Using 3D Printing to Create Personalized Brain Models for Neurosurgical Training and Preoperative Planning

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■ BACKGROUND: **Three-dimensional (3D) printing holds promise for a wide variety of biomedical applications, from surgical planning, practicing, and teaching to creating implantable devices. The growth of this cheap and easy additive manufacturing technology in orthopedic, plastic, and vascular surgery has been explosive; however, its potential in the field of neurosurgery remains underexplored. A major limitation is that current technologies are unable to directly print ultrasoft materials like human brain tissue.**

■ OBJECTIVE: **In this technical note, the authors present a new technology to create deformable, personalized models of the human brain.**

■ METHODS: **The method combines 3D printing, molding, and casting to create a physiologically, anatomically, and tactilely realistic model based on magnetic resonance images. Created from soft gelatin, the model is easy to produce, cost-efficient, durable, and orders of magnitude softer than conventionally printed 3D models. The personalized brain model cost $50, and its fabrication took 24 hours.**

■ RESULTS: **In mechanical tests, the model stiffness ($E = 25.29 \pm 2.68$ kPa) was 5 orders of magnitude softer than common 3D printed materials, and less than an order of magnitude stiffer than mammalian brain tissue ($E = 2.64 \pm 0.40$ kPa). In a multicenter surgical survey, model size (100.00%), visual appearance (83.33%), and surgical anatomy (81.25%) were perceived as very realistic. The model was perceived as very useful for patient illustration (85.00%), teaching (94.44%), learning (100.00%), surgical training (95.00%), and preoperative planning (95.00%).**

■ CONCLUSIONS: **With minor refinements, personalized, deformable brain models created via 3D printing will improve surgical training and preoperative planning with the ultimate goal to provide accurate, customized, high-precision treatment.**

INTRODUCTION

Neurosurgery is a high-risk field with potentially fatal consequences for the patient. It holds the greatest proportion of malpractice claims among all physician specialties.[1] Neurosurgical training programs are held to increasingly greater standards to demonstrate and document trainee competence. At the same time, strict work hour regulations in Europe and North America have decreased drastically the time available to acquire the necessary surgical motor skills and technical judgment.[2] One possible strategy to enhance surgical education within this tightly regulated time window is to increase hands-on training through surgical simulators that closely mimic the operating room experience.[3-6]

Currently, residential training and surgical planning rely almost exclusively on 2-dimensional (2D) computed tomography and magnetic resonance images. Surgical preparedness could be advanced through 3-dimensional (3D) simulators with the goal of providing the spatial awareness and tactile experience of how the brain feels, moves, and responds during a surgical procedure.[7] With physiologically, anatomically, and tactilely realistic models, surgeons could practice complex procedures and preoperatively optimize treatment plans, a desirable goal, which is out of reach with 2-dimensional images alone.[4,8] Recent prototype studies in orthopedic surgery, vascular surgery, and neurosurgery demonstrate how surgical models can improve patient consent,[9]

Key words
- Clinical skills
- Simulation
- Neurosurgery
- 3D printing
- Training

Abbreviations and Acronyms
ABS: acrylonitrile butadiene styrene
3D: three-dimensional
2D: two-dimensional

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help optimize surgical and endovascular procedures,[10] and enhance the surgical training experience.[11]

With rapid advances in additive manufacturing and 3D printing,[12] graspable, 3D models of any organ can now be created directly from 2D computer tomography scans or magnetic resonance images.[13] Although 3D-printed medical models are physiologically and anatomically accurate, they are typically undeformable and tactilely unrealistic.[14] With current 3D printing technologies, it is virtually impossible to reproduce the ultrasoft nature of the human brain and mimic its tactile properties. A major challenge in printing soft structures is that the material deforms significantly during the fabrication process, even under its own weight.[15]

Here we propose a novel method to create a physiologically, anatomically, and tactilely accurate model of the human brain. We adopted a 3-step manufacturing process that uses the undeformable 3D-printed brain model as a template for molding and casting.[16] We created a negative silicone mold of this template, and cast a soft, deformable brain model from a surrogate material that closely mimics the rheological features of the human brain.[17] To explore the realism this model, we performed nanoindentation tests on slices of our brain model and compared them with nanoindentation tests on sagittal slices of mammalian brains.[18] To evaluate the usefulness of the model, we perform a multicenter survey of neurosurgeons and surgical residents in Europe and the United States. We close by discussing their feedback and by identifying potential applications of the model.

