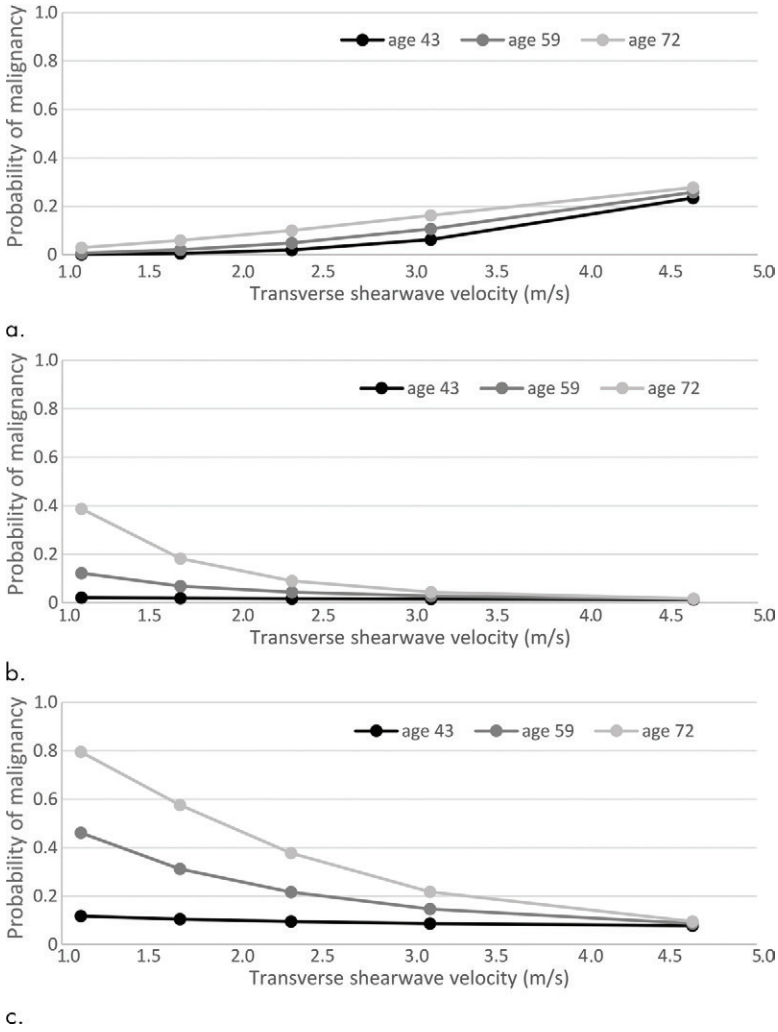


Figure 5: Estimated probabilities of malignancy for different combinations of shear-wave velocity (SWV), age, and lesion position. Estimates calculated for SWV at 5th, 25th, 50th, 75th, and 95th percentiles and age at quartiles within each lesion position category, while holding all other covariates at the reference category (categorical covariates) or at the mean (continuous covariates). **(a)** Subcutaneous, **(b)** deep (intra- or intermuscular), and **(c)** mixed (subcutaneous and deep intra- and/or intermuscular).

As with previous reports, our data suggest that slower SWVs are found in deeply located malignant soft-tissue lesions (12,13). Shear waves propagate faster in stiffer tissues (24); therefore, lower SWVs indicate malignant soft-tissue lesions are softer or less stiff. This is contrary to what has been reported in other organs, such as the breast, prostate, and thyroid, where greater tissue stiffness (and therefore higher SWV) is associated with greater likelihood of malignancy (9,11). Nevertheless, thyroid follicular cell carcinomas can be soft (25) due to greater cellularity and lower fibrous content (26). In contrast to our results in deeply located lesions, higher SWVs in subcutaneous lesions were associated with malignancy. The inverted relationship between superficial and deep lesions may relate to differing bioelastic properties of the lesion subtypes that tend to predominate in either compartment (27) or differing properties of the surrounding tissues, being subcutaneous fat and striated muscle, respectively, which may also be affected by aging. Magarelli et al used strain elastography to evaluate soft-tissue lesions and found that malignant lesions tended to be stiffer, but only evaluated 32 lesions (14). Similarly, Park et al found that malignant soft-tissue lesions were harder compared with subcutaneous epidermoid cysts (28). The strain elastography method used in the previous studies is based on a qualitative mechanical compression technique, which is therefore prone to operator-induced variability.

Limitations of this study include the lack of statistical testing for all malignant subtypes. The umbrella term *soft-tissue sarcoma* encompasses a large range of rare mesenchymal lesions whose constitution may vary greatly; such wide variation does not occur in the other tumor groups evaluated by SWE to date, namely breast and thyroid. However, a small number of malignant soft-tissue lesions tend to predominate (29) and those encountered tend to have fairly consistent overall imaging appearances, namely lobulated mass lesions, which are hypoechoic on US and have high signal intensity on T2-weighted MR images (5). Nonetheless, this reflects clinical decision making, which in the initial workup usually approaches soft-tissue lesions in a binary benign-versus-malignant framework. Our study population

is likely to have a bias toward malignant lesions, given that only those participants who had already been referred for biopsy were included. It should be noted that the numbers within subgroups did become very small when analysis was restricted to lipomatous lesions, which might have affected the robustness of statistical secondary analysis. Although interreader reliability was measured and appeared excellent, no assessment of intrareader variation was performed. Both SWE operators had extensive experience in performing the technique and others' results may not be as reproducible, although a substantial part of the modality is largely semiautomated.

In conclusion, although shear-wave elastography does not have independent predictive ability, its supplemental use is able to improve the classification performance of assessment using US alone when compared with histologic evaluation. Given the ubiquity of lipomatous lesions and the difficulties in managing them, further evaluation of the role of shear-wave elastography in lesion classification should be performed, especially given that its most powerful ability appears to be adding credence to the impression of benignity based on US alone.

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