Developing a deformable model of liver tumor during breathing to improve targeting accuracy in image-guided therapy using finite element simulation

Z. Matin Ghahfarokhi\textsuperscript{a}, M. Salmani-Tehrani\textsuperscript{b} M. Moghimi Zand\textsuperscript{c}\textsuperscript{*}

\textsuperscript{a}Department of Mechanical Engineering, Isfahan University of Technology, Isfahan, Iran. P. O. Box: 8415683111. Tel: (+98) 031-33915219. Mobile: 09132845496. Email: z.matin@alumni.iut.ac.ir

\textsuperscript{b}Department of Mechanical Engineering, Isfahan University of Technology, Isfahan, Iran. P. O. Box: 8415683111. Tel: (+98) 031-33915219. Mobile: 09132057021. Email: tehrani@cc.iut.ac.ir

\textsuperscript{*}Corresponding author: Small Medical Devices, Bio-MEMS & LoC Lab, School of Mechanical Engineering, College of Engineering, University of Tehran, Tehran, Iran.

Postal Code: 14399-55961. Tel: (+98) 021-61114807. Fax: +98-21-88013029. Mobile: 09133108601. Email: mahdimoghimi@ut.ac.ir.

Abstract

Numerical simulation of the motion and deformation of a tumor embedded into liver during respiration can help to locate a tumor for radiotherapy. Here, a 3D FE model to simulate human liver behavior during respiration. First, the cloud of point according to CT image data was imported into CATIA software. Then a spherical tumor was embedded into the different segments of liver tissue in ABAQUS. A quasi-linear hyperviscoelastic constitutive model and an elastic behavior were used to define the liver and tumor properties, respectively. Boundary conditions were defined based on the difference between end-exhale and end-inhale states of liver tissue. Deformation and motion of liver tumor was then determined at intermediate states of breathing. Finally, the new position and the deformed shape of the tumor were investigated, considering the increase of tumor stiffness. The results show that the tumor located in the segment VII has maximum displacement in the \textit{y}-direction. Similarly, a maximum \textit{z}-displacement is observed for the tumor embedded into segment VI, while the tumor embedded into segments II and V experiences a maximum displacement in \textit{x}-direction. Moreover, the maximum motion of tumor rather takes place for the tumor in the segment VI.

Keywords: Breathing, Finite element model, Liver tissue, Point cloud, Tumor

1 Introduction

After skin, the liver is the second largest gland in a living body. It is the only organ which is able to generate or renovate itself by producing new cells. The liver performs many vital functions such as storing iron, drug metabolism, maintaining the hormonal balance and producing bile to help with food digestion [1-3]. On the other hand, the liver cancer and chronic liver disease are the leading cause of death for more than 15000 Americans, each year [3]. These important features and high death rate are reason enough to include the liver in many biomechanical researches.
Nowadays, the use of computer-aided surgery technology is a significant progress in surgical planning for treatment of the diseases [4]. Computer-aided surgery, which is known as a minimally invasive method, results in small operative trauma into human body, less pain, less blood and shorter hospitalization time and cost [5, 6]. Nevertheless, there exist some drawbacks for the surgeon without direct vision of the organs. Medical image methods, e.g. Computed Tomography scan (CT scan), Magnetic Resonance Image (MRI) and so on, play a major role in this technology [7]. However, the accuracy of image-guided therapy is considerably affected by tissue motion and deformation.

The breathing process is an important factor in the tissues movement. During the breathing excursions, the volume of the chest cavity increases and the position of organs close to the diaphragm are bigger influenced than structures around the lung apices [8]. Hence, the liver deformation by breathing is a crucial factor, since liver is in connection with diaphragm [9]. Therefore, precisely locating the tumor within the liver, during interventional procedures, is a challenging research subject [10]. To compensate this problem, several techniques have been used, such as breath holding or taking into account a safety margin around the tumor [11]. In such cases, most of the patients who endure the liver diseases, are aged and weak, and therefore, cannot cooperate well with the physician [12]. Therefore, considerable researches have been conducted to help physician to improve treatment accuracy. Among these, FE simulation is one of the most favorite methods which have been extensively used [13].

