An Experimental and Numerical Study on Tactile Neuroimaging: A Novel Minimally Invasive Technique for Intraoperative Brain Imaging

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-Manuscript category: Original article

-Number of figures: 12

-Number of Tables:0

-Word count: 4455

Abstract:

Background

The success of tumor neurosurgery is highly dependent on the ability to accurately localize the operative target, which may be shifted during the operation. Performing an intraoperative brain imaging is crucial in minimally invasive neurosurgery to detect the effect of brain shift on the tumor's location, and to maximize the efficiency of tumor resection.

Method

The major objective of this research is to introduce the tactile neuroimaging as a novel minimally invasive technique for intraoperative brain imaging. To investigate the feasibility of the proposed method, an experimental and numerical study was first performed on silicone phantoms mimicking the brain tissue with a tumor. Then the study was extended to a clinical model with the meningioma tumor.

Results

The stress distribution on the brain surface has high potential to intraoperatively localize the tumor.

Conclusion

Results suggest that tactile neuroimaging can be used to provide a non-invasive, and real-time intraoperative data on tumor's features.

Keywords: Intraoperative brain imaging; Minimally invasive neurosurgery; Artificial tactile sensing; Computational modeling and analysis.

1. Introduction

Brain tumors are the second most common paediatric cancer, with more than 4,000 cases diagnosed each year in children and adolescents [1]. Despite all medical advances achieved in the field of brain surgery in the last decades, the survival rate of patients with brain tumors has not much improved. The mortality rate from brain tumors remains high; the median survival rate is only 12 to 18 months in patients with glioblastoma and 41 months in patients with anaplastic astrocytomas [2]. Today, neurosurgery is concerned in the diagnosis, treatment and postsurgical rehabilitation of patients with brain and spinal cord tumors. Determinant factors in selecting the suitable therapeutic technique are highly dependent on the type and geometrical features of the tumors [3, 4].

Recent technological advances in medicine offer a new surgical technique called minimally invasive surgery (MIS) to minimize trauma to the normal tissues as well as to reduce the recovery time [5]. MIS is defined by two essential features: accurate identification of the operative anatomy, and a minimally invasive surgical corridor to the target [6]. Endoscopic instruments are mainly used in general MIS to perform the surgery through small incisions. Minimally invasive neurosurgery is colloquially considered as a brain surgery through small opening in the scalp or the skull bone. However, the goal of this surgical practice is to implement MIS to optimize the brain tumor resection with the least possible effect on the brain tissue around the abnormality being dealt with [1, 6]. For minimally invasive neurosurgery, advanced surgical techniques have been developed such as the conformal radiation, laser hyperthermia, focused ultrasound and the image-guided surgery including intraoperative imaging [6]. In particular, the intraoperative imaging technique can be applied as a MIS during Craniotomy (open surgery) to detect the effect of brain shift on tumor's location and consequently to reduce the side effect on normal tissue [7, 8]. Note

that the opening of the skull and of dura mater, the loss of cerebrospinal fluid, the resection of tumor and the reduction of intracranial pressure often contribute to an intraoperative brain deformation, known as “brain shift” [2]. Brain surface may be deformed up to 20 *mm* after the skull is removed and even up to 50 *mm* after the resection of big lesions [9, 10]. Brain shift degrades the accuracy of preoperative data and makes intraoperative tumor delineation very difficult [11]. Today’s medical advancements in intraoperative imaging such as magnetic resonance imaging (iMRI) and computed tomography (iCT) scans help neurosurgeons to compensate for the impact of brain shift, and to perform precise tumor resection with minimal damage to normal tissues and critical structures [11, 12].

As one of the first studies of neuroimaging, Black et al. [13] described the use of iMRI in the operating room to eliminate errors that may arise during surgeries due to shifting or displacement of the brain. iMRI offers an excellent intraoperative image guidance during brain tumor resection and various surgical data such as the location of tumor and its margins, as well as functional and vascular parameters at high resolution [14, 15]. Aside from iMRI, there are reports of intraoperative imaging utilizing CT [16] and ultrasound [17], in an attempt to acquire the real-time data of brain tumor affected by brain shift. Despite all advances in image-guided neurosurgery, intraoperative imaging techniques such as iMRI and iCT are classified as invasive methods since patients are exposed to the harmful impacts of magnetic field and x-ray [1, 18]. Furthermore, they are expensive and time-consuming as each scan takes up to 20 min [2]. Ultrasound also has limited applicability because many tumors do not have enough echogenicity to provide clear real-time images. Therefore, there is a clear need for development and integration of new non-invasive imaging methods to help neurosurgeons intraoperatively achieve optimal tumor resection.