MATERIALS AND METHODS

Magnetic Resonance Imaging

Magnetic resonance images of a healthy 25-year-old female brain were acquired at the Stanford University Center for Cognitive and Neurobiological Imaging via a 3-Tesla scanner (GE MR750, Milwaukee, Wisconsin, USA) with a 32-channel radiofrequency receive head coil (Nova Medical, Inc., Wilmington, Massachusetts, USA)[19] (**Figure 1**).

Brain Surface Model

Volumetric image segmentation and cortical reconstruction were performed by the use of FreeSurfer (Harvard University, Cambridge, Massachusetts, USA), an image analysis tool that is documented and freely available online.[20] FreeSurfer was used to calculate the brain volume, surface area, cortical thickness, and gyrification indices and to create stereolithography files of the left and right cerebral hemispheres (**Figure 2**). Creating the brain surface model is free of cost and takes approximately 4 hours, fully automated, on a standard desktop computer.

3D-Printed Brain Model

Personalized models of the left and right hemispheres were 3D-printed on a FlashForge Creator Pro Dual Extrusion 3D printer (FlashForge, City of Industry, California, USA) with the use of acrylonitrile butadiene styrene (ABS) thermoplastic with a 1.75 $\pm$ 0.05 mm filament diameter and $\pm$0.07-mm filament roundness (GizmoDorks, Temple City, California, USA) (**Figure 3**). The current price for the 3D printer is $900, the plastic filament costs approximately $4 per hemisphere, and the 3D-printing process takes 10 hours, unsupervised. The 3D-printed hemispheres display a personalized, anatomically realistic surface topology (**Figure 4**). ABS, however, has a material stiffness on the order of 1 GPa, 6 orders of magnitude stiffer than brain tissue,[21,22] which suggests that the 3D-printed model itself is unsuitable as a tactilely realistic training tool.

Silicone Mold for Gelatin Model

To create a tactilely realistic, deformable brain model, the 3D-printed brain model was used as a template in a molding-casting process. Flexible brush-on molds were created on the 3D-printed brain using Rebound 25 (Smooth-On, Macungie, Pennsylvania, USA), a brushable platinum-cure silicone rubber with a shore A hardness of 25 and a tensile strength of 700 kPa, along with Plasti-Paste II (Smooth-On), a mother mold to maintain structural integrity. The mixture was brushed onto the left and right hemispheres in 4 layers to create a strong, durable mold for casting (**Figure 5**). The material cost for the silicone mold is $20, and its creation takes approximately 7 hours.

Tactilely Realistic Personalized Brain Model

After probing a selection of suitable organic and synthetic materials with respect to their structural integrity, stiffness, and shear properties, we selected synthetic gelatin as a tactilely realistic material for casting. Broadly used as a tissue simulant, synthetic gelatin is a transparent, shelf-stable gelatin that is mechanically identical to the classical organic 10% gelatin, a mixture of 1000 g gelatin and 9000 mL of

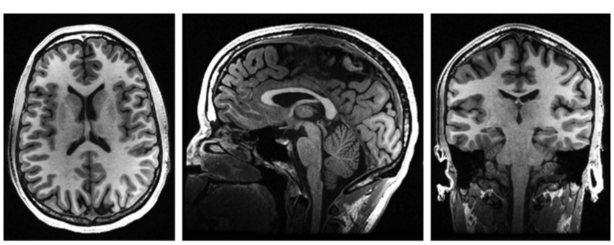

Figure 1. Magnetic resonance image of a healthy 25-year-old female brain. Axial view (*left*), sagittal view (*middle*), and coronal view (*right*).

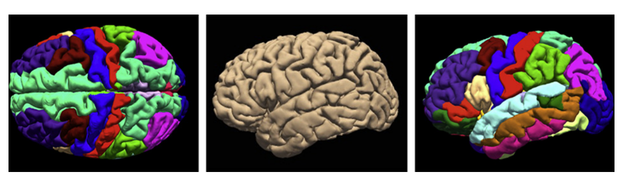

Figure 2. Brain surface model created from magnetic resonance images using FreeSurfer. Axial view (*left*) and lateral view (*middle and right*) with color-coded anatomic regions. The brain has volume of 1228.8 cm^3, a surface area of 1766.9 cm^2, and an average cortical thickness of 0.263 cm.