Nuttu et al. [14] proposed and described a methodology to obtain a FEM of the lung. The proposed method is based on the boundary condition of the lung outer surface. Therefore, by using the method, displacement of different points within the organ during breathing process can be predicted. Zehtabial et al. [15] studied the feasibility of creating a fast 3D model for simulating respiratory lung deformation. Similar study has also performed to provide information on the lung-tumor motions due to breathing. The interesting readers can refer to [16]. Moreover, Lorente et al. [7] modeled the biomechanical response of the liver tissue in real time, using machine learning technique.

Only a few studies have been reported in the field of FE modeling and simulation of organs to aid targeting. Reviewing these researches reveals that none of them was focused on studying deformation and displacement of tumor within the liver. In this paper, a 3D finite element model is developed to simulate behavior of human liver as a whole, using CT image data. The main goal of this study is to investigate the motion and deformation of a tumor embedded into the liver, during respiration. The results of this study would be important for guiding surgeons during interventional procedures, when the liver tumor is to be located for radiotherapy treatment.

For this purpose, four different segments II, V, VI and VII of the liver tissue were separately considered and studied as the tumor location (Figure 1). The reason for choosing these segments is that segments II and VII are located under the diaphragm. Then, these segments endure a lot of displacement. Then, the tumor motion in segments II and VII can be more than other segments. On the other hand, segment V and VI are located on the gallbladder and intestines, respectively. Also, the boundaries of segment V are adjacent to other parts and we guess this proximity will cause less tumor shape in this segment. But, it is expected that the tumor located in section VI will become more shape because this segment is compressed by the upper parts on the intestines.

In the section 2, the biomechanical modeling and finite element simulation of a human liver are described in details. The results of simulations are illustrated in section 3. In sections 4 and 5, a discussion about the simulation results and concluding remarks are presented, respectively.

2 Materials and methods

This section is divided in two subsections. First, the biomechanical modeling for predicting the mechanical behavior of a human liver tissue is introduced in section 2.1. Next, the method used for the finite element simulation of liver is described in section 2.2.
2.1 Biomechanical modeling of a human liver tissue

In this paper, the quasi-linear hyperviscoelastic model, which was previously proposed by Fung [18], is adopted to model the mechanical response of human liver tissue. In this model, the hyperelastic part is described by a reduced polynomial form of the strain energy function [19].

\[ w = c_{10} \left( J^{\frac{2}{3}} I_1 - 3 \right) + c_{20} \left( J^{\frac{2}{3}} I_1 - 3 \right)^2 + \frac{K}{2} (J - 1)^2 \]  

(1)

Furthermore, the time dependent material parameters are used to describe the viscoelastic part of the tissue behavior. For this purpose, relaxation function, \( g(t) \), is defined as introduced in Eq. (2) [19].

\[ g(t) = 1 - \sum_{k=1}^{2} g_k \left( 1 - e^{-\frac{t}{\tau_k}} \right) \]  

(2)

In Eq. (1) \( c_{i0}, (i = 1, 2) \) stand for the elastic material parameters, \( I_1 \) and \( J \) denote the first invariant of right Cauchy-Green deformation tensor and determinant of the deformation gradient tensor, respectively. Also, \( K \) is the bulk modulus which characterizes the compressibility of the soft tissue. The parameters \( \tau_k \) and \( g_k \) in Eq. (2) indicate the times and relaxation coefficients, respectively.

2.2 Preparing Modeling the geometry

In order to demonstrate the displacement of the tumor in the liver tissue during the breathing process, a whole finite element (FE) model of a tumor embedded into the human liver has been created. First, the liver geometry has been obtained from the point cloud according to a CT image data, represented by Suwelack et al. [20], as shown in Figure 2. Importing this point cloud into CATIA software, the curved surfaces have been constructed on the point cloud, using the automatic surface option. Then, the closed surface option was used to convert the surface into a solid volume (Figure 3). The geometrical model was then imported into ABAQUS software. The mechanical properties have been assigned to the FE model of the liver, as mentioned in Tables (1).

The tumor was modeled as an elastic sphere of diameter 10(mm) in the FE simulations. Table (2) presents the tumor location zone within the liver parenchyma. The values of 8(KPa) and 0.49 were assigned to Young’s module and Poisson’s ratio of the tumor, respectively [21, 22].

In next step, the liver was meshed using 4-node linear tetrahedron, hybrid element (C3D4H) and the model of the tumor has consisted of 1242, the 8-node linear brick, hybrid elements. The mesh of the tumor within the liver has been shown in Figure 4.