Recently, tactile imaging is emerging as a new medical imaging modality that translates the sense of touch acquired by tactile sensor into a form of digital image [19, 20]. Any device which measures the information such as force, temperature and vibration by physical touch can be regarded as a tactile sensor [21]. For example, stress imaging, a type of tactile imaging technique, produces a map of pressure or stress on the soft tissue surface due to the contact with a tactile sensor [22]. Particularly, artificial tactile sensing (ATS) closely simulates the manual palpation since the probe of the tactile device with a force sensor acts similarly to human fingers during clinical examination, deforming soft tissue with the probe and detecting resulting changes in the stress pattern [19].

Tactile imaging has a broad range of potential applications in practical and experimental medicine, as many researchers have reported that cancerous tissues are significantly stiffer than normal ones [19, 23]. Wang et al. [23] developed a prototype tactile mapping device (TMD) system composed of a tactile sensor array probe, a 3D camera and a force/torque sensor, which can provide tactile maps of the breast lumps during breast palpation. Ottensmeyer [24] designed a minimally invasive instrument (TeMPeST 1-D) to measure the viscoelastic properties of intra-abdominal organs. Tanaka et al. [25] developed an active palpation sensor for detecting prostate cancer and hypertrophy. Keshavarz and Mojra [26] fabricated a novel tactile sensing robot to characterize the mechanical behaviour of breast tissue during clinical breast examination (CBE). Liu et al. [27] presented a new approach for the localization of tissue abnormalities during MIS using a force-sensitive wheeled probe. Sadeghi-Goughari et al. [7] proposed a haptic-thermal robot to palpate brain surface and measure the temperature for tumor localization during minimally invasive diagnosis in neurosurgery. McKinley et al. [28] designed a novel low-cost palpation probe for robot assisted minimally invasive surgery (RMIS) for localizing subcutaneous blood vessels.

Most of these efforts are based on the clinical observations that tumors are much stiffer than surrounding normal tissues. In the case of brain tumors, it has also been proved that brain tumors are stiffer than the normal neurological tissue. Wang et al. [29] indicated that the glioblastoma tumor can be modelled as an elastic material with the elastic modulus of 26 *kPa* embedded in a brain tissue of 1 *kPa* stiffness. Murphy et al. [30] reported the elastic moduli of the meningioma and the normal brain tissues to be 10 *kPa* and 1 *kPa*, respectively. Also based on this behaviour, the present study proposes tactile neuroimaging as a fast, passive and non-invasive method in brain tumor surgery to intraoperatively localize brain tumor under the effect of brain shift. Since a part of skull is temporarily removed for tumor resection during the minimally invasive intracranial neurosurgery, tactile imaging can be performed on the brain surface to sense the stress variation caused by the stiffness difference between the tumor and the brain. This method has a potential to overcome the drawbacks of the existing intraoperative imaging techniques such as invasiveness and long imaging time, and hence to reduce morbidity in neurosurgery. For the investigation of the feasibility of the proposed method, experimental and numerical analyses were performed on brain phantoms with tumors. The experiments were conducted on silicone phantoms which contained abnormalities mimicking brain tumors, and the results were compared with those from the simulations using finite element analysis (FEA). The brain and tumor tissues were characterized as elastic materials to describe the mechanical behavior of the soft tissues during tactile palpation. Furthermore, virtual tactile neuroimaging was also conducted on a clinical brain model constructed from the MRI data of a real patient with a meningioma tumor to evaluate the applicability of tactile imaging to brain surgery. The resulting tactile data are presented in graphical forms to demonstrate the capability of tactile imaging in the intraoperative detection and localization of brain tumors.

In this paper, results from the tactile analyses are presented in three different forms:

a) Tactile image: force or corresponding stress contour map on the examined surface of the brain
b) Tactile map: force or stress distribution profile with coordinate data on the examined surface
c) Tactile diagram: force or stress distribution on the path defined over the tumor center on the examined surface

Tactile images intuitively show the stress profile on the geometry of brain, to which neurosurgeons can refer during the tumor surgeries. Tactile map contains the tactile data with the exact coordinate on the palpated surface, which can provide the real-time information for robot assisted surgeries, while the tactile diagram can be used to present and compare the results in a detailed manner.

