Modality independent elastography (MIE): Potential applications in dermoscopy

Michael I. Miga, Megan P. Rothney, and Jao J. Ou
Vanderbilt University, Department of Biomedical Engineering, Nashville, Tennessee 37235

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The use of palpation information for skin disease characterization is not as commonly used as in other soft tissues, although mechanical differences within lesions have been noted. For example, regions of hyperkeratosis have the potential to transform into cancerous lesions and likely feature different material properties from those of surrounding normal tissue due to varying cytoarchitecture. As a result, the spatial distribution of lesion mechanical properties may serve to assist a diagnosis or enhance visualization of the complete extent of a cancerous region, i.e., accurate information regarding the margins of disease for surgical therapy. In this work, a multiresolution extension to a novel elastographic imaging method called Modality Independent Elastography (MIE) is used to characterize the mechanical properties of a skin-like phantom embedded with a mock stiff lesion. Simulation studies were also performed to investigate the potential for characterizing realistic melanoma lesions. Elasticity image reconstructions from the phantom experiments localized the stiff inclusion and had good correlation between the Young’s modulus contrast ratio and experimental measurements from material testing. In addition, multiresolution MIE was shown to be a more robust framework than its single-resolution version. Results from the melanoma simulation demonstrate the potential for using multiresolution MIE with dermoscopic images. © 2005 American Association of Physicists in Medicine. [DOI: 10.1118/1.1895795]

I. INTRODUCTION

Skin cancers are a growing health concern in the United States, with total annual cases being reported in the millions by the American Cancer Society. There are three major types of skin cancers [basal cell carcinoma (BCC), squamous cell carcinoma (SCC), and melanoma], with melanoma estimated to be the sixth most prevalent cancer and an estimated 55,100 new cases (within the United States) to be diagnosed in 2004.¹ In general, skin cancers develop from precancerous lesions of the epidermis that have dysplastic changes due to the damage inflicted by ultraviolet solar radiation. As with other cancers, the dysfunctional cells may aggressively compete with normal tissue for nutrients and space. The progression from a benign to malignant state depends upon the degree of cellular differentiation and the spatial extent of the growth, which approximately translates into the pathological determination of grade and stage.

When skin cancers are identified at an early stage and are still small in size, surgical excision is usually straightforward and effective. If the disease has progressed to invade deeper levels of the skin, treatment becomes more difficult and may involve more invasive surgery, radiation, and/or chemotherapy. It is clear that the early detection of cancer is critical in order to formulate a proper treatment plan and achieve the most favorable clinical outcome. However, detection and diagnosis still rely primarily on visual inspection followed by a biopsy of suspect areas for histological analysis. Therefore, a significant proportion of diagnostic technological advances have been concerned with obtaining a better view of the lesion via improved optics (i.e., dermoscopy) or more advanced and novel imaging systems ranging from high-frequency ultrasound to confocal laser microscopy. Addi-

tional strategies involving electrical impedance mismatch, Raman spectroscopy, and cytological smears have also been forthcoming.

As opposed to other methods mentioned above which capitalize on electrical, optical, and biochemical phenomena, we have chosen to pursue an alternative approach to skin health assessment which is based on its mechanical behavior. Detecting changes in tissue by palpation and then associating them with a disease state has had a longstanding history in clinical medicine. Although a health assessment of skin from palpation is performed to a lesser degree, utilizing changes in the mechanical properties to characterize the skin does have precedent within clinical dermatology. One thoughtful review by Edwards and Marks discusses the complex mechanical behavior of skin when subjected to in vitro and in vivo testing. Their review highlights extensive methodologies being used to quantify skin mechanical properties (e.g., uniaxial and biaxial extensometry, torsion stimulators, indentometry, ballistometric tests, shear wave application devices, dynamic suction methods, ultrasonics, and electrodynamometry) and also indicates the difficulties in comparing across these methods. As a result, Edwards and Marks emphasize the necessity for quantitative, reproducible methods to assess skin health given the wide subjectivity in clinical analysis. For example, the work by Draaijers et al. suggests that reliable subjective assessment of the pliability of scars requires more than one observer while measurements using a noninvasive suction device can be accomplished with a single observer. This type of work qualitatively confirms the Edwards and Marks conclusion that the need for technology...
and automation in skin assessment will be essential for reducing inter-rater variability.