The boundary conditions were defined based on the difference between the position of the liver regions at the end-exhale and end-inhale states [23]. Both the displacement and deformation of the tumor with the different stiffness were evaluated and determined to provide the data which can help to improve the accuracy of the image-guided procedures.

3 Results

Table (3) reports the position of the tumor at end of breathing period. The results show that initial range of \( x, y \) and \( z \) coordinates of the tumor within the left lobe are (71.127 to 81.127)(mm), (20.3 to 30.3)(mm) and (95 to 105)(mm), respectively. These coordinate ranges have been changed to (67.8259 to 78.0354)(mm), (3.41504 to 13.2503)(mm) and (106.152 to 112.303)(mm), at the end of breathing period.
The effect of the tumor stiffness is shown in Table (4). In this Table, the location of the tumor in the segment VI is investigated when the tumor stiffness increases by a factor 6.25. This result suggests that the tumor moves a value of 2.09 (mm) for a Young’s modulus of 8(KPa).

Figure 5 plots the displacement of the liver parenchyma in a breathing cycle. As it is seen, the upper surface of the liver endures more displacement than other sections because of placing under diaphragm. Among the segments II and VII, segment II is more constrained due to contact with the stomach. Then it has less motion. Also, segment VI has the less displacement rather than segment V due to locate on the intestines. However, shape of the tumor in the segment VI is more because of compressing between segment VII and the intestines. Moreover, figure 6 represents the displacement map of the deformed tumor in the different location of the liver parenchyma. In order to assess the motion planning of tumor, the displacement of below point of tumor located in the segment VI is displayed in Figure 7.

Also, stress distribution through the liver tumor illustrates in figure 8. Figure 8 shows that the stress is uniformly distributed.

4 Discussions

Computer-aided technology has been recognized as the significant progress in treating of the liver diseases, especially for the image-guided therapy, in which tumor motion and deformation are required. Respiratory process is an important challenge in tumor locating.

In this paper, a 3D model of tumor within the human liver tissue was simulated using CT image data to assess the displacement of tumor and its relation to breathing stages. Primary purpose was to demonstrate how the liver tumor moves and shapes during breathing process. Secondary purpose was to investigate how shape of tumor was changed increasing tumor stiffness.

The results of this study shown that for the tumor located in the segment VII, maximum displacement was observed in the y-direction. However, maximum displacement for the segment VI was recorded in the z-direction and for the segments II and V was occurred in the x-direction. Moreover, the value of maximum shape of liver tumor was occurred in the segment VI. Additionally, the tumor stiffness had not significantly affect the magnitude of motion and deformation. In the breathing stages, the tumor was displaced on a plan based on the first order.

The validity of the obtained results is difficult because of the lack of a similar research task. However, this method can be a basis for development a 4-D dynamic model using intermediate positions of the tumor calculated from end-inhale to end-exhale. Knowing this information, physician can better determine how tumor motion affects the required dose during radiation therapy and surgeons able to demonstrate the tumor location.

5 Conclusions

In this work, a whole finite element model of the human liver tissue has been simulated to targeting of the tumor embedded into the liver during respiration. The tumor has been located in different positions of the liver parenchyma. This model provides a prediction of tumor displacement map using just one CT image data in the breathing stages. This investigation can potentially help surgeons for improving the accuracy of targeting in the image-guided therapy of liver cancer patients.

6 Declarations

Conflicts of Interest: None declared
Sources of funding for the research: None
Ethical Approval: This study does not involve human or animal subjects.
Nomenclature

\( c_{ij0} \)  
Material parameter, Kpa

\( I_1 \)  
First invariant of right Cauchy-Green deformation tensor

\( J \)  
Determinant of the deformation gradient tensor

\( K \)  
Bulk modulus

\( w \)  
Strain energy function

\( g \)  
Relaxation coefficient

Greek Letters

\( \tau \)  
Relaxation coefficient, \( s \)

References

1. Yarpuzlu, B., Ayyildiz, M., Enis Tok, O. and et al. “Correlation between the mechanical and histological properties of liver tissue”, J. Mech. Beh. Biomed. Mat., 29, pp. 403–416 (2014).

2. Matin Ghaahfarokhi, Z., Moghimi Zand, M. and Salmani Tehrani, M. “Analytical solution and simulation of the liver tissue behavior under uniaxial compression test”, Modares Mech. Eng., 16 (9), pp. 47-56 (1395) (in Persion).