2. Tactile imaging experiments

2.1. Experimental setup on the silicone phantoms

To investigate the feasibility of tactile imaging to intraoperative localization of brain tumors, an experimental setup using silicone phantoms was developed. The silicone phantoms contained stiff inclusions embedded in soft matrix to mimic tumors in the brain tissue. Platinum cure silicone (Ecoflex 00-30, SMOOTH-ON inc) was chosen to make two types of inclusions, representing glioblastoma and meningioma, while the matrix was made of Sylgrad 527 silicone (Dow Corning), mimicking brain tissue. Before fabricating the silicone phantoms, the mechanical properties of silicone materials were measured by performing uniaxial compression tests. Three cylindrical samples with diameter of 27 *mm* and height of 30 *mm* were made for each silicone material for the tumors and the brain tissue, respectively. Uniaxial compression tests were performed on the samples at the speed of 0.5 *mm/s* using a TA micro test machine (TA.xt Plus, Stable Micro Systems Ltd, UK) with a 5 *kgf* load cell, as shown in Fig. 1(a). Results from the compression tests are presented in Fig. 1(b). The stress-strain diagrams show the quasi-linear elastic behavior of silicone

materials with stiffness of 27.3 and 10.8 *kPa*, respectively, that are corresponding to the stiffness of glioblastoma and meningioma brain tumors [29, 30]. The silicone material representing brain tissue also shows linear elastic behaviour with stiffness of 2.7 *kPa*. It needs to be mentioned that the stiffness of real brain tissue is around 1~2 *kPa* [29, 30]; however, due to the limitation in the tunability of the silicone, the matrix with 2.7 *kPa* stiffness was fabricated and used for the current project.

Tactile imaging experiments were performed on the silicone phantoms using a probe having a spherical end-tip with diameter of 5 *mm* attached to the TA machine, as shown in Fig. 2(a). The phantom surface was compressed 2 *mm* and the force measured by the load cell was recorded as the response of tactile imaging. Three types of silicone phantoms were fabricated for the experiments:

1) **SP 1** contained a cylindrical inclusion (mimicking glioblastoma tumor) of 27 *mm* diameter and 30 *mm* length embedded within the matrix (brain tissue) with dimensions of $100 \times 80 \times 60$ *mm*, at a depth of 26.5 *mm* from the top surface to the centerline of cylinder ("*h*" in Fig. 2(b)).
2) **SP 2** contained two cylindrical inclusions (glioblastoma and meningioma tumors) with 21.6 *mm* diameter and 24.7 *mm* length, respectively, at a depth of 13.8 *mm*.
3) **SP 3** has the same configuration as SP 2, except two tumors were positioned at a depth of 23.8 mm.

Tactile data were collected at every 5 *mm* distance in the vicinity of the tumor, while at every 10 *mm* distance in the remote area. Fig. 2(c) shows the tactile points layout for SP 2 and 3.

2.2. FEA modeling of the silicone phantoms

Finite element analyses (FEA) were conducted using commercial FEA code (ABAQUS 6.10) to validate the experimental results by comparing them with those derived from numerical analysis. 3D FEA model was developed for SP1. Dimensions of the model and the embedded inclusion were compatible with actual phantom. For 3D FEA model, the tetrahedral element type was selected which is well suited to irregular meshes (Fig. 3). Boundary conditions were applied by considering the cube fixed on all sides except the top surface, which was compressed by 2 *mm* for tactile imaging. The elastic moduli of the tumors and the brain tissue were set to those measured by uniaxial compression tests.

2.3. Results from tactile sensing experiments on silicone phantoms

In this subsection, the results from experimental and numerical analyses on the phantoms model are presented. In the fist step, accuracy of the experimental results was validated by comparing the tactile diagrams from the experiment on SP 1 with the corresponding numerical simulation using FEA as shown in Fig. 4. The figure shows the distribution of force on the phantom surface during examination. The peak in the surface force profile clearly indicates the existence of abnormality embedded in the phantom. Furthermore, the force values are in excellent agreement with the corresponding FEA data.