While the characterization of skin cancer for diagnostic purposes and possibly surgical intervention is an interesting prospect, other investigations have begun to suggest relationships between skin elasticity parameters and other diseases. In a recent study using a noninvasive suction device, Pierard et al. demonstrated a correlation between bone mass density (BMD) and skin elasticity parameters. Specifically, in a 100-woman study in which a portion of the subjects were participating in hormone replacement therapy, a positive correlation existed between BMD of the hip and femoral neck and skin elasticity parameters. The authors clearly state that their goal was not to develop a surrogate BMD assessment test, but the results are nevertheless intriguing. Using a similar device, Yoon et al. demonstrated a relationship between skin elasticity parameters and patients afflicted with diabetes mellitus. Other work has been forthcoming that demonstrates the potential for using noninvasive measurements of skin mechanical parameters as diagnostic information.

To this end, the field of elastography has established methods to spatially characterize the mechanical properties of tissues under various states of deformation with the goal of developing functional parameters to characterize disease. In skin cancer, increases in cell density, atypia in the morphology and orientation of cells, and compositional alterations (e.g., hyperkeratosis) contribute to changes in the local cytoarchitecture. These changes in mechanical structure can propagate from microscopic to macroscopic levels and may manifest as a distortion of the normal anatomy. Given the influence of mechanical structure on the behavior of deforming tissue, elastographic imaging methods may be well suited for detecting and monitoring the growth of these cancerous anomalies. In fact, advances in applying ultrasound elastography and sonography techniques to skin are being reported. Most recently, Gennisson et al. demonstrated the use of a new sonoelastographic probe that measured a distinct difference between dermis and hypodermis shear wave velocities which was subsequently used to estimate Young's modulus. Although interesting, this work is not completely applicable to the clinical goals of understanding the spatial extents of a melanoma lesion.

Following previous work in Ref. 23, we are using a new elastographic method we have termed "modality-independent elastography" (MIE) that combines nonrigid image registration with an elasticity inverse problem. More specifically, image similarity metrics routinely used with image registration methods are recast within a nonlinear optimization algorithm whereby mechanical properties (e.g., Young's modulus) within a biomechanical model of the deforming tissue become the driving parameters for improved image registration. In this way, the MIE method circumvents two potential limitations of current elastographic techniques. First, it is not inherently dependent on preprocessing steps such as homologous feature selection and tracking which drive active contour models or other traditional displacement-based iterative methods (however, it does require the determination of boundary conditions). Second, because it is an image processing technique, MIE is not reliant on a particular imaging modality such as in ultrasound and magnetic resonance elastography, as long as the acquired images provide a sufficient pattern to allow for registration. Building on recently completed work with a dual-mesh implementation, in this paper we present a simplified multisolution elasticity imaging framework for Young's modulus reconstruction. In addition, phantom and simulation experiments demonstrate its utility as a dermoscopic image analysis tool for evaluating skin lesions based on material elasticity.

As a final point, the work presented here represents a potentially new application of the MIE approach for the characterization of skin lesions using optical images. This may have significant implications at many length scales (subcellular, cellular, matrix level, and gross tissue). For example, properly designed, optically based MIE could be used to characterize the structural development of tissues at the cellular scale. This could be important for therapies such as Mohs micrographic surgery. Mohs is a surgical technique which combines surgery and pathological investigation to more effectively remove skin tumors. More specifically, after removing visibly cancerous regions, the surgeon removes an additional thin layer of the site margin and creates a "map" of the border. Upon pathological examination of the removed layer, the "map" can be used to target the remaining cancerous cells. Currently, the Mohs technique is a time-consuming procedure, but the success of the procedure is compelling and has been shown to be cost effective with certain considerations. If MIE skin imaging could accurately assist or replace the pathologic characterization of the margin in less time, this would be of great value for this surgical therapy.

