Production approaches of a human brain tissue phantom for robot-assisted stereotactic biopsy

D D Klimov, M A Buinov, A A Vorotnikov, A M Meleshnikov and Y V Poduraev
Moscow State University of Technology “STANKIN”, 1, Vadkovsky Avenue, Moscow 127055, Russia

E-mail: daniil.klimov@gmail.com

Abstract. The article presents the production approaches of a human brain tissue phantom for robot-assisted stereotactic biopsy. The different types of materials used for the production of brain phantoms are shown. The experiments on the possibility of obtaining a sample of tissue simulating the brain, using a conventional biopsy needle with a side cutting window, are conducted. It is proved that silicone can not be used for production of a phantom of a brain tumor. The approach to the production of a phantom of two materials is proposed for use in the development of new robotic systems of stereotactic brain biopsy, as well as training surgeons.

1. Introduction
Neurosurgery is an essential part of the medical field, which sets innovative trends in surgery in general. Stereotactic brain biopsy is a typical task in neurosurgery that uses minimally invasive surgery. It uses surgical navigation systems to accurately determine the location of targets identified on patient diagnostic images obtained using the computed tomography (CT) or magnetic resonance imaging (MRI). Next, a specialized biopsy needle is inserted through the prepared hole and takes the tissue sample for subsequent analysis.

The process of robotisation is widespread in this area. There are a number of commercial systems that use robots to carry out this procedure; new, more advanced systems are being developed. For testing of such systems, phantoms of the brain tissue are necessary, with the possibility of simulating tumors that correspond to the tissue by mechanical and other properties.

Nowadays, the study of the mechanical characteristics of brain tissue and its changes due to a traumatic brain injury is hindered by the low availability of human tissues for laboratory research, because of problems in ethics, biosafety, and tissue degradation in samples obtained from corpses (due to dehydration of collagen [1]).

In the field of phantomization of the brain tissue, silicones of various hardness, composite hydrogels and some other materials are used for imitating the process of stereotactic robotic biopsy. The specificity of the task is to simulate the mechanical properties of the brain tissue to mimic the effect of the brain shift (for example, for craniotomy) and interaction with the instruments used in neurosurgery.

The additional requirement may be presented by the possibility of obtaining medical images (CT / MRI), for example, imitation of such properties as radiolucency. Solving the problem of creating durable and easy-to-use phantoms will allow more efficiently solving the problems of developing new surgical systems that require testing before moving on to clinical trials.

2. Methods and materials
For successful imitation, the phantom must correspond to the brain at all stages of the operation. In the case of a brain biopsy:

- Identification of the region of interest based on computed tomography, for succeeding stereotactic navigation.
- Providing access to the biopsy needle entry point
- Insertion of a biopsy needle into a predetermined point based on stereotactic navigation.
- Tissue sampling at the region of interest
- Removing the needle with the tissue sample

A popular method is to make a phantom of the brain tissue from a mixture of two different silicones. Commonly two-component silicones with a hardness of 10–70 according to Shore OO are used [2]. Corresponding mechanical characteristics are achieved by changing the ratio of components or the kind of silicone.

Another method was proposed by Antonio E. Forte et al. [3], in which the use of a composite hydrogel consisting of two components - polyvinyl alcohol of a specific molecular weight and a gelling agent phytage. According to the results of some studies [4, 5], it closely imitates the mechanical properties of brain tissue.

In certain cases, the materials based on gelatin are used in a concentration of 5–10%, and even such an unconventional material as cheese [6], to simulate various types of brain tumors.

3. Implementation

To ensure a complete simulation of the process and a clear demonstration of the biopsy needle hitting the phantom of the tumor, certain requirements are imposed on the material:

- the tissue cutting window of the biopsy needle should be able to collect a sample
- the material of the phantom of the tumor should differ in color from the “healthy” tissue of the brain phantom
- tumor phantom material must have different radiolucency

To begin with, silicone was chosen as the starting material for phantom production. It is easily accessible, simple to use material, allowing adequately simulating the mechanical properties of the human brain. Another advantage is durability. Silicone also allows using various dyes and contrast agents.

To check the material compliance with the requirements stated above, five specimens of different hardness were produced according to Shore: OO-10, OO-30, OO-50, A-10, A-25 (figure 1 a). In the experiments, a specialized brain biopsy needle with a side cutting window was used — the sampling procedure corresponded to the sequence of actions during the actual operation.

![Figure 1. a) Silicone specimen of hardness A25 during testing b) obtained sample of the brain tumor phantom from composite hydrogel](image-url)
The needle consists of two nested tubes with a rectangular window that opens when the inner tube is rotated 180°. It was introduced into the sample in a closed form, after which a window was opened and with the help of a syringe connected to the upper part of the tube, low pressure was created in the tube, which allowed the tissue to be drawn into the cutting window. Finally, the window was closed to cut a tissue sample for later retrieval.

Although the mechanical properties of silicone are close to brain tissue when the needle is inserted, the tissue cutting window of the needle was not able to separate the sample that simulates the tumor. Therefore, none of these materials can adequately simulate the procedure of brain tissue biopsy.

In this regard, it was decided to conduct similar experiments with the composite hydrogel. It was made according to the recipe provided in [3] with a concentration of 2.5% polyvinyl alcohol and 1.1% phytage. The process of fabrication and sample preparation for the experiment requires specialized equipment and takes about 27 hours.

In the beginning, both ingredients dissolve in the appropriate amount of deionized water at a temperature of 90 °C under vigorous stirring in a magnetic stirrer for one hour. Then, the solutions are mixed at a temperature of 70 °C for 30 minutes. Since the main processes of bond formation in the hydrogel occur during the freezing and thawing cycle, the resulting mixture must be poured into a mold in a climate chamber for 15 hours (figure 2 b), followed by a slow defrosting to room temperature [5].

