Enhancement of ARFI-VTI Elastography Images in Order to Preliminary Rapid Screening of Benign and Malignant Breast Tumors Using Multilayer Fractional-Order Machine Vision Classifier

JIAN-XING WU, (Member, IEEE), HSIAO-CHUAN LIU, PI-YUN CHEN, CHIA-HUNG LIN, YI-HONG CHOU, AND K. KIRK SHUNG, (Life Fellow, IEEE)

1Department of Electrical Engineering, National Chin-Yi University of Technology, Taichung City 41170, Taiwan
2Department of Biomedical Engineering, NIH Transducer Resource Center, University of Southern California Los Angeles, CA 90089, USA
3Department of Physiology and Biomedical Engineering, Mayo Clinic College of Medicine, Rochester, MN 55905, USA
4Department of Oncology, Taipei Veterans General Hospital, Taipei City 11217, Taiwan

Corresponding authors: Jian-Xing Wu (jian0218@gmail.com) and Chia-Hung Lin (eechl53@gmail.com)

This work was supported by the Ministry of Science and Technology of Taiwan under Contract MOST 108-2218-E-167-007-MY2 and Contract MOST 109-2635-E-167-001, and in part by the Hospital Research Ethics Committee and the Institutional Review Board (IRB), Taipei Veterans General Hospital, Taipei City, under Contract V103C-059.

ABSTRACT
Breast tumor ranks fourth among various cancers in terms of mortality rate in Taiwan, and it is also the most commonly prevalent cancer in females. Early detection of any malignant lesions can increase the survival rate and also decline the mortality rate through current advanced medical therapies. Acoustic radiation force impulse (ARFI) is a new imaging technique for distinguishing breast lesions in the early stage based on localized tissue displacement, which is quantitated by virtual touch tissue imaging (VTI). Digital ARFI-VTI is an initial breast imaging modality and appears to be more effective in women aged >30 years. Therefore, image enhancement process is a key technique to enhance a low-contrast image in a region of interest (ROI) for visualizing texture details and morphological features. In this study, two-dimensional fractional-order convolution, as a 2D sliding filter window (eight filters are selected), is applied to enhance ARFI-VTI images for an accurate extrapolation of lesions in an ROI. Then, the maximum pooling is performed to reduce the dimensions of the feature patterns from 32×32 to 16×16 size. A multilayer machine vision classifier, as a generalized regression neural network (GRNN), is then used to screen subjects with benign or malignant tumors. With a 10-fold cross-validation, promising results such as mean recall (%), mean precision (%), mean accuracy (%), and mean F1 score of 92.92±3.43%, 80.42±6.45%, 87.78±2.17%, and 0.8615±0.0495, respectively, are achieved for quantifying the performance of the proposed classifier. Breast tumors visualized on ARFI-VTI images can be useful as digitalized images for rapid screening of malignant from benign lesions by the proposed machine vision classifier.

INDEX TERMS
Acoustic radiation force impulse, virtual touch tissue imaging, Elastography, fractional-order convolution, multilayer machine vision classifier.

I. INTRODUCTION
Breast cancer is the most frequent cancer in females and affects about 2.1 million women each year worldwide; it also accounts for the highest number of breast cancer-related deaths. According to the Ministry of Health and Welfare in Taiwan, cancer ranked the first in terms of its mortality rate on the list of the top 10 causes of death in 2018. The number of people with cancer has also been statistically increasing, a phenomenon that has received worldwide attention. Breast cancer in females ranks the fourth in terms of its mortality rate among various cancers, and it is also the most commonly prevalent cancer in females and the leading cause of death ranking the first among females aged between 45 and 69 years [1], [2]. The signs and symptoms of breast cancer include a lump in the breast, a change in breast size and shape, dimpling of the skin, fluid coming from the nipple, a newly inverted nipple, or a red/scaly patch of skin [3], [4]. Current medical techniques have helped in advancing the diagnosis and treatment of breast cancer. Early detection of any breast...
cancer can increase the survival rate and also steadily decline the mortality rate. Therefore, an assistive decision-making method must be developed for rapid clinical screening of benign or malignant tumors in the breast. We propose an automatic screening method for the classification of tumor types using ARFI elastography [5]–[9].

A malignant tumor in the breast is a heterogeneous tissue with varying intratumoral molecular expression. Histopathological analysis is the gold standard in breast cancer diagnosis using imaging techniques. Therefore, digitalized breast imaging examinations, such as breast magnetic resonance imaging (MRI), breast computed tomography (CT), X-ray mammography, and ultrasound image [5]–[10], are assistive tools that can be used to screen benign or malignant tumors for making personalized decisions regarding cancer treatment. Mammography and ultrasound methods are primarily used for breast screening to assess the risk of breast cancer. Breast MRI captures both the anatomical and functional tumor characteristics to assess the presence of tumor heterogeneity on a computer monitor. Noninvasive MRI does not use ionizing radiation and can capture useful characteristics of tumors; however, a limitation of this technique is that it cannot capture tumor heterogeneity. Detailed imaging examination is generally used to evaluate difficult-to-assess abnormalities, lumpectomy sites, and the chemotherapy treatment seen on mammography and ultrasound image, while biopsy is required for detecting abnormalities in special cases. The decision for the patient to undergo biopsy depends in particular on breast imaging reporting and data system (BI-RADS) category assessment.

Breast MRI is generally used as a second-line examination tool for diagnosing the possibility before surgery. X-ray mammography is used for early detection, but it can easily result in high false positive rates and also cause pain and discomfort during the screening process. Dense breast tissue can appear white or light gray on an X-ray image, and hence it is difficult to interpret in younger females [10]. This examination is not suitable for younger subjects (suitable for women aged ≥45 years). Breast ultrasound imaging is a noninvasive, nonradiation, and early detection method that has been widely used in clinics [11]–[16]. It is the standard initial breast imaging modality and appears to be more effective in women aged 30–39 years than mammograms (first-line examination). However, traditional B-mode ultrasound imaging has certain drawbacks such as speckle noise and low contrast. Poor-quality images can reduce the observable features to detect the possible abnormalities, such as gray-grade, textural, and morphological features. Furthermore, the diagnostic results depend on the operator’s clinical experience and operation skill [17], [18]. Mean and median filtering methods are used to reduce speckle noises (salt and pepper noise). Median filter, as a nonlinear filter, is a promising method to reduce noises performs better than the mean filter. However, these filters cannot handle the entire image. For small or moderate levels of Gaussian noise, the median filter is effectively removes noise and preserves the edges with the fixed window size [19]. The middle pixel value is calculated by sorting all the pixel values from the surrounding neighborhood in numerical order. However, the median filter has a limitation when dealing with large amounts of noise (that is, high levels of noise) [20]. In addition, modified median filters have good capability for reducing noise, but their models are complicated.