II. METHODS

A. Model of phantom/skin elasticity

One critical component within all model-based inverse problem frameworks is the selection of a computational model to represent the continuum of interest. In our phantom and simulation studies, we have elected to employ a linear elastic model to simulate the skin. These assumptions (e.g., symmetry, isotropy, etc.) allow the simplification of Cauchy's law from 36 stiffness constants to 2 and employ the equation

$$\nabla \cdot \sigma = 0,$$

where $\sigma$ is the two-dimensional (2-D) Cartesian stress tensor and is defined as

$$\sigma = \begin{bmatrix} \sigma_x & \tau_{xy} \\ \tau_{yx} & \sigma_y \end{bmatrix}.$$

The constitutive relationships for the material can be written as
\[
\begin{bmatrix}
\sigma_x \\
\sigma_y \\
\tau
\end{bmatrix} = \frac{E}{(1-\nu)^2} \begin{bmatrix}
1 & \nu & 0 \\
\nu & 1 & 0 \\
0 & 0 & \frac{1-\nu}{2}
\end{bmatrix} \begin{bmatrix}
\frac{\partial u}{\partial x} \\
\frac{\partial v}{\partial y} \\
\frac{\partial u}{\partial y} + \frac{\partial v}{\partial x}
\end{bmatrix},
\] (3)

where \( E \) is the Young’s modulus, \( \nu \) is Poisson’s ratio, and \( u, v \) are displacements in the \( x \) and \( y \) directions, respectively. For this work, Poisson’s ratio was assumed to be constant at 0.485 for our skin phantoms and tissue simulations. This value was found by searching the reconstruction parameter space for an optimal value that achieved maximum similarity when comparing the homogeneous model-deformed image to its acquired counterpart. The constitutive relationships expressed in (3) represent a two-dimensional approximation to a three-dimensional system which assumes a symmetric, isotropic, thin specimen in equilibrium and stresses that are constrained to lie within the plane, i.e., the classic plane stress approximation.\(^{31}\) Using the Galerkin method of weighted residuals to integrate this set of partial differential equations, a finite element framework is generated and can be solved to represent a displacement field for a given distribution of Young’s modulus values.\(^{32}\) The boundary conditions for our studies below were either manually derived from a structured grid representation as in the phantom system or prescribed by the user in the case of the simulation studies.

**B. Modality-independent elastography (MIE)**

The MIE framework begins with the acquisition of a baseline predeformed “source” image and a post-deformed “target” image. The “source” image set is used to create a well-resolved finite element mesh of the tissue domain. In previous work, a second coarse mesh was also specified on the domain and was used specifically as the mechanical property reconstruction grid.\(^{30}\) In this work, a new single-mesh region-based multiresolution MIE approach has been employed which simplifies previous dual-grid techniques with the generation of a structured regionalization using a \( K \)-means clustering algorithm based on the element centroids of the well-resolved mesh. A \( K \)-means clustering algorithm iteratively partitions the element centroids into a given number (\( K \)) of regions (where \( K \) is the user-defined number of desired clusters) such that the sum of all point-to-region centroid distances over all regions is minimized. The advantage of using the \( K \)-means clustering approach as opposed to a regular grid is that the clustering approach can more appropriately fit irregular domains (e.g., the circular domain for the dermoscopic image set). For this work, the implementation in the MATLAB (MathWorks, Natick, MA—www.mathworks.com) statistics toolbox was used. Figure 1 illustrates an example of this approach on a circular domain whereby the element centroids have been clustered into 16 separate homogeneous, isotropic regions.

The method has been adapted to a multiresolution strategy whereby coarser resolutions (i.e., fewer regions) can be initially reconstructed to provide better initial guesses to subsequent resolutions. The use of hierarchical multiresolution structures within both rigid and nonrigid registration algorithms has a longstanding precedent and lends credence to its application here.\(^{33–35}\) In this work, six progressively finer resolutions were used within each reconstruction (16, 36, 64, 144, 256, 400 regions).

Once the mesh and \( K \)-means resolutions have been specified, the reconstruction algorithm begins by assigning an initial modulus value to each region (a homogeneous initialization is assumed) at the first resolution, weighted residual equations are integrated, boundary conditions are applied, and the matrix equation system is generated:

\[
[A(\widetilde{E}_E)](u) = \{b\},
\] (4)

where \([A(\widetilde{E}_E)]\) represents the model stiffness matrix based on the current distribution of properties \( \widetilde{E}_E \), \( \{u\} \) is the vector of unknown tissue displacements, and \( \{b\} \) is the vector of known forces acting on the system and boundary conditions. Upon the calculation of tissue displacements, the source image can be deformed. This model-deformed source image is then compared to the target image using an image similarity method\(^{23,30}\) which is calculated over a number of discrete spatial zones (e.g., for all reconstructions, approximately 400 similarity zones were designated within the image for a comparison). Modulus values in the regions are updated based on maximizing the similarity between the deformed source image and the target image over all the similarity zones until a tolerance is reached or the desired number of iterations has been completed.