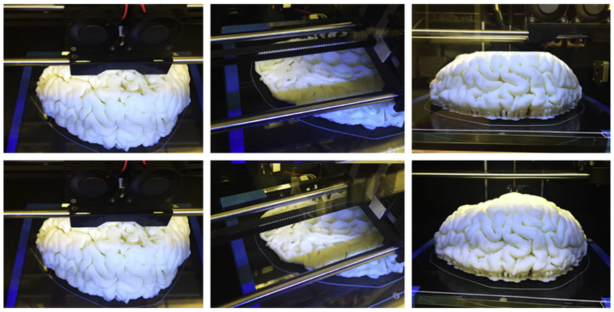

Figure 3. 3-Dimensional printing of personalized brain model. Hemispheres were printed individually with acrylonitrile butadiene styrene thermoplastic with a filament diameter of 1.75 mm and a material stiffness of 1 GPa.

water.[17] With a density of 1060 kg/m^3, synthetic gelatin has a density similar to most soft biological tissues. With a material stiffness on the order of 10 kPa, it is 5 orders or magnitude softer than common 3D-printable materials and only an order of magnitude stiffer than brain tissue.[23] The silicone mold was cast with 10% synthetic ballistic gelatin (Clear Ballistics, Fort Smith, Arkansas, USA) to create a personalized model with realistic physiological, anatomical, and mechanical properties (**Figure 6**). The material cost for the gelatin model is $22, the gelatin is re-usable via melting and molding, and the creation of the gelatin model takes 3 hours.

Mechanical and Functional Assessment

To characterize the mechanical features of the gelatin model, 3 nanoindentation tests were performed on 5-mm-thick brain model slices and compared with similar nanoindentation tests on sagittal slices of mammalian brains.[18] To quantify a possible mechanical degradability of the model, brain model slices were tested fresh and 3 months after fabrication. To characterize the functional features of the model, the deformable gelatin model was evaluated by 10 neurosurgeons and residents from King's College London, Oxford University, and Stanford University. Surgeons were asked to assess the model and its usefulness as a neurosurgical training and planning tool (**Figure 7**).

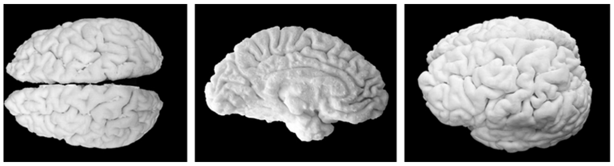

Figure 4. 3-Dimensional printed brain model. Axial view (*left*), sagittal view (*middle*), and lateral view (*right*) illustrate the realistic, personalized surface topology.

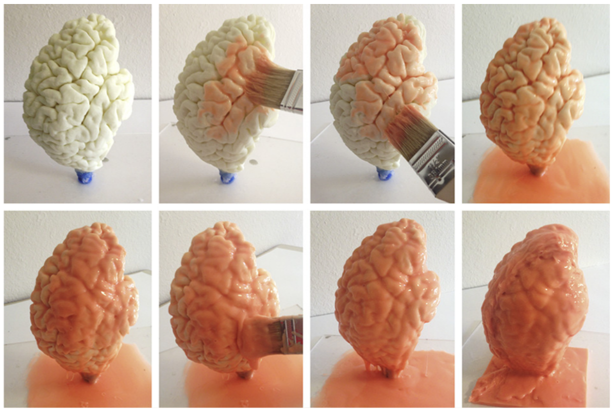

Figure 5. Silicone mold for gelatin model. Flexible brush-on molds were created on the 3-dimensional–printed model using a brushable silicone rubber along with a mother mold to maintain structural integrity while casting.

RESULTS

The proposed method successfully produced a physiologically, anatomically, and mechanically realistic personalized brain model. The model is based on magnetic resonance images, which were successfully converted into a printable stereolithography file using FreeSurfer. The FreeSurfer analysis revealed the specific brain dimensions with a volume of 1228.8 cm^3, a surface area of 1766.9 cm^2, an average cortical thickness of 0.263 cm, and left and right gyrification indices of 2.937 and 3.011. These anatomic features were accurately captured by the 3D-printed structure. The 3D-printed model was used as a template for molding and casting a tactilely realistic, deformable brain model. Created from soft gelatin, this model is durable, deformable, and orders of magnitude softer than its 3D-printed template.

Mechanical Testing

In nanoindentation tests, the gelatin model displayed conceptually similar characteristics as the mammalian brain: It behaved like an ultrasoft, viscoelastic polymer (**Figure 8**). With a stiffness of $E = 25.29 \pm 2.68$ kPa, brain model slices (right) were less than an order of magnitude stiffer than mammalian brain slices (left) with a stiffness of $E = 2.64 \pm 0.40$ kPa. The shape of the indentation curve of the surrogate material

Figure 6. Personalized tactilely realistic brain model. The silicone mold was cast with gelatin to create a personalized model with realistic physiological, anatomical, and mechanical properties. Axial view (*left*), sagittal view (*middle*), and lateral view (*right*).