Manual palpation is common used by clinicians, such as tumor growth, tissue scarring, and fibrotic tissue. In recent years, acoustic radiation force-based elasticity technique uses the acoustic force to deform soft tissues, and then the dynamic displacement response of these tissues is ultrasonically measured to estimate the tissue’s mechanical properties, such as heterogenous, non-linear, anisotropic, and viscoelastic breast tissues. Both qualitative elasticity metrics and images can be reconstructed these dynamic displacement responses from measurement data, leading to offer promising information for diagnosis and monitoring disease progression. Hence, ARFI elastography has been used as a radiation force-based imaging method [13]–[16] to create a qualitative 2-D map for evaluating tissue stiffness or strain in response to external compressions [21], [22]. On the basis of the stress–strain relationship, the measured tissue deformation in responses to external mechanical excitation can be related to tissue stiffness. This method produces a compression to the tissue with an impulsive, harmonic, and steady-state radiation force excitation [13]–[15], [22], [23]. For external compressions, the lesions indicate the difference between benign tumors and malignant tumors based on softer and stiffer tissues. This technique uses short-duration acoustic pulses with a fixed transmitting frequency to locate tissue displacement, such as virtual touch tissue quantification (VTQ) [22] and virtual touch tissue imaging (VTI) [16], [17], [22], [23]. In the VTI method, a numerical algorithm (mathematical) can be used to transform the strain changes of tissue stiffness to a grayscale image to visualize the tissue stiffness in a region of interest (ROI) [18], [24]–[26]. Therefore, the ARFI-VTI technique can be used to locate lesions for needle biopsy and to guide aspiration. Moreover, the texture and gray scale can be used to distinguish malignant (Figure 1(a)) and benign tumors (Figure 1(b)) from normal tissue.

In VTI imaging, malignant and benign lesions appear with bright and dark intensity, respectively, with malignant lesions representing a texture with high-intensity gray level (bright component), as shown in Figure 1(a). Therefore, texture analysis and classification methods using digital ultrasound images can be applied to screen benign and malignant lesions. Thereafter, artificial intelligence methods such as fuzzy-based neural network, radial basis function network, support vector machine network, wavelet neural network, and convolutional neural network [18], [24]–[29] can be selected to implement a decision-making classifier using ultrasound images for screening benign and malignant lesions. In addition, a filter to reduce speckle noise in both B-mode and ARFI-VTI images is lacking; speckle noise will degrade the fine details and lesion’s edge definition and also limit the
contrast resolution when detecting small and low-contrast lesions. Therefore, image enhancement process is a key technique to modify gray-scale levels that can adjust the lesion contrast in an ROI for visualizing texture details and morphological features. In this study, fractional-order convolution (FOC) operation [30]–[34] is applied for image enhancement and segmentation with the application of multiscale image texture enhancement method. Along with enhancing high-frequency and medium-frequency components, the FOC method can significantly retain low-frequency components in a nonlinear manner, which can highlight edge information and texture details and filter noises. Therefore, two-dimensional (2D) FOC operations are applied with suitable fractional-order parameters to enhance the ARFI-VTI images. Then, 2D FOC [31]–[33], maximum pooling process, flattening process, and generalized regression neural network (GRNN) [35]–[37] are integrated into a multilayer decision-making classifier, which can automatically screen benign and malignant lesions. The experimental results with a 10-fold cross-validation will demonstrate the feasibility of the proposed computerized assistive method. Compared with conventional methods, the proposed computerized assistive method can also improve the classification accuracy rate.

The remainder of this article is organized as follows: Section II describes the methodology, including ARFI-VTI imaging, the 2D fractional-order convolution, and the fully connected network-based decision-making classifier. Sections III and IV present the results and discussion, in comparison with the traditional neural network, and the conclusion, respectively.

II. METHODOLOGY

A. ULTRASOUND B-MODE AND VTI IMAGING

In this study, conventional B-mode breast ultrasound images were obtained using the IU22 system (Philips Healthcare, Bothell, WA, USA) with 7–12 MHz linear-array transducer (depth: <50 mm), and they were preliminary reviewed to locate the possible lesion site. Then, breast ARFI-VTI images were obtained from the ACUSON S2000 system (Siemens Medical Solutions, Mountain View, CA, USA) [16]. A short-duration acoustic pushing pulse (frequency: 2.6796 MHz) in ARFI imaging was transmitted to generate internal tissue excitation (depth: 1–20 mm) in the ROI by using the transducer, followed by a series of intensity pulses (frequency of 3.08 MHz and pulse repetition frequency of 3–12 kHz). This ARFI pushing pulse could be used to track tissue displacement or strain response to reflect the differences in tissue stiffness. Then, the ROIs were manually drawn and mapped to ARFI-VTIs using a mapping algorithm. Histopathological evaluations were conducted to confirm the breast tumor types (such as fibroadenomas or types of carcinomas), including benign and malignant breast tumors. Two expert clinicians (with >30 years of experience in the radiological field) confirmed and agreed on possible lesion types. The ARFI-VTI images were collected from 80 subjects, and they were divided into two subsets of trained images for training the multilayer machine vision classifier in the learning stage and untrained images for evaluating the classifier with cross-validation in the recalling stage.

B. IMAGE ENHANCEMENT PROCESS

Ultrasound imaging may involve speckle noise, which will affect image quality and hamper diagnostic decisions. Hence, image enhancement process with convolution operation is required to adjust gray-scale levels and filter noise in low-contrast images, such as conventional ultrasound images and ARFI-VTI images. The FOC operation was selected in this study; it can retain low-frequency components and enhance high-frequency and medium-frequency components. Using the definitions proposed by Grünwald–Letnikov [33], the general formula can be deduced as follows:

\[
\frac{d^v s(t)}{dt^n} \approx t^{-v} n^v \sum_{h=0}^{n-1} \Gamma(h - v) \frac{1}{\Gamma(h + 1)} s(t - ht/n) \tag{1}
\]

where \(s(t)\) is the time-varying signal in a 1D signal; \(v\) is the fractional-order parameter, \(0 < v < 1\); \(n \in \mathbb{R}\); \(\Gamma(\cdot)\) is the gamma function; \(n\) is the number of sampling points, \(h = 0, 1, 2, 3, \ldots, n-1\). For digital image processing, a discrete fractional-order differentiator for the discrete signal or image process can be proximately expressed in the general form [33]–[35]:

\[
D^v_t s(t) \approx s(t) + (-v)s(t - 1) + \frac{(-v)(-v+1)}{2}s(t - 2) + \cdots + \frac{\Gamma(-v+1)}{ht\Gamma(-v+h+1)}s(t - h) + \cdots \tag{2}
\]

The 2D image plotted on horizontal (\(x\)) and vertical (\(y\)) directions, with each pixel value at location \((x, y)\) in an ARFI-VTI image, can be expressed as \(s(x, y) \in [0, 255]\); then the fractional differential expression can be expressed as [33]

- horizontal direction:

\[
D^v_x s(x, y) \approx s(x, y) + (-v)s(x - 1, y) + \frac{(-v)(-v+1)}{2}s(x - 2, y) + \cdots + \frac{\Gamma(-v+1)}{ht\Gamma(-v+h+1)}s(x - h, y) + \cdots \tag{3}
\]

- vertical direction:
vertical direction:

\[ D_x^v s(x, y) \approx s(x, y) + (v) s(x, y - 1) + \frac{(v)(v+1)}{2} s(x, y - 2) + \frac{\Gamma(v+1)}{h! \Gamma(v+h+1)} s(x, y - h) + \ldots \tag{4} \]

where \( x = 1, 2, 3, \ldots, p \) and \( y = 1, 2, 3, \ldots, q \) are the image width and height, respectively. As shown in Equations (3) and (4), where \( h \to n = 2m - 2 \), the dimension of fractional-order mask, \((2m-1) \times (2m-1)\), can be designed, and \( n \) should be an even number \((n = 2, 4, 6, \ldots)\) to ensure that the fractional-order mask has a specific center. Hence, a \( 3 \times 3, 5 \times 5, \ldots, (2m-1) \times (2m-1) \) fractional-order mask, \( m = 2, 3, 4, \ldots \), can be designed for the local convolution process [32], [33]. In this study, the size of \( m = 2 \) was selected to construct \( 3 \times 3 \) mask matrices. Hence, we can implement eight fractional-order masks with three coefficients, “1”, “(−v)”, and “+(v)(v+1)/2”, including the directions of negative \( x \)-coordinate, negative \( y \)-coordinate, positive \( x \)-coordinate, positive \( y \)-coordinate, left downward diagonal, right upward diagonal, left upward diagonal, and right downward diagonal, as presented in Figure 2(a). The fractional-order masks have a rotation capability and can be rotated clockwise every \( 45^\circ \) (rotation invariant).