With respect to the optimization framework for MIE, it can be represented as a least squared error objective function:

\[
\phi(\widetilde{E}) = \min\{|S(\widetilde{E}_s) - S(\widetilde{E}_E)|^2\},
\] (5)

where \( S(\widetilde{E}_E) \) is the similarity value achieved when comparing the target image to itself (i.e., the maximum value for the similarity metric) and \( S(\widetilde{E}_E) \) is the similarity between the model-deformed source image and the target image using the current estimate of the elastic modulus, \( \widetilde{E}_E \). Equation (5) can be solved by employing a Newton–Raphson-based approach:
\[
[[J^T][J] + \alpha[I]](\Delta \tilde{E}) = [J^T](S(\tilde{E}_d) - S(\tilde{E}_e)) \tag{6}
\]

where \([J]\) is the \(M \times N\) Jacobian matrix of the form \(J = \partial S(\tilde{E}_d)/\partial \tilde{E}\), \(M\) is the number of similarity measurement zones, and \(N\) is the number of material property regions and is equivalent to \(K\) as designated in the \(K\)-means clustering algorithm. The details of Eq. (6) have been reported previously.\(^{23,30}\) Because \([J^T][J]\) (an approximation to the Hessian matrix) tends to be ill conditioned, it is regularized with an empirically determined \(\alpha\) parameter found in the standard Levenberg–Marquardt approach.\(^{36}\) The determination of this regularization parameter is described in Ref. 37. Figure 2 is a flow chart of the new multiresolution MIE approach.

In previous work, we have analyzed the performance of our MIE algorithm with respect to four standard image similarity metrics found within the literature: the sum of squared differences, normalized mutual information, the correlation...
coefficient (CC), and the gradient correlation coefficient (GC).\textsuperscript{30} Within this work, the correlation coefficient and gradient correlation coefficient were used for the similarity measurements.

Briefly stated, the CC operates on the distribution and mean intensity values of the overlapping regions of two images where \( I_1 \) would represent the intensity values within the “target” image and \( I_2 \) would be the model-deformed “source” image. The correlation coefficient can be calculated by the expression

\[
CC = \frac{\sum (I_1(i) - \bar{I}_1)(I_2(i) - \bar{I}_2)}{\sqrt{\sum (I_1(i) - \bar{I}_1)^2 \sum (I_2(i) - \bar{I}_2)^2}}, \quad \forall \in I_1 \cap I_2, \quad (7)
\]

where \( \bar{I}_1, \bar{I}_2 \) are the mean intensity values within each respective image, and \( i \) is the \( i \)th pixel within the respective image. The GC metric is calculated by applying the correlation coefficient to images that have been processed by any of the standard edge detection functions (e.g., Canny, Sobel, etc.).

C. Phantom construction

A phantom was constructed that was approximately 25 cm long, 15 cm wide, and approximately 2 mm thick. The inclusion-surrounding bulk material of the phantom was Smooth-On\textsuperscript{TM} Evergreen 10 polyurethane with an additive to allow permanent marker to adhere to the material surface (Smooth-On, 2000 Saint John Street, Easton, PA). A cylindrical inclusion was placed centrally within the membrane phantom that was approximately 5 cm in diameter and was made of a stiffer polyurethane material (Smooth-On\textsuperscript{TM} Evergreen 50). The inclusion material was chosen for its relative stiffness to that of Evergreen 10 and its color which is the same (to study the case of non-pigmented lesions). After the phantoms had set, a permanent marker was used to draw

15 cm \( \times \) 15 cm grid with 1 cm \( \times \) 1 cm squares on the phantom surface. Figure 3(a) shows the skin phantom used for data collection in this series of experiments.

D. Image acquisition protocol

To acquire the pre- and post-deformed images of the stretched skin phantom, the membrane was first secured in customized clamps attached to a milling vise to form a translation stage and then brought level with a nominal applied load to define the baseline position. Images were taken by a commercial web camera (Logitech QuickCam Pro 4000, 960 \( \times \) 1280 pixel resolution) that was rigidly mounted above the membrane at a single location to ensure a fixed field of view and frame of reference for the duration of the experiment. A series of five total images was collected (eight-bit grayscale) via laptop control of the camera—the baseline predeformation position and four subsequent positions with incremental stretches of approximately 5 mm each. Figure 4
is a schematic of the experimental setup, while Fig. 3(a)–3(e) shows an example dataset.

