Ultrasound Elastography: Prostate Cancer Detection Assessment Using A Phantom

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1 Abstract

Prostate cancer early detection is critical for a desirable treatment outcome. If detected at early stage, prostate cancer can often be cured. Due to the high prevalence of prostate cancer among men worldwide, with a relatively high cause of death, it is important to have a technique for early tumor detection to improve the lives of cancer patients. An emerging imaging modality for prostate and breast cancer assessment is ultrasound elastography. Clinical ultrasound elastography is based on strain imaging that qualitatively determines tissue stiffness but not the true Young’s modulus distribution. Furthermore, the stress uniformity assumption associated with strain imaging results in a poor sensitivity and specificity of this clinical tool. To enhance this technique, strain images can be processed for tissue elastic modulus reconstruction. The proposed technique is to iteratively calculate stress values using Finite Element Method (FEM) and reconstruct the Young's modulus distribution using Hooke's law until desired values are achieved. Since tissue geometry is difficult to obtain using strain imaging, the proposed method is unconstrained and does not require tissue geometry. The strain images of a prostate phantom were processed using this computationally intensive method in order to validate the technique. The results were to assess the effectiveness of such a clinical tool for cancer diagnosis.

2 Introduction and Theory

According to the Canadian Cancer Society[1]), prostate cancer is the second most common cancer in men worldwide. A method for detecting tumors at early stage would therefore result in a large number of optimal cancer treatment outcomes and cured cancer patients. Current prostate detection techniques are known to be inefficient due to their low sensitivity and specificity. An alternate developing method, elastography, uses variations in prostate tissue stiffness as a contrast mechanism for prostate
cancer diagnosis. According to a current research paper by Weaver [2], remodelling of extracellular matrix collagen as a result of tumor progression causes progressive tissue stiffening. Tumor tissue commonly has two times the stiffness or greater as compared to normal healthy tissue. Strain imaging followed by implementing the developed elastography techniques can potentially lead to high sensitivity and specificity for prostate cancer diagnosis in order to respectively reduce over treatment as well as to accurately diagnose patients that are ill. Strain images lead to qualitative tissue stiffness reconstruction. Strain imagining differentiates soft and hard parts of tissue, however the assumption of tissue stress uniformity can be inaccurate, especially when dealing with clinical applications. The reality is that deviations from stress uniformity result in artifacts in the elastogram. Figure 1 shows a B-mode prostate ultrasound image containing a tumor with clearly defined boundaries. The strain image in the right half of figure 1 shows a strain image of the prostate. Based on the colours in the image, the tumor relative to other tissues is difficult if not impossible to detect.

![Figure 1. B-mode prostate image (a) and strain image (b). The white arrows in the B-mode image indicate a prostate tumor. The strain image displays stiffness using a colour scale. The elastogram displays numerous artifacts as a result of the stress uniformity assumption.](image)

The above observations show that strain imaging is unreliable for tumor detection. The solution is to use an elastography technique that incorporates the tissue stress field leading to calculating the Young's
modulus spatial distribution. Mousavi et al. [3] recently presented an unconstrained elastography technique about the reconstruction of prostate tissue Young's modulus. The process requires a strain image, and using a stress field calculated by FEM, the Young's modulus distribution is updated iteratively using Hooke's law. A prostate mimicking phantom was built in order to validate the accuracy of the proposed technique.

3 Methods

For this project there were four stages for obtaining results. First a prostate phantom was constructed followed by phantom tissue gold standard compression tests. Prostate phantom imaging was performed and finally post processing was done with the help of Abaqus and Matlab.

3.1 Phantom Construction

A phantom was built to mimic the elastic properties of a cancerous prostate. Appropriate proportions of gelatine, agar, water, glycerol, sigmacell, and formaldehyde were measured as determined from a previous phantom construction performed by Mousavi et al. [3]. The addition of agar to the phantom largely attributes to the stiffness of the phantom tissue. Figure 2 shows the relationship between agar concentration and phantom tissue stiffness. Extrapolation allowed for estimation of the appropriate amount of agar for the phantom tissue constructions.
The stiffness of tumors was aforementioned to be two times or greater than that of the prostate. After measuring each ingredient as displayed in figure 3, the appropriate amounts of water was heated to 70ºC in a beaker containing a magnetic stir stick. Gelatin was slowly added to the water followed by further heating of the solution to 80ºC. Agar was added slowly until the solution reached 90ºC. Formaldehyde and glycerol were then added and finally sigmacell completed the solution. Solutions were made to represent and mimic the elastic properties of the prostate, surrounding tissue, and two tumors of differing stiffness.
Figure 3. The weighed ingredients are shown above on the left. The phantom making apparatus is visible on the right including a prostate mould, beakers, and a hot plate.