With the appropriate fractional-order parameters, \( 0 < v < 1 \), the original image was convolved to obtain the fractional-order gray gradient for 2D digital image processing. A spatial domain-based convolution operation can be implemented on the negative \( x \)-coordinate and negative \( y \)-coordinate, as shown in Figure 2(b). The fractional-order gray gradient can be defined as

\[ \nabla^v s(x, y) = \left[ \begin{array}{c} G_x^v s \\ G_y^v s \end{array} \right] = \left[ \begin{array}{c} \frac{\partial^v s(x, y)}{\partial x^v} \\ \frac{\partial^v s(x, y)}{\partial y^v} \end{array} \right] \tag{5} \]

and normalize the fractional-order gradient

\[ \nabla^v s = \frac{|G_x^v s| + |G_y^v s|}{255} \tag{6} \]

With the use of operators \( G_x^v s \) and \( G_y^v s \), the 2D fractional-order convolution operations are used to enhance the original image by convolving both horizontal and vertical directions and can be expressed as

\[ G_x^v s(x, y) = \sum_{i=-\lfloor \frac{k-1}{2} \rfloor}^{\lfloor \frac{k-1}{2} \rfloor} \sum_{j=-\lfloor \frac{k-1}{2} \rfloor}^{\lfloor \frac{k-1}{2} \rfloor} M_x(i, j) s(x + i, y + j) \tag{8} \]

\[ G_y^v s(x, y) = \sum_{j=-\lfloor \frac{k-1}{2} \rfloor}^{\lfloor \frac{k-1}{2} \rfloor} \sum_{i=-\lfloor \frac{k-1}{2} \rfloor}^{\lfloor \frac{k-1}{2} \rfloor} M_y(i, j) s(x + i, y + j) \tag{9} \]

where \( M_k = M_k^T = \begin{bmatrix} 0 & v & 0 \\ -v & 0 & 0 \\ 0 & 0 & 1 \end{bmatrix} \), the fractional-order masks are rotation-invariant, and the summation of elements is nonzero; \( h' = 3 \) is the dimension of the mask matrix for the \( 3 \times 3 \) fractional-order mask; \( i \) and \( j \) are the indices of rows and column number in the mask matrix, respectively. The 2D FOC is the process involving both horizontal and vertical-direction scans with the fractional-order sliding window, which multiplies each element by the corresponding input image pixel values, as shown in an example in Figure 2(b).

C. MAXIMUM POOLING AND FLATTENING PROCESS

After the 2D FOC process was completed, maximum pooling, which is a pooling process (down-sampling) with a \( 2 \times 2 \) sliding window (\( 2 \times 2 \) max filter), was used to pick the largest value in each subpattern from left to right and top to bottom. The pooling results are downsampled feature pattern and are derived from the largest value of maximum operation, for example, \( \max(0.5, 0.3, 0.1, 0.2) = 0.5 \) in Figure 2(c). This process was used to reduce the dimension of the feature pattern and also can retain the key information and the conformity of various features within the ROI. In this study, the dimension of the feature pattern can be reduced from \( 32 \times 32 \) (1,024 elements) to \( 16 \times 16 \) (256 elements), as shown by symbols (2) and (3) in Figure 3, respectively. Then, the pooled feature pattern was flattened from a matrix form (\( 16 \times 16 \)) to a vector form (\( 1 \times 256 \)), as shown by symbol (4) in Figure 3. The flattened pattern was fed into the pattern layer of multilayer machine vision classifier. The pooling process reduced the amount of feature data and computation time during pattern recognition task [27]–[29], [38].

D. GRNN-BASED MULTILAYER CLASSIFIER

After the flattening process, we can obtain the feature patterns in vector form and fully link them to the pattern layer of GRNN-based classifier as an input vector, \( \Phi = \{\phi_1, \phi_2, \phi_3, \ldots, \phi_{256}\} \). For ARFI-VTI images, collected images, \( \Phi(k) = \{\phi_1(k), \phi_2(k), \phi_3(k), \ldots, \phi_{256}(k)\} \), \( k = 1, 2, \ldots, K \), where \( K \) is the total number of training images, are consequently used for pattern training, pattern classification, and validation in the multilayer network. In this study, a GRNN is used to create a screening model with multiple inputs and corresponding outputs, consisting of input layer, pattern layer, summation layer, and output layer, as seen in Figure 3. The number of input node, pattern nodes, and output nodes can be determined by the dimension of the input and output vectors and the number of input–output paired training patterns. Then, optimization methods, such as gradient descent, least-square-error, and particle swarm optimization (PSO) algorithms [35], [37], [39], can be used to adjust the optimal network parameters, improving the prediction performance of classifier model.

For training GRNN-based classifier, considering \( K \) input–output paired training patterns, as input variable vector be a multi-dimensional feature pattern \( \Phi(k) = \{\phi_1(k), \phi_2(k), \phi_3(k), \ldots, \phi_{256}(k)\} \) and the output response variable be \( Y(k) = \{y_1(k), y_2(k), \ldots, y_{m(k)}\}, k = 1, 2, \ldots, K \),
the generalized algorithm for GRNN can be expressed as follows [33]–[35]:

Step 1) use input training patterns, \( \Phi(k) \), to set the connecting matrix \( W^{IP} \) between the input and pattern layers:

\[
W^{IP} = [w_{ki}]^T = [\phi_1(k), \phi_2(k), \phi_3(k), \ldots, \phi_N(k)]
\]  

(10)

where \( N \) is the number of input nodes, \( i = 1, 2, 3, \ldots, N \), \( N = 256 \) in this study, and the dimension of the matrix \( W^{IP} \) is \( K \times N \).

Step 2) set the connecting matrix, \( W^{PS} = [w_{kj}], j = 1, 2, 3, \ldots, m \) between the pattern and summation layers:

\[
W^{PS} = [y_1(k), y_2(k), \ldots, y_m(k)], 1^T
\]  

(11)

where \( m \) is the number of output nodes, \( j = 1, 2, \ldots, m \), \( m = 2 \) in this study, and the dimension of the matrix \( W^{PS} \) is \( K \times m + 1 \). The two output variables \( (y_1, y_2) \) are coded using binary code 0 / 1. The lesions can be divided into two types, and the coding for the two types is as follows: (1) benign tumor (Class #B): \( y_1, y_2 = [1, 0]; \)

---

**FIGURE 2.** Two-dimensional fractional-order convolution. (a) Eight combinations of fractional-order convolution masks to perform image enhancement, (b) Fractional-order convolution process with horizontal and vertical direction scans, (c) Maximum pooling operation.

**FIGURE 3.** The structure of fractional-order machine vision classifier, including 2D fractional-order convolution process (symbol 2), pooling process (symbol 3), flattening process (symbol 4) and multilayer fully connected network (GRNN network).
malignant tumor (Class #M): \([y_1, y_2] = [0, 1]\). Then, the dimensions of the connecting matrix \(W^{PS}\) will be \(K \times 3\) for \(m = 2\).