E. Material testing protocol

Material testing was performed in order to determine the accuracy of the reconstructed Young’s modulus values. When the phantoms were poured, specimens of both the bulk and stiff polyurethane were allowed to cure in separate containers from the membranes. These samples were then cut into 1 cm × 1 cm × 1 cm cubes. Compression testing was performed on an EnduraTEC ELF 3200 material tester (EnduraTEC Systems Group, Minnetonka, MN). The polyurethane was assumed to be elastic, homogenous, and isotropic.

The Enduratec material testing protocol involved ramping the actuator linearly from the zero position to 24% strain at 2% strain increments. The max strain value was chosen to extend slightly beyond the range of observed strain in the experiment shown in Fig. 3 which was approximately 22% strain for the bulk material. Although the stiffness inclusion material only experienced approximately 1%–2% strain, stress values were reported for the full strain range up to 24%. Between each change in axial position a three second dwell time was imposed to allow viscoelastic responses to subside. Stress–strain plots were produced for both the bulk material and the inclusion material. Three samples of each material were tested and an average curve was calculated.

F. Phantom experiment

To quantitatively test the MIE method within the context of dermoscopic applications using optical images, a series of studies using the elastic membrane of Fig. 3 were employed within the setup of Fig. 4. The single inclusion phantom was considered to be representative of a single lesion on the skin surface (nonpigmented in this case). The multiresolution MIE technique was used at each successive deformation for a total of four elasticity image reconstructions per similarity metric (in this case CC and GC only). The computational domain for these calculations involved 1051 nodes and 1973 elements. Boundary conditions were generated by analyzing the pre- and post-deformed structured grid and estimating the domain’s deformation. The Young’s modulus reconstructions were then compared to the elasticity values as generated from the material testing protocol. It should be noted that only Young’s modulus contrast was compared in these evaluations. This is due to the manner in which boundary conditions are prescribed in the model system. Currently, the approach is driven by displacement boundary conditions (i.e., Dirichlet type) which consequently make the elastic model only sensitive to Young’s modulus contrast. Without knowledge of an applied stress at the boundary or a prescribed material property within the domain, absolute properties cannot be determined. In addition, it must also be noted that the reconstructions were constrained to a region of the phantom that was smaller than the overall phantom. This was a result from observing that at higher stretch states, out-of-plane distortions of the membrane became more prominent in the periphery.

G. Simulation experiments

In an effort to test the algorithm within the context of a more realistic image acquisition scenario for skin cancer, a simulation study was performed on an image of the 1 cm melanoma lesion shown in Fig. 5(a). In addition, a grid structure was not specifically applied to the lesion image so as to test whether the natural skin-texture itself contained sufficient image information for reconstruction. The lesion was provided by the Dermatology Image Atlas project (www.dermatlas.org, Image Name: melanoma_1_040510, Contributed by Eric Ehrsam, M.D.) and represents a 1 cm pigmented melanoma plaque, located on the left arm of a 35-year-old woman. For the simulation boundary conditions, an annulus-shaped mechanical stretching device was assumed which would systematically stretch two semicircular regions apart by 2 mm. The melanoma was assumed to have a 2:1 elasticity contrast level with normal tissue, i.e., the melanoma was twice as stiff as the surrounding skin. The computational domain for the inverse problem contained 1294 nodes and 2459 elements. In addition, the mesh used to generate the forward-problem data was approximately 10%
more resolved than the mesh used for reconstruction. This introduced a small degree of variability to the boundary conditions and image deformation to simulate potential acquisition noise. Figure 5(b) and Fig. 5(c) illustrates the localized application of the stretching and the simulated solution for both horizontal and vertical displacements, respectively. Upon completion, these image data was used as input to the multiresolution MIE algorithm. Results are reported using the CC and GC image similarity methods.