The tactile image from the experiment on SP 2 containing two tumors with different stiffness are presented in Fig. 5(a). It can be observed that the level of the peak force varies depending on the stiffness of tumor embedded under the tactile point. An increase of the tumor's stiffness from 10.8 *kPa* to 27.3 *kPa* results in an elevation of the maximum sensed force in the tactile map from $0.072\ N$ to $0.138\ N$. Fig. 5(b) displays the top view of the tactile image of SP 2, while the rectangles drawn around the high force region indicate the location of embedded tumors with their corresponding size (21.6 *mm* diameter and 24.7 *mm* length). It is obvious that tactile

data from the phantom experiment exactly predict the location of tumors and also provide some estimated information on the size and margins of the tumors. Fig. 5(c) presents the tactile images from SP 3 that was designed to investigate the sensitivity of tactile imaging to the tumor depth. The comparison between Figs. 5(a) and 5(c) indicates that as the tumors recede further inside the phantom, the corresponding force response sensed on the tissue surface decreases. This can be more clearly visualized with tactile diagrams in Fig. 5(d) that show the decrease of maximum sensed force for glioblastoma from 0.138 N to 0.030 N with the increase in the depth of tumor from 13.8 to 23.8 mm, while that for meningioma from 0.072 N to 0.027 N. It needs to be mentioned that the increase of tumor depth also generates more widespread pattern of sensed force above the tumor.

3. Virtual tactile neuroimaging of the clinical brain model

After performing tactile imaging on phantom models with the compatible stiffness of brain tumors and validating the feasibility of tactile imaging in intraoperative localization of brain tumors, a computational analysis on a clinical brain model with meningioma tumor was developed. To simulate the mechanical response from the brain containing a tumor during intraoperative tactile imaging, virtual tactile neuroimaging using FEA was carried out on a clinical brain model.

3.1. Geometrical and tactile data of brain and tumor

Precise information on the geometries of brain and meningioma tumor was derived from the MRI data of a 41 year-old female patient who was referred to the neurosurgeon in our research team to treat her brain tumor. MRI image data with and without contrast were acquired at the imaging facilities of the Iran Gamma Knife Center in Tehran. A large heterogeneous ill-defined residual posterior parafalcine meningioma was noted with peri-lesional edema (Fig. 6).

The MRI image data were transferred to the Mimic (version 3.2.0.2) and SolidWorks (2013) software to generate the 3D solid models of brain and meningioma tumors, as shown in Fig. 7. In this model, the tumor was approximated with a sphere with diameter of $40\ mm$.

3.2. Finite element mesh and boundary conditions

For the FEA of tactile neuroimaging, the brain model was meshed with tetrahedral elements (Fig. 8). Elastic moduli of the brain tissue and meningioma were set to $1\ kPa$, $10\ kPa$, respectively [30].

To apply boundary conditions, the brain model was divided into two parts: the bottom one was in contact with the skull bone and the top one was open for tactile neuroimaging. The bottom surface of the brain was considered to be fixed in normal direction (Z-direction) while the top one was compressed by $2\ mm$ to simulate artificial palpation of the brain tissue during tactile neuroimaging. The brain and tumor tissues were considered to be bonded together to make the strain values continuous across boundary.

4. Results from virtual tactile neuroimaging

4.1. Mesh convergence

To minimize the computational load while maintaining the accuracy of the virtual tactile neuroimaging, FEA simulations were performed using 4 different element sizes for the brain model and the results are presented using the tactile diagrams. As shown in Fig. 9, the stress data for 3.5 *mm* and 4 *mm* element sizes are close to those for 3 *mm* case, with the maximum error less than 3% and 6%, respectively. On the other hand, the FEA using 5 *mm* element size yielded the maximum error exceeding 10% compared to 3 *mm* case. Therefore, the element size of 4 *mm* was

selected for FEA model for efficient computation without compromising accuracy, which resulted in the total number of elements of 171,546.

4.2. Tactile data of the reported patient

The tactile image and tactile map for the brain model with meningioma are presented in Fig. 10. Tactile image in Fig. 10(a) indicates an abnormality in the left posterior region of the brain, where notable stress increase is observed in the vicinity of the tumor region. In the tactile map in Fig. 10(b), it is shown that the peak stress is about twice the stress in surrounding region. The overshoot of the stress in the tactile map is the indicative of the intraoperative location of meningioma tumor and the intraoperative coordinates on the brain surface which have the shortest distance to the surgical target. The tactile map also provides estimated information on the real-time tumor's margins, and the area of the overshoots describes the estimated boundary between tumor and normal tissue.