**Step 3**) feed the training or testing pattern vector (\(\Phi(k)\) or \(\Phi(0)\)) to the pattern layer and calculate the output of the pattern layer as follows:

\[
g_k = \exp[-\sum_{k=1}^{K} (\phi_i - w_{kj})^2 / 2\sigma_k^2], \quad i = 1, 2, 3, \ldots, N \quad (12)
\]

where \(\sigma_k\) is the smoothing parameter, all variables, \(\sigma_k\), in pattern layer, \(k = 1, 2, 3, \ldots, K\), are equal to the same variable \(\sigma\). The optimal smoothing parameter, \(\sigma_{opt}\), can be obtained using the PSO algorithm [37], [39], [40].

**Step 4**) feed the output of the pattern layer to the output layer and calculate the output, \(y_j\), of the output layer, \(j = 1, 2, 3, \ldots\):

\[
y_j(k) = \sum_{k=1}^{K} w_{kj} \times g_k \left/ \sum_{k=1}^{K} 1 \times g_k \right. = s_j(k) \left/ \sum_{k=1}^{K} g_k \right. \quad (13)
\]

The final output of GRNN-based classifier can be decided by hard limit function:

\[
y_j^* = \begin{cases} 1, & y_j \geq 0.5 \\ 0, & y_j < 0.5 \end{cases}, \quad j = 1, 2 \quad (14)
\]

\[
f = \text{sign}(y^*) = \begin{cases} 1, & y_1^* = 1 \in \text{Class #B} \\ 2, & y_2^* = 1 \in \text{Class #M} \end{cases} \quad (15)
\]

where “0.5” is the threshold value set to confirm the final decision, and the output \(f\) is the numerical value representing the two classes coded by numbers 1 and 2 for Classes #B and #M, respectively.

In Equation (12), a suitable smoothing parameter, \(\sigma_{opt}\), must be determined to enhance the classification accuracy, which is required to refine the optimal parameter in the GRNN-based classifier. The GRNN learning model adjusts this parameter only in the learning stage. Hence, this adaptive scheme can improve the drawback of the conventional backpropagation multilayer neural networks that require the adjustment of overall network parameters. Hence, the objective function/mean squared error (MSE) function is expressed as follows:

\[
MSE = \frac{1}{K} \sum_{j=1}^{2} \sum_{k=1}^{K} (T_{j}(k) - y_j(k))^2 \leq \varepsilon \quad (16)
\]

where \(\varepsilon\) is the specified tolerance error (convergent condition) to terminate the training stage. The optimization algorithm was used to determine the optimal smoothing parameter, \(\sigma_{opt}\), which was intended to minimize the MSE by iteration computation. While the training stage allowed the MSE to reach a small value, terminating the training stage takes a considerable amount of time. Hence, the experienced tolerance error was set \(\varepsilon = 10^{-2}\).

**E. TRAINING GRNN-BASED CLASSIFIER WITH PSO ALGORITHM**

In training stage, the PSO algorithm is adopted to adjust and optimize the smoothing parameter, \(\sigma_{opt}\), to minimize the MSE function. In PSO algorithm, each particle agent is encoded with the center position and velocity, which are represented by a \(G\)-dimensional vector, as center position vector \(\delta^p = [\sigma_{p1}^g, \sigma_{p2}^g, \sigma_{p3}^g, \ldots, \sigma_{pg}^g] \) and velocity vector \(\Delta \delta^p = [\Delta \sigma_{p1}^g, \Delta \sigma_{p2}^g, \Delta \sigma_{p3}^g, \ldots, \Delta \sigma_{pg}^g, \ldots, \Delta \sigma_{ps}^g, \ldots, \Delta \sigma_{pg}^G] \), \(p = 1, 2, 3, \ldots, p_{max}\), where agent \(g = 1, 2, 3, \ldots, G\), where \(G\) is the particle population size (\(G = 20, 30, \) and 40 in this study); \(p\) is the number of iterations. Its algorithm adjusts the optimal parameter in iteration computations. A global search is performed to find the desired optimal parameter and can be expressed the center position and velocity, as follows [33], [35], [37], [38]:

- velocity:

\[
\Delta \sigma_{g}^{p+1} = \Delta \sigma_{g}^p + c_1 \text{rand}_1(\sigma_{best_g} - \sigma_{g}^p) + c_2 \text{rand}_2(\sigma_{best} - \sigma_{g}^p) \quad (17)
\]

- acceleration parameters: \(c_1 = (b_1 - 1) \frac{p}{p_{max}} + a_1, c_2 = (b_2 - a_2) \frac{p}{p_{max}} + a_2\)

- central position (optimal smoothing parameter):

\[
\sigma_{g}^{p+1} = \sigma_{g}^p + \Delta \sigma_{g}^{p+1} \quad (18)
\]

where parameters, \(\text{rand}_1 \in (0, 1)\) and \(\text{rand}_2 \in (0, 1)\), are the uniform random numbers between 0 and 1; \(p_{max}\) is the maximum iteration number; two parameters, \(c_1\) and \(c_2\), are the time-varying acceleration parameters—the first term, \(c_1\), is the cognitive component, and the second term, \(c_2\), is the social component; \(a_1, b_1, a_2,\) and \(b_2\) are constant values, of which the experienced values are \(c_1\) from 2.5 to 0.5 and \(c_2\) from 0.5 to 2.5, respectively [35], [39], [40]. While cognitive component, \(c_1\), has a higher value, the search region will expand at each search stage. Multiple particles are allowed to determine the individual best solution, \(\sigma_{best_g}\), around the search space. Monotonously decreasing the parameters, \(c_1\) and \(c_2\), enables the search region to gradually approach the global best solution, \(\sigma_{best}\), with fine-tuning at the end of the search stage. The term \(p/p_{max}\) is also used to control the acceleration parameters, \(c_1\) and \(c_2\), which pulls each particle toward the best solution.

**F. COMPUTER-AIDED DECISION-MAKING IMPLEMENTATION**

The proposed digital image processing and screening methods include (1) searching the possible lesion (as shown by the green-bounded box in Figure 4) in the ROI, (2) performing the 2D FOC, maximum pooling process, and flattening process, and (3) screening of benign and malignant breast tumors. The proposed algorithms were designed on a tablet PC using a high-level programming language in LabVIEW programming software (NI™, Austin, TX, USA) and MATLAB software (1994-2019, The MathWorks, Inc. USA). The prototype
A. ROI ENHANCEMENT AND LESION REGION BOUNDING

In convolution processes, the horizontal and vertical fractional-order masks with fractional-order parameter, \(v\), were used to move the sliding window over the ROI and a local convolution operation was performed. The value of the parameter \(v\), assigned from 0 to 1, could not totally fit the ARFI-VTI image enhancement. Based on previous studies [32], [33], appropriate parameters were suggested to assign as \(v = (0.0, 0.3) \approx [v] \approx 0.0 < v < 0.3\), as seen in the image enhancement for malignant and benign tumors in Figures 5(a) and 5(b), respectively. The fractional-order masks had a rotation capability and were rotated every 45 degrees (rotation invariant) in eight directions, as seen in Figure 2(a). This implied that the fractional-order mask was able to enhance the high-frequency edge information in the region where the gray gradient changes and also retained the low-frequency contour information of the original image. Hence, these fractional-order masks could be used to describe the edges that are present and to remove noise for machine vision image processing. Figures 5(a) and 5(b) show image enhancement with different fractional-order parameters for malignant and benign tumors. The experimental results also reveal that the image enhancement appeared to be similar and stable from the fractional-order \(v = 0.05\) to 0.30. Thus, the fractional-order mask with \(v = 0.10\) was assigned for all experiments in this study.