III. RESULTS

A. Material testing

During the material testing phase, additional cyclic testing was performed in which viscoelastic behavior was noted. As a result, a waiting period was utilized at each strain level to allow viscoelastic responses to subside. The stress/strain behaviors at these quasi-static time periods for the bulk material and inclusion are shown in Figs. 6(a) and 6(b). In addition, discrete finite difference approximations were made at the various strain levels to estimate a Young’s modulus value. Table I represents a distribution of values calculated within the strain ranges tested. Once each modulus was calculated for each acquired strain level, a distribution of Young’s modulus contrast ratios was calculated and is expressed by Eq. (2):

![Figure 6](image)

**Table I.** Young’s elastic modulus values at several experimental strain levels.

<table>
<thead>
<tr>
<th>Material strain (%)</th>
<th>Bulk material (kPa)</th>
<th>Inclusion material (kPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>112.5</td>
<td>868.0</td>
</tr>
<tr>
<td>8</td>
<td>154.3</td>
<td>1635.0</td>
</tr>
<tr>
<td>12</td>
<td>180.0</td>
<td>2125.0</td>
</tr>
<tr>
<td>16</td>
<td>182.5</td>
<td>2375.0</td>
</tr>
<tr>
<td>23</td>
<td>206.3</td>
<td>2412.5</td>
</tr>
</tbody>
</table>
To assist in determining inclusion-to-bulk contrast ratios for different bulk strain levels in each experimental stretch as reflected in Fig. 3, an exponential curve fit was prescribed:

$$\text{CR}(\varepsilon = \varepsilon_{\text{bulk}}) = A + B e^{-C\varepsilon},$$  \hspace{1cm} (9)

whereby $A = 4.0$, $B = 5.0$, $C = 13.8$. The root mean square contrast ratio error between model and acquired data over the entire acquired strain range was 0.093. The quality of the exponential model can be seen in Fig. 6(c). Using the expression described in (9), a series of Young’s modulus contrast ratios values could be tabulated as a function of the specific strain levels used within the experiments of Fig. 1. These levels were determined by manually measuring strain levels within regions of the bulk material from the optical images. Table II reports the approximate contrast ratio for Young’s modulus at the various bulk material strain levels experience during the stretching experiments using Eq. (9).

### B. Multiresolution MIE phantom reconstructions

Figures 7 and 8 are representations of the multiresolution elasticity image reconstruction performance for each of the different stretch states shown in Fig. 3 using CC and GC as the basis for image similarity, respectively. The boundary

<table>
<thead>
<tr>
<th>Bulk material strain</th>
<th>Contrast ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stretch 1: 8%</td>
<td>5.7</td>
</tr>
<tr>
<td>Stretch 2: 12%</td>
<td>5.0</td>
</tr>
<tr>
<td>Stretch 3: 16%</td>
<td>4.6</td>
</tr>
<tr>
<td>Stretch 4: 23%</td>
<td>4.2</td>
</tr>
</tbody>
</table>

---

**Table II. Contrast ratios for each experimental strain level.**

**Fig. 7.** An illustration of elasticity image reconstructions using CC where each column represents the respective stretch relative to Fig. 3 (e.g., 3a–3b represents the stretch from base to the first increment). The top image shows the location of a transect as designated by the T and the gray scale associated with Young’s Modulus (Pa). The middle row represents the reconstructed elasticity images at each stretch state with the contour showing the actual inclusion location. The bottom row shows the elastic property contrast ratio as compared to that predicted with the material testing (shown as dark box-like contour) along the transect T.
contour represents the inclusion location as shown within the image. The contrast ratios designated within the transect images of Figs. 7 and 8 were based on Table II.

Figure 9 shows elasticity images at varying stage resolutions within the multiresolution MIE reconstruction (reconstruction shown is the GC–3a–3b stretch regime).

To test the effect of the multiresolution framework, the same optical images were provided to our algorithm using a 400 property region resolution with an initial guess of homogeneity (i.e., coarser resolution solutions were not used as initial guesses). In results not reported here, the CC reconstruction was able to localize and quantify the stiff region similar to that of Fig. 7 at the high stretch states but was much worse with respect to the initial stretch state (i.e., 3a–3b image reconstruction).

Figure 10 represents the GC result for the four stretch states using the single 400 region high resolution parametrization. In Fig. 10(a) (3a–3b stretch state), the inclusion is localized but the contrast resolution is poor compared with its multiresolution counterpart in Fig. 8, first column. At subsequent stretch states (3a–3c, 3a–3d, and 3a–3e), the elasticity image has not converged to an acceptable representation of the inclusion. Interestingly, the distance traveled by grid squares within the homogenous regions near the stretching edge within the second stretch state (3a–3c) is approximately the size of one grid square (∼1 cm).

