A Novel Phantom Tissue Model for Skin Elasticity Quantification

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1 Background

Skin cancer is the most common form of cancer in the U.S., resulting in one out of the five Americans developing skin cancer at some point in their lifetime [1]. Though melanoma accounts for only 2% of these cases, it is the leading cause of skin cancer deaths; as with all cancer, early detection before metastasis is vital for patient survival, stressing the need for effective diagnostic devices [2]. While research progresses toward new skin cancer detection devices, successful adoption of these technologies requires a robust, repeatable method for large-scale validation. Tissue mimicking phantom models have proven to be adequate as they are able to accurately model the mechanical, optical, and acoustical properties of skin.

Several types of bio-based and synthetic materials are used to simulate tissue. Agar-based tissue phantoms at different concentrations were used to test ultrasound as a stiffness imaging technique for cancerous lesions [3]. Other groups have utilized polydimethylsiloxane (PDMS) in combination with titanium oxide (TiO_2) and nanorose particles to mimic both the biochemistry and optical properties of skin with incorporated lesions [4]. Specifically, they created a two-layer model consisting of a nanorose-containing top lesion layer and an underlying skin layer with only PDMS and TiO_2. Other materials, such as porcine skin gelatin, collagen, lipid scattering particles, polyacrylamide gels, and epoxy resins have also been used to simulate skin tissue for optical spectroscopy, imaging, and dosimetry [5].

To adequately mimic the properties of skin tissue, it is important that phantom tissue models be composed of layers that represent the three different layers of the skin: epidermis, dermis, and hypodermis. The epidermis, the outermost, and stiffest skin layer, serves as a waterproof barrier against the environment. The dermis is comprised of hair follicles and sweat glands that allow for sensory and temperature regulation. Finally, the hypodermis, the innermost, and thickest layer consists mostly of connective and adipose tissue for energy storage. Due to the prevalence of adipose tissue, the hypodermis is the least stiff layer. While some groups have developed phantoms resembling the epidermis and dermis layers, phantoms composed of all three layers are rare [6].

In addition to containing properties analogous to normal skin, a phantom model needs to incorporate a model for the cancerous lesion. One important parameter that can be exploited to distinguish melanomas from surrounding normal skin tissue is stiffness. When cells plated on polystyrene were allowed to adhere and spread on an extracellular matrix, it was discovered that the elastic moduli of normal melanocytes was 308 ± 18 Pa while that of metastatic melanomas increased to $10{,}001 \pm 90$ Pa [7]. Analysis of mechanical stiffness of normal melanocytes in comparison to melanomas also revealed a 2.5- to 6-fold increase in stiffness, further demonstrating elastic properties of the skin as a good measuring tool for diagnosing melanomas [8,9].

Our research group is developing a skin cancer diagnostic device for tissue characterization. This device measures the full-field tissue elasticity to determine if a lesion is cancerous. To determine elasticity, the device uses a weak vacuum to apply a force and structured light to measure the tissue deformation. A mass within the tissue with contrasting stiffness will cause the tissue to deform differently. Thus, this paper will focus on the creation of a phantom tissue model that mimics the mechanical properties of skin in order to drive mechanical design and validate the measurement method prior to human clinical trials.

2 Methods

For the purpose of detecting melanomas, the design requirements of tissue-mimicking phantom models were twofold: (1) achieving accurate thicknesses for each layer of the skin and (2) modeling the elasticity of normal skin relative to melanomas.

The layer thickness is approximately 50 μm to 1 mm for the epidermis, 1–2 mm for the dermis, and the hypodermis varies from 1 mm to 5 cm [10,11]. Different models have been used to estimate the Young's Modulus of the individual skin layers. The Young's Modulus of the epidermis is typically found to be 1 MPa [12]. The value for the dermis is much less, ranging from 35–300 kPa [10,12]. The hypodermis, composed of mostly fat, is even lower, with values of 2–35 kPa [10,12].

A malignant melanoma lesion initially grows horizontally within the epidermis; after which it starts to penetrate into the dermis. Tumor thicknesses typically start at 0.25 mm for early stage tumors and grow to 4 mm or more if left untreated. Thickness is positively correlated with the stage of the cancer and inversely related to the probability of survival [13]. The diameter of a lesion can range anywhere from 1 to 5 cm [14].

The elasticity and thickness of human skin is not constant, and varies significantly depending on several factors, most notably, location on the body. Design Circle, Inc., a medical product development firm, fabricated the phantom models according to the specifications for layer thickness, diameter, color, and stiffness shown in Table 1. A proprietary synthetic rubber was poured into a custom mold for each layer.

The property specifications for the initial prototype phantom models reflected those for an average person's abdomen. While sufficient for an initial validation, future models will incorporate varying stiffness and thickness values to simulate other body regions. Due to the use of synthetic rubber for the material, Young's modulus values were converted to durometer according to the method proposed by Mix and Giacomin [15].

3 Results

After the phantom models were fabricated, the stiffness of each layer was quantified to determine how close the final model matched the proposed specifications. An Admet Universal Materials Testing system with a 1 N force transducer was used to determine the stiffness of each layer. Each layer was measured three times and the mean value was compared to the specification.

The epidermis and hypodermis were well outside the target specifications. The epidermis was 74.4% stiffer than the specification with a 1744 kPa mean measurement. The hypodermis was 63.8% less stiff with a mean measured value of 18.1 kPa. However, the dermis and lesion were within 15% at 22 1 kPa and 343 kPa, respectively.

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Table 1 Phantom tissue model specifications

			Stiffness	
	Thickness (mm)	Diameter (cm)	Young's modulus (kPa)	Durometer (Shore OO)
Epidermis	0.25	12	1000	87
Dermis	2	12	200	55
Hypodermis	30	12	50	15
Melanoma lesion	1.5	1.5	400	73

Finite element analysis (FEA) was performed to predict how the phantom model would deform. The measured properties and dimensions were used to form custom materials within ANSYS 16.0. A pressure ramped from 0 to 100 mbar was applied to a 6 cm diameter area. The center deflection for a phantom model with a lesion is 10.67 mm versus a model without a lesion at 9.98 mm, resulting in a 6.9% difference. The phantom models were measured by the prototype device described at the end of the Sec. 1. The average device measurement deviated from the FEA results by 10.0% and 18.6% for the models with and without a lesion, respectively.

4 Interpretation

Differences in the measured stiffness of the individual layers of the phantom versus the specifications are likely due to the conversion between Young's Modulus and durometer. Durometer is a nonlinear hardness measurement from 0 to 100, with 100 being equivalent to a material with infinite hardness.

The epidermis was at the higher end of the Shore OO scale so it was more sensitive to error. Since the phantom model is used to validate a prototype diagnostic device with FEA results, a stiffer epidermis is adequate as long as the increased stiffness is taken into account. The hypodermis was well below the specified stiffness value; however, this was advantageous. The lowest possible stiffness of the synthetic rubber was thought to be 50 kPa and therefore, above the acceptable range for the hypodermis. The measured value of 18.1 kPa fits within the actual range.

The phantom tissue model presented in this brief has shown initial promise as a viable solution to mimic human skin. The model adequately validated the prototype system as the measured results were within 20% of the FEA results. This model provides a low cost, robust, and repeatable method to enable validation of a prototype device that diagnoses skin cancer through the quantification of tissue stiffness.

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