ARFI ultrasound assessments are affected by imaging depth variation among different subjects between focal depths of 1 and 20 mm, thus degrading the fine details and lesion’s edge definition and causing difficulty in detecting small and low-contrast lesions in poor-resolution images. Figure 6 shows the digital image processes with intensity inhomogeneity for malignant and benign lesions. The 2D FOC operations could enhance the visibility of lesion structures in the ROI, as shown in the malignant and benign tumors in Figures 6(a) to 6(d). For example, the gray gradient distributions of malignant lesions appeared as rough shapes and indicated higher gray gradient values as \(>0.5130\) and \(>0.6425\), as depicted by the green regions in Figures 6(a) and 6(b), respectively. In the lesion regions with high-frequency variations, the gray gradient values exhibited more variability. Furthermore, homogenous regions had a flat shape and contained lower gray gradient values for benign lesions, as shown by the blue region in Figures 6(c) and 6(d), respectively. In contrast to malignant lesions, the gray gradient values had little variations with smooth textures. Hence, the fractional-order convolution operation resulted in a gradient intensity for the segmentation of lesion structures within the ROI. For bounding the specific region, the lesion’s minimum gray gradient value as a threshold value could be determined by the contour search algorithm [32], [42]. Then, the lesions could be automatically drawn on each ARFI-VTI image by the threshold value by detecting the brighter pixel in the ROI. Hence, the FOC could easily detect the differences in gray gradients to indicate the isolines and to search the lesion

of computer-aided decision-making application software was implemented for screening breast lesions, as seen in Figure 4.

In digital image processing, each breast ARFI-VTI image was converted from the DICOM format into a tagged image file (TIF) format. The TIF format has the advantage of losslessness and short computation time for routine image examinations [32]. Each size of ROI was specified as a 32×32 pixel-sized image, 8 bites/pixel, with 0–255 gray-scale values. ARFI-VTI images were obtained from the 80 subjects (age range: 31–97 years; mean age: 51.39±13.84 years, tumor size: 39.66±19.75 mm, grade tumor size: T0–T3 [41]) enrolled at TVGH, Taipei City, Taiwan, as depicted in Table 1. Hence, in clinical applications, feature patterns were mined by the graphical user interface (screenshot in Figure 4) and were collected into an image database. The patterns can be divided into two groups of dataset: one subgroup for training the classifier in the training stage and another subgroup for evaluating classifier performance in the recalling stage by recall (%), precision (%), accuracy (%), and F1 score.

### TABLE 1. Experimental profile of the enrolled subjects.

| Subject | Benign Lesion | Malignant Lesion | Total |
|---------|---------------|------------------|-------|
| Age Range | 34 | 46 | 80 |
| Mean | 35 - 97 | 35 - 97 | 31 - 97 |
| Age (year) | 11.34 | 12.70 | 13.84 |
| Tumor Size (mm) | 39.67 | 38.65 | 39.66 |
| Grade Tumor Size (T0-T4) | T1-T3: 20–70mm | T0-T3: 0–70mm | T0-T3: 0–70mm |
| Size (T0-T4) in diameter | in diameter | in diameter | in diameter |

Note: T0: < 10 mm in diameter; T1: 10–20 mm in diameter; T2: 20–50mm in diameter; T3: > 50mm in diameter [41]

III. EXPERIMENTAL RESULTS AND DISCUSSION

The feasibility study of the proposed digital image processing and screening methods was validated, as detailed below.
contours for further applications in image segmentation, feature extraction, and classification analysis in specific areas or the ROI.

**B. GRNN-BASED CLASSIFIER TRAINING AND TESTING**

A total of 320 ARFI-VTI images were collected from the 80 enrolled subjects (TVGH IRB approval number V103C-059), including 176 images for malignant tumors and 144 images for benign tumors. A total of 122 images (50 malignant tumors and 72 benign tumors) were randomly selected from different enrolled subjects to train the machine vision classifier in the learning stage, and the remaining images were also randomly selected from different enrolled subjects to evaluate the performance of the classifier with a 10-fold cross-validation in the recalling stage. In the cross-validation stage, the dataset was divided into two subsets of 122 trained images (72 benign and 50 malignant tumors) and 122 untrained patterns (72 benign and 50 malignant tumors or 50 benign and 72 malignant tumors) in each test. In this study, these trained and untrained images were randomly selected from the dataset for 10-fold cross-validation, as shown in Tables 2 and 3. We randomly fed the subset of 122 images (about 38% of the dataset) for training purposes and then evaluated the specificity, sensitivity, and accuracy with the untrained images (about 38% of the dataset) using 10-fold cross-validation by also randomly selecting the trained and untrained images into 10 groups.

In the learning stage, after 2D FOC and pooling computations, we were able to obtain 122 paired input–output training pattern \( \Phi(k) = [\phi_1(k), \phi_2(k), \phi_3(k), \ldots, \phi_{256}(k)] \) and \( \gamma(k), \gamma_2(k) = \{\text{benign, malignant}\}, k = 1, 2, 3, \ldots, 122 \), for training the GRNN-based classifier. The output patterns were encoded as the binary values “1” or “0” for possible class identification as follows: (1) benign class: \([1, 0]\) and (2) malignant class: \([0, 1]\). Thus, we were able to construct the classifier consisting of 256 input nodes, 122 pattern nodes, 3 summation nodes, and 2 output nodes, as depicted in Figure 3. Then, the PSO optimization algorithm was used to search the optimal network parameter \( \sigma \). The PSO algorithm with time-varying acceleration coefficients [35], [37], [39], [40], particle groups, \( G = 30 \) (experienced value [35], [37]), and maximum iteration number of \( p_{\text{max}} = 50 \) was used to optimize the smoothing parameter. In the training stage, we performed at least 5 runs with random initial parameters for training the GRNN-based classifier. For the convergent condition, tolerance value \( \varepsilon \leq 10^{-2} \) and optimal smoothing parameters could be guaranteed to minimize the mean squared error (MSE), as shown in Figure 7(a), which indicated the MSE versus the number of iterative computations, respectively. It could be observed that the iteration computing process required \(<20 \) iterative computations (CPU execution time: \(<1.2450 \text{ s}\) to reach the pre-specific convergent condition. The average optimal parameter, \( \sigma_{\text{opt}} = 0.0036 \), can be obtained to minimize the objective function. As shown in Figure 7(b), the convergent condition could also be validated as each particle agent guaranteed to adjust its central position (smoothing parameter) using the velocity, which rapidly reached the convergent condition (particle population size, \( G = 30 \); about 17 iterations and 510 computations). For the training patterns, the PSO algorithm with the time-varying acceleration coefficients had stable solutions to search the near-optimal parameter and a guaranteed classification accuracy of 100.00% in the training stage.
In the recalling stage, the remaining images were randomly divided into two subgroups, including (1) subgroup #1 from 1- to 5-fold cross-validation: 72 malignant and 50 benign classes and (2) subgroup #2 from 6- to 10-fold cross-validation: 50 malignant and 72 benign classes, as presented in Tables 2 and 3. A 10-fold cross-validation method was used to evaluate the performance of the GRNN-based classifier. As shown in Table 2, cross-validation with two subgroups of untrained images was performed by randomly interchanging trained patterns and untrained patterns [43]. These two groups of patterns were randomly selected from the dataset, with a subset of 122 patterns in the learning stage and 122 untrained patterns for evaluating the performance of the classifier. Table 2 shows the experimental results for the GRNN-based classifier, with a mean recall and precision of 92.92±3.43% and 80.42±6.45%, respectively, for identifying the “malignant tumors (TP),” and a mean accuracy of 87.78±2.17% for identifying the possible correct classes (TP and TN). The mean precision, as a positive predictive value (PPV), was greater than 80.00% for evaluating classifier’s performance for screening the possible “malignant” present. Thus, the feasibility of the GRNN-based classifier with the PSO algorithm could be verified and validated.