It is evident that by using a single high resolution parametrization as opposed to a multiresolution approach, a local minimum is found and the elasticity image degrades considerably. Consequently, the error magnitude for the image shown in Fig. 8, the second column is a factor of 50% smaller than that of Fig. 10(b) thus demonstrating that Fig. 10(b) indeed represents a local minimum (it should be noted that all parameters were identical—number of similarity zones, filtering, regularization, relaxation, etc.).

C. Multiresolution MIE melanoma reconstruction simulations

In addition to the experimental results shown above, several similar simulations were executed using a pigmented melanoma image. Figure 11 shows the elasticity image reconstruction and transect results using the multiresolution MIE framework for both CC and GC. Figure 12 illustrates the inter-resolution results from the GC reconstruction shown in Fig. 11.

IV. DISCUSSION

The elasticity image results from phantom (Figs. 7–9) and simulation (Figs. 11 and 12) studies demonstrate the utility of the multiresolution MIE approach. In addition, comparing
the results in Figs. 8 and 10 clearly illustrates that instances can exist in which a single-resolution approach will fail whereas the multiresolution succeeds. A separate but related concern which is still under investigation is the degree and content of the image pattern needed to facilitate reconstruction; however, the preliminary elasticity image results from the melanoma simulations reported herein suggest that a sufficient intensity content exists in standard dermoscopic images.

Another important advance in this paper over previous work is the comparison between reconstructed elastic properties and their separately measured counterparts. The stress–strain curves shown in Figs. 6(a) and 6(b) and modulus values in Table I demonstrate a nonlinear elastic behavior. A good representative exponential fit to the Young’s modulus contrast ratio data was achieved in Fig. 6(c) and provides a direct comparison to MIE-derived Young’s modulus properties. One shortcoming is that because MIE is completely driven by displacement boundary conditions, only the contrast in Young’s modulus values can be compared. However, the goal within this work is to investigate elastic properties as a mechanism for contrast within medical images.

Overall, the elastic image reconstructions shown in Figs. 7 and 8 demonstrated good localization with a varied performance in maintaining lesion shape integrity for both the CC and GC similarity methods, respectively. It appears that at high strain levels, MIE was less successful at capturing the anticipated contrast ratio. In fact, in both CC and GC, the ratio was overestimated, thus producing more contrast. It should be noted that the reconstructions shown were performed on a domain that represented only a portion of the image that surrounded the inclusions (~3–4 cm from the inclusion border). This was due to our inability to completely control the physical boundaries of the phantom given the large mismatch between the stiffness values of the two materials. This manifested itself as out-of-plane warping of the phantoms, i.e., a wrinkling at edges as the strain on the skin phantoms increased. The spatial location of these membrane distortions was more prominent with the distance from the inclusion. By making a more localized reconstruction region, the influence of these distortions was minimized although some effects are undoubtedly present. Ultimately, these out-of-plane motions would be interpreted as planar strains in the optical image acquisition system shown in Fig. 4. Although this variability in shape integrity existed, successful localization was achieved for all stretch states. It was encouraging that at small stretch states, where the model is most appropriate, proper quantitative contrast ratios were achieved (stretch states 3a–b, 3a–c in Figs. 7 and 8). Further encouragement was provided by successful localizations at high stretch states whereby nonlinear behavior is undoubtedly present and the small-strain assumptions are compromised (although the quantitative contrast ratio was not as satisfying). Undoubtedly, a large-deformation model is necessary at these higher strains to match contrast ratios at this level; however, if proper empirical characterizations could be done using the linear model over many stretch states, effective contrast thresholds could be determined for the characterization of lesions. In addition, these results were also promising in that successful Young’s modulus contrast and localization was achieved with a nonpigmented lesion. This indicates that only the deflections of the surrounding image pattern and not the lesion image intensity itself are responsible for the changes in the elastic modulus values. This enthusiasm must be tempered by the realization, however, that the in vivo model may require more thought with respect to boundary conditions. Undoubtedly, the influence of subcutaneous tissue connectivity would influence the results here if these additional constraints were applied. Given the inherent link between the image formation and the validity of the computational model, more work needs to be performed prior to clinical deployment.
Although these results are encouraging, not all reconstructions exhibited the same peak modulus or lesion localization. One reason could be the accuracy to which boundary conditions were determined for each stretch state. It is possible that the manual delineation of boundary conditions or the observed wrinkling at high stretch states resulted in some boundaries being mapped less precisely than others. In some of the reconstructions, significant boundary artifacts can be observed. For example, in the second and fourth column of Fig. 7, a Young’s modulus peak is shown in the lower right hand region of the boundary. A second candidate for reconstruction inaccuracies across stretch states could be the degree of model-data mismatch. It is interesting to note the correlation between increased stretch and the marked decrease in accuracy of the contrast-ratio transect plots. At the smaller stretches, 3a–b and 3a–c, both CC and GC reconstructions perform better in both localization and quantification while both show overpredictions within transects for stretch states, 3a–d and 3a–e. A model-data mismatch would seem a likely source for this change in performance, considering that the elastic model used is a small-strain model and the levels of strain are less in the first two stretch states. One somewhat qualitative observation that can also be made is that the GC-based method appears to reconstruct somewhat better than the CC-based method. This is also the case within the melanoma simulations. Interestingly, in Ref. 30, a similar experience was found in that the GC method outperformed other methods with respect to our phantom reconstructions. The principal difference between the CC and GC similarity methods is the form of the image to be used when calculation the correlation coefficient. GC employs the edge map of the image while CC uses the raw acquired image. The increased performance by GC may indicate that areas of structured...
sharp gradient intensities influence the MIE approach more significantly than more gradual intensity changes. However, this statement must be tempered with the realization of Fig. 10 whereby structural decorrelation has occurred although arguably at much larger length scales as compared to those in traditional USE.