3. www.liverfoundation.org

4. Matin Ghaahfarokhi, Z., Moghimi Zand, M. and Salmani Tehrani, M. “Proposing a new nonlinear hyperviscoelastic constitutive model to describe uniaxial compression behavior and dependence of stress-relaxation response on strain levels for isotropic tissue-equivalent material”, Sci. Iran., (2018), accepted.

5. Samur, E., Sedef, M., Basdogan, C. and et al. “A robotic indenter for minimally invasive measurement and characterization of soft tissue response”, Med. Image Anal., 11, pp. 361–373 (2007).

6. Dehghani Ashkezari, H., Mirbagheri, A., Behzadipour, S. and et al. “A mass-spring-damper model for real time simulation of the frictional grasping interactions between surgical tools and large organs”, Sci. Iran. B, 22(5), pp.1833-1841 (2015).

7. Lorente, D., Martínez-Martínez, F., Rupérez, M. J. and et al. “A framework for modeling the biomechanical behavior of the human liver during breathing in real time using machine learning”, Expert syst. Appl., 71, pp. 342-357 (2017).

8. Baxa, J., Ferdova, E. and Ferda, J. “PET/MRI of the thorax, abdomen and retroperitoneum: Benefits of the breathing-synchronized scanning”, Eur. J. Radiol., 94, pp. A35-A43 (2017).

9. L. Mescher, A., “Junqueira's basic histology”, Mc-Graw Hill companies.

10. Dhont, J., Vandemeulebroucke, J., Burghelea, M. and et al. “The long-and short-term variability of breathing induced tumor motion in lung and liver over the course of a radiotherapy treatment”, Radiother. Oncol., 126(2), pp. 339-346 (2018).

11. Keall, P. J., Mageras, C. S., Balter, J. M. and et al. “The management of respiratory motion in radiation oncology report of AAPM Task Group 76”, Med. Phys., 33, pp. 3874-3900 (2006).

12. Srimaltheeravalling, G., Leger, J., Ezell, P. and et al. “A study of porcine liver motion during respiration for improving targeting in image-guided needle placements”, Int. J. CARS., 8, pp. 15-27 (2013).

13. Saghaei Nooshabadi, Z., Abdi, E., Farahmand, F. and et al. “A meshless method to simulate interactions between large soft tissue and a surgical grasper”, Sci Iran. B, 23(1), pp. 295-300 (2016).
14. Nutu, E., Petrescu, H. A., Vlasceanu, D. and et al. “Development of a finite element model for lung tumor displacements during breathing”, *Mater. Today*, 3, pp. 1091-1096 (2016).
15. Zehtabian, M., Faghihi, R., Mosleh-Shirazi, M. A. and et al. “A fast model for prediction of respiratory lung motion for image-guided radiotherapy: A feasibility study”, *Iran J. Radiat. Res.*, 10(2), pp. 73-81 (2012).
16. Bäck, A. “Systematic evaluation of lung-tumor motion using four-dimensional computed tomography”, Phys. Med., 52(1), pp. 3-4 (2018).
17. Paulsen, F. and Waschke, J. “Sobatta: Atlas der Anatomie des Menschen”, URBAN&FISCHER verlag (2010).
18. Fung, Y. C. “Biomechanics, Mechanical Properties of Living Tissues”, Second ed. Springer-Verlag, New York (1993).
19. Nava, A., Mazza, E., Furrer, M. and et al. “In vivo mechanical characterization of human liver”, *Med. Image Anal.*, 12, pp. 203-216 (2008).
20. Suwelack, S., Roehl, S., Dillmann, R. and et al. “Quadratic corotated finite elements for real-time soft tissue registration”, In MICCAI workshop: Comput. Biomech. Med. (2011).
21. Gordic, S., Ayache, J. B., Kennedy, P. and et al. “Value of tumor stiffness measured with MR elastography for assessment of response of hepatocellular carcinoma to locoregional therapy”, *Abdom. Radiol.*, 42 (6), pp. 1685-1694 (2017).
22. Leroy, A., Payan, Y., Voirin, D. and et al. “Finite element model of the liver for computer-assisted hepatic tumor ablation”, Proceedings of BBE, (2001).
23. Brock, K. K., Hollister, S. J., Dawson, L. A. and et al. “Technical note: Creating a four-dimensional of the liver using finite analysis”, *Am. Assoc. Phys. Med.*, (2002). http://onlinelibrary.wiley.com/doi/10.1118/ 1.1485055/ full

**Biographies:**

**Z. Matin Ghahfarokhi** received her Bachelor of Science degree in Mechanical Engineering of Biosystem from Shahrekord University, Iran in the year 2008 and her Master of Science degree in Mechanical Engineering from the same institute in the year 2011. Now she is researching as a Ph.D student in Mechanical Engineering, in the Department of Mechanical Engineering, Isfahan University of Technology, Iran.