![Figure 2. a) The process of the preparation of the ingredients of the composite hydrogel b) Freezing of the mixed hydrogel in a climatic chamber.](image)

Unlike silicone samples, composite hydrogel showed good results and allowed extracting the sample in accordance with the procedure of brain biopsy (figure 1 b). It is worth noting that phantoms from composite hydrogel have a short lifetime. Under the influence of atmospheric air, the material loses its shape and mechanical properties after 48 hours.

4. Results
Despite the fact that the composite hydrogel showed compliance with the requirements for the material of a phantom of a brain tumor, its use to create a “healthy tissue” of a phantom of the brain is impractical due to its low strength and fragility.

Unlike phantoms made of silicone, a composite hydrogel does not hold a shape on its own and needs specialized external support. In this regard, difficulties arise in combining the brain phantom and tumor phantom, which are distinguished by the presence of a dye and various X-ray transparency (concentration of a contrast agent). The initial location of the tumor phantom inside the brain phantom changes over time with movement, as well as in a stable position under the influence of gravity. This leads to the fact that during the time between obtaining medical images using computed tomography...
and the beginning of the operation, the phantom of the tumor can unpredictably shift. It follows that this approach is poorly applicable in the field of stereotaxis, where everything is based on the conjunction of the position of the anatomical structures of the patient on medical images and during surgery.

For the phantom prototype, a hybrid approach was used, which implies the use of a simpler and more durable silicone brain and a tumor phantom of the composite hydrogel. This makes it possible to simulate a tumor by introducing a contrast agent targeted into the tumor phantom, thus simplifying navigation based on medical images. It is also possible to introduce dye, for additional visual assessment of hitting the desired area after the completion of the procedure.

The prototype of the brain phantom was made of silicone with a hardness of OO-50 according to Shore, of two halves (figure 3 a), and a hemispherical recess was left in each separate hemisphere. The phantom of a tumor made of the composite hydrogel with the addition of red food coloring (E122) was placed (figure 3 b). The phantom of the tumor is easily detected in the image obtained using computed tomography (figure 3 c), as the two materials differ in radiolucency. The brain phantom is placed in a plastic skull which is fixed in a silicone shell that mimics the soft tissue of the patient’s head. The upper part of this shell is removable, for the convenience of multiple manipulations. The inner surface of the skull phantom was covered with a layer of silicone 1-2 mm thick to simulate the dura mater.

The phantom prototype was used in the research based on the joint project of Moscow State University of Technology "STANKIN" and A.I.Yevdokimov Moscow State University of Medicine and Dentistry in which a Multifunctional Automated Robotic System (MARS) is developed. The main task of the phantom development is to provide the opportunity to test the implementation of a robotic and manual brain biopsy procedure in various areas of the patient’s head, ensuring the reuse of phantom elements.

Figure 3. a) Casting mold for the silicone phantom b)The prototype of the phantom for brain biopsy c) CT-image of the phantom for brain biopsy

5. Conclusion
The authors carried out work on stages from literary and patent search to the first metrological examination, as a result of which it was found that the use of silicones does not solve the problem of simulating the tissue sampling using a needle for brain biopsy.

According to the above mentioned aspects, it becomes evident that phantoms, which have been successfully used for mimicking brain tissue for different tasks, are not always suitable for use in robot-assisted stereotactic biopsy. Therefore, the issue of developing new phantoms and, above all, materials for them, becomes urgent.

Composite hydrogels, in turn, are well suited as a phantom material of brain tissue. The phantoms of a similar hybrid structure can be used both in the training of surgeons and in the development of robotic systems for stereotactic brain biopsy.

In the future, the authors intend to continue improving the phantom, in particular, to imitate various types of brain tumors in such parameters as shape, the similarity of appearance in medical images and mechanical characteristics.
6. Acknowledgments

This work was supported by the Ministry of Science and Higher Education of the Russian Federation as part of State Assignment no. 9.3408.2017/4.6. This work was carried out using equipment provided by the Center of Collective Use of MSTU "STANKIN".

References

[1] Pantoni L, Garcia J H and Gutierrez J A 1996 Cerebral white matter is highly vulnerable to ischemia Stroke 27(9) 1641–7

[2] Chanda A, Callaway Ch, Clifton C and Unnikrishnan V 2016 Human Tissue Simulants for Study of Traumatic Brain Injury Biofidelic human brain tissue surrogates, Mechanics of Advanced Materials and Structures DOI:10.1080/15376494.2016.1143749

[3] Forte A, Galvan S, Manieri F, Rodriguez y B F and Dini D 2016 A composite hydrogel for brain tissue phantoms Mater. & Design P 227–38

[4] Leibinger A, Forte A, Tan Zh, Oldfield M, Beyrau F, Dini D and Rodriguez y B F 2015 Soft Tissue Phantoms for Realistic Needle Insertion. A Comparative Study Annals of biomedical engineering 44 DOI: 10.1007/s10439-015-1523-0

[5] Tan Zh, Dini D, Rodriguez y B F, Forte F and Elia A 2018 Composite hydrogel: A high fidelity soft tissue mimic for surgery Mater. & Design 160 886–94

[6] Sidhu D S, Ruth J D, Lambert G and Rossmeisl J H 2017 An easy to produce and economical threedimensional brain phantom for stereotactic computed tomographic-guided brain biopsy training in the dog* Veterinary Surgery 00:000-000 Retrieved from: https://doi.org/10.1111/vsu.12657