4.3. Sensitivity of tactile neuroimaging to tumor's features

Brain tumors have the ability to reproduce cancer cells and to invade the surrounding normal tissue. Due to the aggressive behavior of brain tumors, their features such as size and stiffness may vary with respect to the development stage and the degree of malignancy. Effects of tumor's features including tumor size and stiffness were investigated using the brain model with different types of tumors. The sensitivity of tactile data to the tumor stiffness and its size are presented in Figs. 11 and 12, respectively. Here, E and D denote the tumor stiffness and its diameter, respectively.

In Fig. 11, the diameter of meningioma was fixed at 40 *mm* and the stiffness was increased from 5 *kPa* to *15 kPa*, which was selected according to clinical data. Tactile images in Fig. 11(a) graphically illustrates that as the stiffness of the tumor gets smaller, the size of high stress region decreases. The tactile diagram in Fig. 11(b) also shows the decrease in peak stress with the decrease

of tumor stiffness. For example, a decrease of the tumor's stiffness from $10\ kPa$ to $5\ kPa$ results in the decline of peak stress from $0.101\ kPa$, about twice higher than the surrounding region, to $0.083\ kPa$, about 1.5 times higher. It is notable that the trend of stress variation in the high stress region around the tumor was similar in all three tactile diagrams, with the stress being amplified proportional to the tumor stiffness. This is consistent with the results from tactile imaging experiments using silicone phantoms shown in Fig. 5.

To show the effect of tumor size on the performance of tactile neuroimaging, the diameter was changed from 40 *mm* to 30 *mm* while the stiffness of meningioma tumor was fixed at 10 *kPa*, and the results are presented in Fig. 12. As one may easily expect, as the size of tumor decreases, the size of high stress region around tumor decreases. However, tactile diagram in Fig. 12(b) suggests that the size of the tumor also affects the peak stress. A decrease of the tumor's diameter from 40 mm to 30 mm results in a reduction of peak stress from $0.101\ kPa$ to $0.0756\ kP$. Therefore, it is speculated that by using the peak stress and stress profile around the peak, it should be possible to identify tumors with different characteristics.

5. Discussion and future work

In this paper, we performed the tactile imaging experiments on silicone phantoms and compared the results with those from numerical simulations using FEA. Virtual tactile neuroimaging simulations on the clinical brain tumor models were also conducted to investigate the feasibility of the method in intraoperatively identifying and localizing the brain tumor and its margins. We presented tactile imaging data in two different ways; tactile image and tactile map. Tactile images indicate the force or stress levels using color map, which can be used as visible data for neurosurgeons to intuitively identify the location of tumors in 3D space during brain tumor surgeries. On the other hand, tactile maps show the stress profile versus the coordinate data of

brain surface; thus, it can be a useful roadmap for robot assisted brain surgery. The occurrence of overshoot in the stress level on the brain surface confirms the applicability of tactile data in the delineation of tumor location affected by brain shift (Figs. 5 and 10). In summary, the tactile data can provide the real-time intraoperative information on the stress distribution on the brain surface, which may serve as an intraoperative assisting tool to help neurosurgeons compensate for the effect of brain shift and to achieve the goal of maximum tumor resection with the least morbidity.

The practical feasibility of tactile neuroimaging as an intraoperative imaging tool is considered in comparison with existing techniques. In general term, the mainstream imaging methods for brain tumor surgery include iMRI and iCT. They both are classified as semi-invasive techniques since patients are exposed to harmful impacts of magnetic field and x-ray, but the tactile neuroimaging is completely noninvasive, and just examine the brain surface using tactile sensors. Other than this, its main advantages over iMRI and iCT are reflected in its simple mechanism and affordable cost. To develop a clinical model for the tactile neuroimaging, we just need to design an apparatus by embedding some high resolution tactile sensors which would make it very cost-effective. However, both iMRI and iCT are highly expensive and labor-intensive imaging modalities. Moreover, the patients with implanted stents made of magnetic materials are not permitted to be treated by surgical techniques containing MRI tube; while tactile imaging can be applied to these patients without any problems.