After a brief cool down period, the solutions were poured into the appropriate moulds. The prostate shown in the left of figure 4 was first created and refrigerated for solidification. A hollow circular object was then used to insert holes into the prostate phantom to serve as moulds for phantom tumors one and two.

Figure 4. Phantom prostate moulds are shown on the left. On the right, holes were inserted into the prostate to allow for the implanting of the tumors.

Tumor solutions were poured into the prostate followed by enclosing the prostate in a rectangular
container in order to pour the surrounding tissue solution. Refrigeration of the moulds led to their solidification and completion. Samples of each solution were taken in cylindrical moulds to later determine the phantom tissue's gold standard Young’s moduli using uniaxial testing. The samples and moulds are shown in figure 5.

![Cylindrical samples of each phantom tissue are shown in the figure along with the completed prostate phantoms.](image)

**3.2 Uniaxial Test**

The cylindrical samples of the phantom tissues underwent uniaxial gold standard compression tests to measure their Young's moduli. The uniaxial testing machine is shown in figure 6, it recorded force-displacement data which was used for accurate estimations of the stiffness of each phantom tissue. The machine was calibrated after each trial to ensure accuracy. The dimensions of each cylindrical sample were measured as required for determining their Young's modulus. Each sample was tested twice to reduce noise.
3.3 Phantom Imaging

A circular hole was cut into the surrounding phantom tissue adjacent to the prostate mimicking rectum phantom. Ultrasound transmission gel was applied for impedance matching purposes. Several B-mode images for tumor recognition were acquired using both the circular and linear array as seen in figure 7 below.

Strain images were taken over the period of three separate phantom tissue compressions. Many frames
were captured during the period of a compression that lasted for several seconds. Frames from the strain imaging provided the data required for post processing Young's Modulus reconstruction. Strain image acquisition is shown in figure 8.

![Figure 8. Strain images were acquired using the circular array during phantom tissue mechanical stimulation.](image)

### 3.4 Post Processing

To calculate the stress field of the phantom prostate during the strain imaging mechanical stimulation, FEM was used. Using an ultrasound B-mode image similar to as seen in figure 9, geometry of the finite element model was determined. Boundary conditions were set to zero displacement at the edges of the phantom which were considered sufficiently far from loading with the exception of where the ultrasound probe applied compression.
Figure 9. Shown is a B-mode image of the prostate phantom. The rectangular boundaries where no tissue displacement occurs are clearly visible.

The ultrasound imaging provided the strain along the y direction (axial) and assuming the phantom was linearly elastic and isotropic, the Young's modulus was reconstructed with the help of Hooke's two dimensional equation shown in equation 1. Note that the tissue was considered nearly incompressible so Poisson ratio, \( \nu \), was considered close to 0.5.

\[
\frac{1}{E} = \frac{\varepsilon}{\sigma_{yy}} - \nu \sigma_{xx}
\]

The Young's moduli were then calculated iteratively beginning with an arbitrary Young's modulus input assigned to each element followed by stress calculations with the help of FEM. The US strain image allowed for the Young's modulus to be calculated using Hooke's law. A median filter followed by a Gaussian smoothing filter was applied to the elements to achieve convergence and continuity as well as to preserve tissue boundaries. The Young's moduli were then used to recalculate the stress field until convergence was achieved. Figure 10 is a flow chart of the iterative Young's modulus reconstruction.
Using manual selection of tissue regions in the reconstructed image, the Young's moduli were estimated and compared with respect to the surrounding tissue modulus. Two frames from each of three strain imaging tests were analyzed to provide more accurate results. Other post processing measures included visual selection of tumor location. This was used to compare actual tumor location found in the B-mode image to the tumor location as found in the reconstructed image.