In addition, 2D first-order or second-order convolution, as seen in Figures 8(a) and 8(b), maximum pooling operation, and GRNN-based classifier could also be integrated into a multilayer machine vision classifier. In this study, the GRNN-based classifier with the 2D second-order (Laplacian) convolution was implemented to train a classifier. The PSO algorithm was also used to determine the optimal parameter in the training stage with the time-varying acceleration parameters and specific convergent condition. For the same enrolled subjects and image dataset, with the 10-fold cross-validation in the recalling stage, Table 3 revealed a mean recall and precision of 81.92±10.41% and 75.40±14.14%, respectively, for identifying “malignant tumors (TP),” and a mean accuracy of 79.43±6.53% for identifying the possible classes. In contrast to the GRNN-based classifier with the second-order convolution, the experimental results indicate that the proposed screening classifier had higher recall, precision, and accuracy in the clinical indication. The proposed classifier also had a higher F1 score (0.8615±0.0495) than GRNN-based classifier with second-order convolution (0.7774±0.0962) for measuring the harmonic mean of recall and precision indexes.

C. DISCUSSION
Ultrasound imaging could cause speckle noise due to a phase-sensitive transducer, which would affect image quality and degrade the diagnostic decisions for identifying the lesion’s fine details in the ROI. Hence, an image enhancement process is needed to modify the gray-scale levels and readjust
the image contrast by using one-dimensional (1D) or 2D convolution process and histogram method [47], [48]. In the convolution process, such as in benign tumors, Figure 8(c) depicts the comparisons with the fractional-order convolution mask (fractional-order, \( v = 0.1 \)) and the traditional Laplacian mask (mask sized 3 \( \times \) 3, second-order derivative) and Sobel mask (mask sized 3 \( \times \) 3, first-order derivative) convolution masks [32], [34]. Through Sobel mask operation (first-order mask, as shown in Figure 8(a)), we were able to obtain the enhanced lesion feature, but the texture in an ROI was different from the original image. The Laplacian mask (second-order mask, as shown in Figure 8(b)) operation produced grayish edge line and other region resulted in making dark (background). However, first-order and second-order derivatives are sensitive to noise, such as speckle noise in B-mode ultrasound imaging or ARFI-VTI images, due to which these operators would exaggerate the effects of noise. Second-order derivatives would exaggerate noise twice, as shown by the feature patterns in Figures 8(c) and 8(d). Images with noise, the noises might also be enhanced at the same time and easily lead to wrong information in an ROI. Hence, it can be observed that the feature patterns in the vector form could be easily categorized into the class of malignant tumors by using the machine vision classifier. In addition, it was difficult to draw the breast lesion contours precisely. Both first-order and second-order mask still suffer from drawbacks, such as the sensitivity of sliding filter window size, shape, and parameter assignment.

The histogram method is a simple process to determine the threshold value for detecting the lesion contours in the ROI. In histogram processing, a histogram of a grayscale image represents the frequency distribution of gray levels. However, this method is also sensitive to noise and has difficulty detecting the boundary in poor-quality or low-contrast digital images. In the frequency domain, the wavelet or Fourier method involves designing a frequency domain filter to remove speckle noise from ultrasound images with a definite cutoff frequency. However, in real-time application (real world), obtaining the noise background and cutoff frequency from the original image’s frequency is difficult. In addition, these processes require the optimal threshold cut-off frequency to remove speckle noise with the adaptive algorithms and involve complex computations [49], [50]. Adaptive filters are also designed in the frequency domain by using the genetic algorithm and PSO method, which still require complex computations.

Hence, in digital image processing, image enhancement with noise removal obtained by the FOC was as clear as the first-order and second-order masks, as depicted in Figures 8(c) and 8(d), respectively. The possible lesion in the ROI was enhanced to detect the texture and edges in multiscale by controlling the fractional-order parameter. As presented in Figure 5, the experimental results reveal that the lesion’s feature pattern in the ROI was distinguishable and stable from the fractional-order as \( v = (0.0, 0.3) \) for all ARFI-VTI images. Meanwhile, considering the higher quality digital images, enhanced texture details would increase the accuracy for further automatic pattern recognition.

In a clinical context, breast X-ray photograph is a non-machine learning-based method and also is a first-line examination method for screening breast tumors. It uses low-dose X-rays to view the breast tissue, as seen in the malignant tumor in Figure 9(a), and could detect calcification or small tumors, as well as asymptomatic stage 0 breast cancer. However, with X-ray images in high breast density are difficult to interpret because lesions might be shadowed by the dense tissues. As a result, tumors in women with high breast density, such as dense breast or intermediate mixed-type breast density in Chinese women [42], [43], as seen in Figure 9(b) [44], may not be identified accurately, thereby increasing patients’ risk of developing breast cancer. Hence, this examination method is suitable for females aged 45 years and above or specific subjects. Ultrasound examination, such as B-mode imaging and elastography using shear wave with VTI and VTQ [16], [17], [22]–[24], as shown in Figures 9(c) to 9(f), are suitable for screening breast tumors for females aged 30 years and above. Among the current techniques [23], VTI showed sensitivities of >95% and >85% and specificities of >90% and 100% with positive predictive values of >95% and 100% for identifying benign and malignant lesions; VTQ showed sensitivities of >70% and 100% and specificities of 100% and 100% with positive predictive values of 100% and >75% for identifying benign and malignant lesions. Compared with VTQ, VTI is more reliable.
as an assistive diagnostic tool in assessing breast lesions. Its method can also be used to guide and locate for needle biopsy of mass tissue for pathology examinations. In addition, digital medical images could be transferred to a computer and electronically enhanced through an image enhancement process. These images could also magnify and optimize parts of the breast tissue to view the entire breast on an image. Both breast X-ray and ultrasound imaging require coordination of clinical symptoms, palpation, and mammography to reduce the chances of misdiagnosis.

164232 VOLUME 8, 2020
**FIGURE 8.** Image enhancement comparisons with the fractional-order, Laplacian, and Sobel masks. (a) Sobel (first-order) mask, (b) Laplacian (second-order) mask, (c) image enhancement comparisons with the fractional-order, Laplacian, and Sobel masks for benign tumor; (d) image enhancement comparisons with the fractional-order, Laplacian, and Sobel masks for malignant tumors.
TABLE 4. Comparisons between GRNN-based classifier with the 2D FOC and 2D second-order convolution and RDF-based classifier with the 2D FOC.