**Mahdi Moghimi Zand** is a Faculty Member in the School of Mechanical Engineering, College of Engineering, University of Tehran and Director of Small Medical Devices, Bio-MEMS & LoC Lab. Dr. Moghimi Zand’s research is multi-disciplinary and revolves around Vibrations, MEMS, Computational Mechanics, Bio-Medical Engineering and Nano Technology. He also has had different research and visiting faculty positions at Georgia Tech, Sharif University of Tech, Michigan State University and University of Tehran.

**Mehdi Salmani-Tehrani** completed his undergraduate studies, M.Sc. and Ph.D. degrees, all at the Isfahan University of Technology, IRAN. He is now an assistant professor at the Isfahan University of Technology, where he has been a faculty member since 2011. His research interest mainly focuses in metal forming analysis, and recently, in biomechanics studies.
Figure 1. Segmental anatomy of the liver [17]
Figure 2. A point cloud of CT image data for the normal human liver
Figure 3. Geometry of the finite element model for the human liver
Figure 4. The meshed FE model of the tumor within the human liver
Figure 5. The displacement of the liver parenchyma in a breathing cycle
Figure 6. Displacement map of the deformed tumor in a) segment VII b) segment VI c) segment II d) segment V
Figure 7. Displacement of tumor during breathing process
Figure 8. The displacement of the liver parenchyma in a breathing cycle
Table 1. The material parameters of the liver [19]
Table 2. The position of the tumor within the liver
Table 3. The final position of the tumor within the liver
Table 4. The position of the tumor in the segment VI for different stiffness
Figure 2.

Figure 3.

Figure 4.
Figure 5.

Figure 6.
Figure 7.

Figure 8.
Table 1.

| c_{10} (KPa) | c_{20} (KPa) | g_1  | \tau_1 (s) | g_2  | \tau_2 (s) |
|--------------|--------------|------|------------|------|------------|
| 9.85         | 26.29        | 0.51 | 0.58       | 0.15 | 6.89       |

Table 2.

| Number of the model | Location in liver | X(mm)          | Y(mm)          | Z(mm)      |
|---------------------|-------------------|----------------|----------------|------------|
| 1                   | segment VII       | -21.464 to -31.464 | 26.748 to 36.748 | 95 to 105  |
| 2                   | segment VI        | -69.816 to -79.816 | -45.887 to -55.887 | 95 to 105  |
| 3                   | segment II        | 71.127 to 81.127  | 20.3 to 30.3    | 95 to 105  |
| 4                   | segment V         | -25.802 to -35.802 | -57.132 to -67.132 | 95 to 105  |

Table 3.

| Number of the model | X(mm)          | Y(mm)          | Z(mm)      |
|---------------------|----------------|----------------|------------|
| 1                   | -29.4616 to -40.4237 | 4.9948 to 13.8333 | 109.281 to 119.865 |
| 2                   | -71.4393 to -81.0651 | -61.0469 to -70.0071 | 100.578 to 112.36 |
| 3                   | 67.8259 to 78.0354  | 3.41504 to 13.2503 | 106.152 to 112.303 |
| 4                   | -28.5048 to -38.1829 | -75.892 to -86.61464 | 98.1535 to 108.203 |

Table 4.

| Young’s modulus (KPa) | X(mm)          | Y(mm)          | Z(mm)      |
|-----------------------|----------------|----------------|------------|
| 8                     | -71.4393 to -81.0651 | -61.0469 to -70.0071 | 100.578 to 112.36 |
| 10                    | -71.4165 to -81.0768 | -61.0249 to -70.0274 | 100.567 to 112.363 |
| 20                    | -71.3475 to -81.1072 | -60.9565 to -70.0895 | 100.541 to 112.362 |
| 50                    | -71.12724 to -81.1187 | -60.8723 to -70.1571 | 100.548 to 112.307 |