The results from the melanoma simulations provide a more realistic representation of the types of images that can be acquired within the clinic. These images provide their own challenge in that although the lesion is pigmented, the surrounding structured pattern of the grid used in the phantom was not present. In this case, it was desirable to test MIE without the presence of the structured grid. Overall, the elasticity images and transects were satisfying, with the GC qualitatively outperforming the CC method. One interesting observation is related to the apparent suppression of modulus noise within the GC elasticity image as compared to the CC. This is more than likely due to the suppression of low-frequency image characteristics associated with extracting edges within the source and target images.

Figures 9 and 12 demonstrate the multiresolution aspect to our approach by showing the reconstructions at all six resolutions used within the generation of our images. One beneficial aspect is the availability of intraresolution elasticity images which represent accurate, albeit coarse, assessments of image progression. In addition, these intra-resolution images could be used to dynamically alter the $K$-means clustering approach to locally refine the reconstruction process for the next resolution (although not done in this study). This would alter the algorithm representation in Fig. 2 by replacing precomputed resolution maps with an internal process block which calculated $K$-means regions dynamically based on areas of interest found during the reconstruction process.

V. CONCLUSIONS

In this paper, a novel multiresolution extension to Modality Independent Elastography (MIE) has been implemented which simplifies previous work (a dual-grid technique) and is shown to be more robust than the single-resolution version. In addition, the multi-resolution architecture implemented facilitates the monitoring of reconstruction quality at intermediate resolutions. To test the approach, a membrane experimental setup was created which utilizes sets of optical images for the reconstruction process. The use of optical images to generate Young’s modulus reconstructions does represent a new modality within MIE development and could potentially be used within dermoscopic applications.

Results from phantom and simulation experiments demonstrated that the multiresolution MIE approach is viable within the context for both nonpigmented and pigmented lesions, respectively. The nonpigmented phantom experiment highlighted direct comparisons between images of Young’s modulus contrast and their independently measured counterparts, as provided by mechanical testing. Overall the results indicated good localization and quantification. However, results did indicate a dependence on the fidelity of the reconstruction and the degree of applied deformation. In addition to the phantom experiment, a simulation using a clinical image of a pigmented melanoma were reported and illustrated excellent localization and quantification.

Despite potential limitations in elasticity image resolution when compared to traditional MRE and USE, MIE’s adaptability to an optical image-registration platform at multiple scales is an intriguing possibility. Furthermore, this extension to another modality demonstrates that MIE-based approaches to elastography represent a new class of algorithms that may yield potentially new frameworks for disease characterization.

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1 Corresponding author.