| Method                  | 2D FOC + GRNN-based Classifier | 2D Second-order Convolution + GRNN-based Classifier | 2D FOC + RDF-based Classifier [51] |
|-------------------------|---------------------------------|--------------------------------------------------|-----------------------------------|
| Trained Dataset         | 122                             | 122                                              | 122                               |
| Untrained Dataset       | 122                             | 122                                              | 122                               |
| Training Algorithm      | PSO Algorithm                   | PSO Algorithm                                    | Batch Normalization [52]          |
| Image Processing Layer  | 2D FOC, Maximum Pooling, and Flattening Processes | 2D Second-order Convolution, Maximum Pooling, and Flattening Processes | 2D FOC, Maximum Pooling, and Flattening Processes |
| Multilayer Classifier Topology | 256-122-3-2                      | 256-122-3-2                                      | 256-122-1-2                      |
| Memory Storage (byte)   | (256 × 122 × 4 bytes), (122 × 2 × 4 bytes), and (122 × 1 × 4 bytes) | (256 × 122 × 4 bytes), (122 × 2 × 4 bytes), and (122 × 1 × 4 bytes) | (122 × 2 × 4 bytes) |
| Maximum Iteration       | 50                              | 50                                               | ×                                 |
| Convergent Condition    | ≤ 10⁻²                          | ≤ 10⁻²                                           | ×                                 |
| Iterative Computation   | < 20                            | < 20                                             | ×                                 |
| Computation             | < 600 (G = 30)                  | < 600 (G = 30)                                   | ≈ 0.0100                          |
| Mean CUP Time (sec)     | < 12450                         | < 1,1250                                         |                                   |
| Cross-Validation        | 10-fold Cross-Validation         | 10-fold Cross-Validation                          | 10-fold Cross-Validation           |
| Mean Recall (%)         | 92.92 ± 3.43                    | 81.92 ± 10.41                                    | 90.78 ± 4.29                     |
| Mean Precision (%)      | 80.42 ± 6.45                    | 75.40 ± 14.15                                    | 79.63 ± 4.17                     |
| Mean Accuracy (%)       | 87.86 ± 2.10                    | 79.43 ± 6.53                                     | 86.08 ± 3.04                     |
| Mean Negative Predictive Value (%) | 94.22 ± 1.63                  | 81.09 ± 11.19                                    | 91.56 ± 5.49                     |
| Mean F1 Score           | 0.8615 ± 0.0495                 | 0.7774 ± 0.0962                                  | 0.8474 ± 0.0299                  |

Note: Negative Predictive Value (%) = \( \left( \frac{TN}{TN + FN} \right) \times 100\% \), where \( TN \) and \( FN \) are true positive and false negative, respectively.

In pattern recognition, multilayer machine learning methods and deep learning neural networks have been proposed to solve the nonlinear separable classification problems for multiclass classifications. Deep learning methods, such as the multilayer perceptron network and convolutional neural network, were used to design a classifier for classification and pattern recognition [27]. However, these methods require assigning multiple convolutional layers and pooling layers in the feature extraction stage and multiple hidden layers in fully connected weights. Hence, the structure of the multilayer network, hidden nodes in the hidden layers, connected weighting parameters, convolution mask sizes, convolutional mask parameters must be determined, whereas the large amount of training patterns are major concerns that increase the rate of the design cycle and computational time. The proposed structure of the multilayer fractional-order machine vision classifier is easy to determine by using the input-output paired training patterns and the type of classification. After the classifier was constructed, PSO algorithm is employed to find the optimum smoothing parameters by using <20 iterative computations (< 600 computations with particle population size, \( G = 30 \)) to reach the pre-specific convergent condition. In contrast to GRNN-based classifier with 2D second-order convolution, the proposed GRNN-based classifier was superior in specificity, sensitivity, and accuracy in clinical indication. Literature [51] had also proposed a random decision forest (RDF)-based classifier for the screening of breast benign and malignant tumors. Integrated 2D FOC process, maximum pooling process, and flattening process, and RDF-based classifier were carried out using a multilayer machine vision classifier. This classifier determined the network parameters using batch normalization method [52] for subdecision trees without iteration computations and required less parameter assignment in the training stage. This method also requires a less storage memory for storing network parameters.
parameters (4 bytes per digital storage) than the GRNN-based classifier. In the breast lesions, GRNN-based classifiers indicated a higher mean recall and precision for identifying TP cases, and a negative predictive value (NPV = 94.22 ± 1.63%) for identifying TN cases (benign tumors) as shown in Table 4. In contrast to the RBF-based classifier with 2D FOC, the proposed GRNN-based classifier also provided a promising clinical indication in terms of mean accuracy (for identifying both TP and TN cases) and F1 score (for measuring recall and precision) for screening breast lesion. GRNN- and RDF-based classifiers could continually improve the network parameters with new training patterns in the retraining stage. Therefore, the mechanism of their pattern could be applied in medical devices or commercial off-the-shelf platforms such as software medical device or software in a medical device [53], [54].

IV. CONCLUSION

In this study, we developed a multilayer fractional-order machine vision classifier for rapid screening of benign and malignant tumors in the breast tissue. Based on the ARFI-VTI images, we applied the 2D fractional-order convolution to process breast ultrasound images of inhomogenous intensity, low contrast, and speckle noise variance, which was able to non-linearly enhance the high-frequency edge information with gray gradient changes and retain the low-frequency smoothing region in digital images. Therefore, its process could enhance the visibility of lesion structures in an ROI for further image segmentation, feature extraction, and classification applications. Then, the lesion contours could be automatically drawn by the contour search algorithm. For bounding the specific region, the lesion contours were used to guide aspiration for further needle biopsy and histopathological analysis. In the image processing, the fractional-order convolution masks based on G-L definition exhibited better ability in image enhancement for the ARFI-VTI images, which could control the fractional-order parameter, \( v \), in multiscale. In all the enrolled ARFI-VTI image processes, we suggested the use of two convolution masks sized 3 × 3 and fractional-order, \( v = 0.10 \) (appropriate range: (0.0, 0.3)). We compared the experimental results of gray gradient images processed by the fractional-order convolution mask with those processed by the traditional convolution mask. The fractional-order convolution was able to well enhance the texture details of the ARFI-VTI images.

In contrast to the GRNN with Laplacian convolution and RDF with 2D FOC, in terms of the 10-fold cross-validation, the proposed classifier had promising results for identifying “malignant” and “benign” tumor present. These experiments, with >80% mean recall and precision (PPV), demonstrated a high confidence in screening malignant tumors. The superior performances indicated that the proposed multi-layer fractional-order machine vision classifier has the ability to screen abnormalities in breast ARFI-TVI elastography. In real-world applications, abnormality interpretation in several medical images usually requires repetitive interpretation by humans. Therefore, the proposed intelligent methods could provide a vital role in medical automatic diagnostic applications by conducting rapid screening of the class of a lesion so that clinicians can focus on clinical treatment. In future research, Harris Corner Detector with Gaussian function can be used to reduce image noise and aliasing artifacts through the 2D convolution process in computer vision applications. This approach uses a nonlinear Gaussian filter to enhance the lesion’s feature pattern in an ROI. We can also combine the 2D fractional-order and Harris Corner convolution and the random decision forest-based classifier (also with minimal parameter tuning and assignment) to enhance the classification performance and screening accuracy. In addition, these imaging and classification algorithms could be easily implemented in a PC-based assistive tool in clinical applications for assisting radiologists. Hence, preliminary rapid screening without manual inspection can be performed in initial breast imaging modality.