4 Results

The force-displacement data obtained from the uniaxial testing along with the cylindrical sample dimensions were input into Matlab code provided by Mousavi et al. [3]. Stress-strain graphs were produced and using linear regression the Young's moduli for each phantom tissue was approximated and averaged for each of two compression tests.
Figure 11. A stress-strain relationship is shown for one of the phantom tissue uniaxial tests. Linear regression was performed where strain was moderate to attain a consistent Young's modulus.

The ratios of the Young's moduli were taken with respect to the surrounding tissue. They were found to be 5.4, 8.7, and 9.3 for the prostate, tumor 1, and tumor 2 respectively.

Figure 12. The image shows the ratios of the Young's moduli with respect to the surrounding tissue as determined by the uniaxial loading.
Six strain image frames from the three ultrasound compressions were processed which produced a matrix representing the Young's moduli distribution. Using manual selection of phantom tissue regions the Young's moduli were averaged and recorded as ratios with respect to the surrounding tissue. Figure 13 shows the manual selection of regions that represented the surrounding, prostate, tumor 1, and tumor 2 tissues.

Figure 13. The segregated areas in the image represent tumor 1, the prostate, surrounding tissue, and tumor 2 from left to right. The values within each region were averaged to estimate the Young's modulus.

The ratios with respect to the surrounding tissue were found to be 2.2, 6.0, and 8.9 for the prostate, tumor 1, and tumor 2 respectively.

Figure 14. The image shows the ratios of the Young's moduli with respect to the surrounding tissue as determined by the
The reconstructed image was evaluated based on tumor location using manual selection. The centres of tumors 1 and 2 were selected in a corresponding B-mode image and measured from the centres of the tumors as seen in the reconstructed image. This was done with each of the six processed frames and the tumor misallocation averages were found to be 5.21 mm and 5.68 mm for tumors 1 and 2 respectively. The manual selection process is displayed in figure 15.

Figure 15. The top left shows the B-mode image for tumor site identification. The reconstructed colour image is shown on the right for comparisons of tumor location.

5 Discussion

A similar trend of increasing stiffness was found when comparing the ratios as calculated using the gold standard uniaxial test and the proposed Young's modulus reconstruction method. Both of which are shown in figure 16.
Although the elasticity of the prostate compared to the surrounding tissue appeared quite different, fortunately the important ratios for tumor detection are that of tumor 1 and 2. The resultant contrast between the tumors and surrounding tissue was clearly visible. According to Hoffman's paper[4] on screening for prostate cancer, spheroid tumors with a radius of 4.92 mm or greater are important to consider when diagnosing prostate cancer. This indicates that the result for tumor misallocations of approximately 5 mm is reasonable considering that most suspicious tumors detected would have overlapping boundaries as found in the B-mode image compared to the reconstructed image.

The unfortunate truth is that strain images are not 100% accurate, nor is the gold standard uniaxial test. The strain rate of the phantom during strain image acquisition was overlooked, however it should be similar to the strain rate during the uniaxial test to avoid the effects of time dependant tissue stiffness. The meshing in Abaqus, boundary conditions, and behavioural assumptions were
imperfect which caused some concern for the stress calculations in the Young's modulus reconstruction. The manual selections of tissue regions and tumor sites incorporate inter observer variability as a potential source of error. In the future, an indentation technique could be used in place of the uniaxial test to achieve a more accurate true Young's modulus for the phantom tissues since lesser information would be lost as a result of decreased sample preloading. FEM boundary conditions could potentially be improved and implementing a finer FEM mesh would lead to greater resolution. Ultimately the method should be improved to better locate tumors and calculate the Young's modulus ratios in order to diagnose prostate cancer more effectively. Ideally, a faster program would replace Abaqus to allow post processing to be performed in real time, considering it required several minutes to perform the iterative technique.

6 Conclusions

In conclusion, the objective of this experiment was to evaluate the clinical potential of the proposed Young's modulus reconstruction technique for the purpose of prostate cancer diagnosis. Strain images only gave qualitative information concerning tissue elasticity, however after post processing, quantitative analysis was performed to identify tumor presence if a region of tissue was significantly stiffer than other regions of the prostate. The process was validated using a tumorous prostate mimicking phantom and the results were acceptable pertaining to tumor detection. The elasticity reconstruction method has shown potential for clinical utility and future improvements could make it a leading technique for prostate cancer diagnosis.

7 Acknowledgements

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8 References