Although tactile imaging is proposed as an intraoperative method to achieve the accurate localization of brain tumor, this technique does not have the ability yet to provide the detailed information on the tumor properties such as its margin, size, depth and stiffness. As presented in Fig. 5(b), the tactile data can just provide the 2D location and an estimated data on the tumor's margin. Since tactile neuroimaging examines only the brain surface and does not have any accesses

to inside the tissue, exact estimation of tumor margins requires the combination of the tactile image on the brain surface with an inverse algorithm. However, the tactile diagrams in Figs. 11 and 12 suggest that tactile neuroimaging are sensitive enough to differentiate the tumor's characteristics such as size and stiffness. As the next step, we plan to develop an estimation algorithm based on the inverse analysis to better predict the stress variations on brain surface versus tumor's properties such as size, depth and stiffness, in addition to 2D location. These intraoperative data related to the tumor characteristics may significantly contribute to an improvement of tumor resection practice by updating delineation of the tumor margins.

On the other hand, a new fused system can be developed by combining the tactile imaging with the existing techniques, that have the ability to make anatomical images, to enhance the intraoperative imaging capability. For example, the results from tactile neuroimaging can be integrated with ultrasound and elastography data to examine the characteristics of the brain tumor including 3D location, stiffness and size. Utilizing the tactile data on the brain surface regarding the intraoperative location of brain tumor, the ultrasound probe can be efficiently positioned for ultrasound imaging inside the brain, and be manipulated for elastography for stiffness measurement. Combination of these real time data can help us in improving the resolution and efficiency of imaging procedure.

6. Summary

Experimental and computational brain models were developed to study the feasibility and applicability of the tactile neuroimaging for brain tumor localization and intraoperative delineation of its margins. To this end, variation of brain surface stress was selected as the indicative factor of tumor existence. Tactile results were presented as tactile images and tactile maps to improve the diagnostic ability of neurosurgeons.

Results suggested the feasibility of tactile neuroimaging in intraoperative localization of intracranial brain tumors including meningioma and glioblastoma. Overshoot of the surface stress in tactile map was used as the indication of tumor existence. Decrease of the tumor stiffness resulted in the reduction of the maximum stress sensed on the brain surface. Increase of tumor depth also resulted in the decrease of the maximum stress, but the stress profile became more widespread. The size of tumor, an important indicator of the degree of malignancy, can also be sensed by tactile neuroimaging; a marked elevation in the maximum stress occurred with the increase of tumor size. It can be stated that the proposed tactile neuroimaging has a potential as a non-invasive technique that can detect and localize brain tissue abnormalities, which may allow neurosurgeons to compensate for the effects of the brain shift during MIS.

Ethical approval

The patient data were obtained and approved by the appropriate ethical body of the Iran Gamma Knife Center in Tehran, Iran. According to the Helsinki agreement, the whole study was thoroughly explained to the patient and the consent for participation in research was obtained.

Acknowledgement

This research was supported in part by NSERC (Natural Sciences and Engineering Research Council) of Canada under grants RGPIN/2015-05273, RGPIN/2015-04118, and RGPAS/354703-2015.

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Figures:

Fig. 1. (a) Uniaxial compression test on different samples using TA machine, **(b)** stress-strain diagrams for obtaining stiffness properties of tissue and tumor samples.

Fig. 2. (a) Experimental setup and the silicone phantom under test, **(b)** configuration of silicone phantoms (SP 2 and SP 3), and **(c)** tactile spots on top surface of the phantom.

Fig. 3. Meshing of the FEM model for silicone phantoms.

Fig. 4. Tactile diagrams of the silicone phantom (SP 1) and the corresponding numerical data.

Fig. 5. Tactile images from the experiments on **(a)** SP 2, **(b)** SP2 with tumor margin **(c)** SP 3, and **(d)** the corresponding tactile diagrams.

Fig. 6. (a) Axial, **(b)** Sagittal, **(c)** Coronal MRI images of reported patient.

Fig. 7. 3D solid model of the brain containing the meningioma.

Fig. 8. Mesh analysis of the brain and tumor.

Fig. 9. Tactile diagrams from the FEA simulations of brain tumor model using four different mesh sizes

Fig. 10. (a) Tactile image and **(b)** tactile map of the brain model with meningioma.

Fig. 11. (a) Tactile images and (b) tactile diagrams for meningioma with different stiffness.

Fig. 12. (a) Tactile images and (b) tactile diagrams for meningioma tumor with different sizes.