ABBREVIATIONS

| Abbreviation | Description |
|--------------|-------------|
| ARFI | Acoustic Radiation Force Impulse |
| VTI | Virtual Tissue Imaging |
| ARFI-VTI | Acoustic Radiation Force Impulse- Virtual Tissue Imaging |
| VTQ | Virtual Tissue Quantification |
| ROI | Region of Interest |
| G-L | Grünwald–Letnikov |
| FOC | Fractional-Order Convolution |
| GRNN | Generalized Regression Neural Network |
| PSO | Particle Swarm Optimization |
| RDF | Random Decision Forests |
| COTS | Commercial off-the-Shelf |
| PPV | Positive Predictive Value |
| NPV | Negative Predictive Value |
| SaMD | Software as a Medical Device |
| SiMD | Software in a Medical Device |

REFERENCES

[1] X. Yao, Y. Gan, E. Chang, H. Hibshoosh, S. Feldman, and C. Hendon, “Visualization and tissue classification of human breast cancer images using ultrahigh-resolution OCT,” Lasers Surg. Med., vol. 49, no. 3, pp. 258–269, Mar. 2017.
[2] J. Deeba, N. Albert Singh, and S. Tamil Selvi, “Computer-aided detection of breast cancer on mammograms: A swarm intelligence optimized wavelet neural network approach,” J. Biomed. Informat., vol. 49, pp. 45–52, Jun. 2014.
[3] (May 2019). Breast Cancer Treatment (PDQ)-Patient Version. [Online]. Available: https://www.cancer.gov/types/breast/patient/breast-treatment-pdq#section/all?redirect=true
[4] C. Saunders and S. Jassal, Breast Cancer. Oxford, U.K.: Oxford Univ. Press, ch. 13, Oct. 2015.
[5] J. Dahl, G. Pinton, M. Palmieri, V. Agrawal, K. Nightingale, and G. Trahey, “A parallel tracking method for acoustic radiation force impulse imaging,” IEEE Trans. Ultrason., Ferroelect., Freq. Control, vol. 54, no. 2, pp. 301–312, Feb. 2007.
[6] C. Fierbeinteao-Braticevici, D. Andreoussou, R. Usvat, D. Cretoiu, C. Baicus, and G. Marinocchi, “Acoustic radiation force imaging sonoelastography for noninvasive staging of liver fibrosis,” World J Gastroenterol., vol. 15, no. 44, pp. 5525–5532, 2009.
[7] M. Friedrich-Rust, K. Wunder, S. Kriener, F. Sotoudeh, S. Richter, J. Bojunga, E. Herrmann, T. Poynard, C. F. Dietrich, J. Vermehren, S. Zeuzem, and C. Sarrazin, “Liver fibrosis in viral hepatitis: Noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography,” Radiology, vol. 252, no. 2, pp. 595–604, Aug. 2009.
JIAN-XING WU (Member, IEEE) was born in 1985. He received the B.S. and M.S. degrees in electrical engineering from the Southern Taiwan University of Science and Technology, Tainan, Taiwan, in 2007 and 2009, respectively, and the Ph.D. degree in biomedical engineering from National Cheng Kung University, Tainan, in 2014. He is currently a Postdoctoral Research Fellow with the X-ray and IR Imaging Group, National Synchrotron Radiation Research Center, Hsinchu, Taiwan, from 2014 to 2017. He is also a Postdoctoral Research Fellow with the Department of Niche Biomedical LLC, California NanoSystems Institute at UCLA, Los Angeles, USA, from 2017 to 2018. He has been an Assistant Professor with the Department of Electrical Engineering, National Chin-Yi University of Technology, Taichung, Taiwan, since 2019. His research interests include artificial intelligence applications in electrical engineering and biomedical engineering, biomedical signal processing, medical ultrasound, medical device design, and X-ray microscopy.

HSIAO-CHUAN LIU received the M.S. degree in biomedical engineering from National Yang-Ming University, Taipei, Taiwan, in 2005, and the Ph.D. degree in biomedical engineering from the University of Southern California, Los Angeles, CA, USA, in 2019. He is currently a Research Fellow with the Mayo Clinic, Rochester, MN, USA. His current research interests include cell mechanics, acoustic tweezers, shear wave and surface wave elastography, imaging processing, and clinical ultrasound.

PI-YUN CHEN received the Ph.D. degree from the Graduate School of Engineering Science and Technology, National Yunlin University of Science and Technology, Yunlin, Taiwan, in 2011. She is currently an Associate Professor with the Department of Electrical Engineering, National Chin-Yi University of Technology, Taichung, Taiwan, where she has also been the Chief of the Department of Electrical Engineering, since 2019. Her current research interests include neural network computing and its applications, fuzzy systems, and advanced control systems.

CHIA-HUNG LIN was born in Kaohsiung City, Taiwan, in 1974. He received the B.S. degree in electrical engineering from the Tatung Institute of Technology, Taipei, Taiwan, in 1998, and the M.S. and Ph.D. degrees in electrical engineering from the National Sun Yat-sen University, Kaohsiung, Taiwan, in 2000 and 2004, respectively. He is currently a Professor with the Department of Electrical Engineering, Kao-Yuan University, Kaohsiung, from 2004 to 2017. He is currently a Professor with the Department of Electrical Engineering, National Chiao-Tung University of Technology, Taichung, Taiwan, where he has been a Researcher of the Artificial Intelligence Application Research Center, since 2018. His research interests include neural network computing and its applications in power system and biomedical engineering, biomedical signal and image processing, healthcare, hemodynamic analysis, and pattern recognition.

YI-HONG CHOU is the Chief of the Ultrasound Section at the Taipei Veterans General Hospital and a Professor of radiology with the National Yang Ming University School of Medicine, Taipei, Taiwan. He was the Former President of Society of Ultrasound in Medicine (SOMROC), the Former Chairman of Education Committee of the Asian Federation of Societies for Ultrasound in Medicine and Biology (AFSUMB), and the Former Associate Editor of the Ultrasound in Medicine and Biology, the official journal of World Federation of Ultrasound in Medicine and Biology (WFUMB). His scientific interests include ultrasound image analysis, computer-aided diagnosis and detection, and ultrasound-guided minimally invasive techniques. He is currently the President of the Radiological Society of the ROC, the Treasurer of the AFSUMB, the Chairman of Education Committee of the SUMROC, the Editor-in-Chief of the Journal of Medical Ultrasound (JMU), the official journal of the AFSUMB. He has been active in scientific and teaching programs nationally and internationally and has organized a number of international congresses, workshops, and symposia, particularly on ultrasound and imaging of the Breast and Emergency and Critical Care. He has expertise in all imaging modalities of abdominal and breast diseases, and emergency medicine and critical care.

K. KIRK SHUNG (Life Fellow, IEEE) received the B.S. degree in electrical engineering from Cheng Kung University, Tainan, Taiwan, in 1968, and the Ph.D. degree in electrical engineering from the University of Washington, Seattle, WA, USA, in 1975. He was appointed as the Dean’s Professor of Biomedical Engineering, an endowed position, at the Viterbi School of Engineering, University of Southern California (USC), Los Angeles, CA, USA, in 2013, where he has been a Professor of biomedical engineering, since 2002, and has been the Director of the NIH Resource Center on Medical Ultrasonic Transducer Technology, since 1997. He has published more than 500 articles and book chapters. His current research interests include ultrasonic transducers, high-frequency ultrasonic imaging, and ultrasound microbeam. He is a Fellow of the American Institute of Ultrasound in Medicine and a Founding Fellow of the American Institute of Medical and Biological Engineering. He was a recipient of the IEEE Engineering in Medicine and Biology Society Early Career Award, in 1985, and the coauthor of a paper that received the Best Paper Award for the IEEE TRANSACTIONS ON ULTRASONICS, FERROELECTRICS, AND FREQUENCY CONTROL (UFFC), in 2000. He received the Holmes Pioneer Award in Basic Science from the American Institute of Ultrasound in Medicine, in 2010, the Academic Career Achievement Award from the IEEE Engineering in Medicine and Biology Society, in 2011, and the IEEE Biomedical Engineering Award in 2016. He was elected as an Outstanding Alumnus of Cheng Kung University, in 2001. He was selected as the Distinguished Lecturer of the IEEE UFFC Society, from 2002 to 2003. He is an Associate Editor of the IEEE TRANSACTIONS ON ULTRASONICS, FERROELECTRICS, AND FREQUENCY CONTROL and the IEEE TRANSACTIONS ON BIOMEDICAL ENGINEERING AND MEDICAL PHYSICS.