Figure 7. Surgical evaluation. Neurosurgeons and residents evaluated the size, stiffness, cutting properties, haptic anatomy, surgical anatomy, and visual appearance of the model.

closely mimicked the rheology of mammalian brain tissue: Both curves displayed a straight loading curve, a drop in force at constant deformation characteristic of viscous relaxation, a slightly concave upward unloading curve, and a negative force towards the end of unloading characteristic of soft matter adhesion between the probe and the indenter tip. The mechanical properties of the brain model altered only moderately over time: With a stiffness of E = 27.64 ± 0.37 kPa (red curves), fresh model slices were slightly stiffer than 3-month-old model slices with a stiffness of E = 22.93 ± 1.08 kPa (blue curves) but otherwise displayed a similar rheological response.

Surgical Feedback

Feedback surveys from 10 neurosurgeons and residents revealed a general satisfaction with the model and a broad area of potential use (**Figure 9**). Surgical satisfaction with model stiffness (43.75%), cutting properties (43.75%), and haptic anatomy (56.25%) could still be improved, whereas surgical anatomy (81.25%), visual appearance (83.33%), and model size (100%) very perceived as very realistic. The model was perceived as very useful for patient illustration (85.00%), teaching (94.44%), learning (100.00%), surgical training (95.00%), and preoperative planning (95%). All surgeons responded that they would actively use the model for one or more of these purposes (100%).

The survey suggests that the model will be very useful when training and planning surgical procedures including but not limited to tumor removal (70%), aneurysm treatment (70%), Sylvian fissure dissection (20%), and electrode placement (10%). The model could be improved anatomically by including the vasculature (60%), ventricles (40%), individual tumors (30%), the Sylvian fissure (20%), brainstem (10%), arachnoid mater (10%), and the cerebrospinal fluid (10%). By the use of different colors for the different brain regions, the model could also be improved visually (20%). The overall feedback was very positive on the basis of the rationale that only a few surgical training and planning tools are currently available, and that none of these has tactilely realistic mechanical properties.

DISCUSSION

Effective surgical training and careful preoperative planning are significant to the success of any neurosurgical procedure. In this technical note, we explored the potential of current 3D printing technologies and created a personalized brain model to improve the surgical training experience and the preoperative planning process on an individualized patient-specific basis. Taken together, the material cost for a personalized brain model is $50, and the entire fabrication process takes 24 hours, of which 12 hours are fully automated.

Our model fabrication is straightforward, easy to reproduce, and time and cost efficient. It relies on a 3-step manufacturing process including 3D printing, molding, and casting. 3D printing, also known as additive manufacturing, uses 2D cross-sectional images to create 3D objects through computer-controlled layered deposition.[14] It is increasingly recognized as a powerful technology in the medical field,[13] where cross-sectional images are readily available from radiographs, computed tomography

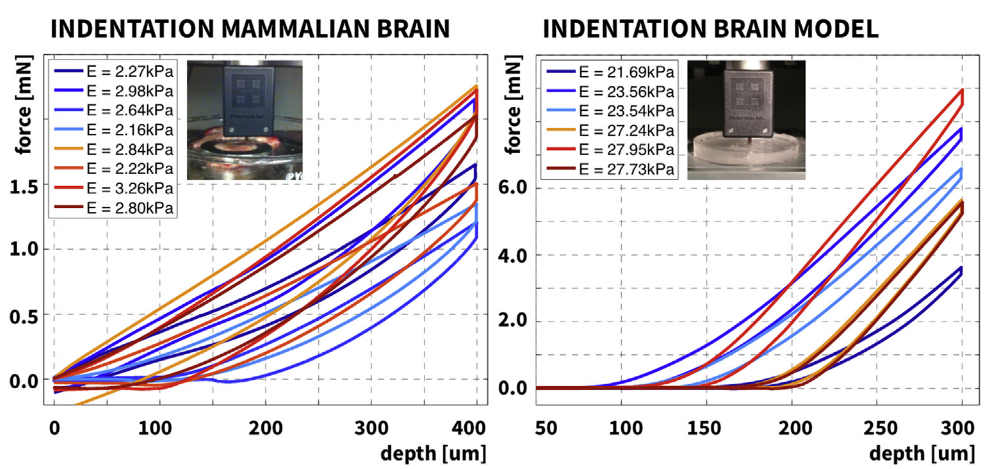

Figure 8. Mechanical testing. Similar to mammalian brain slices (*left*), brain model slices (*right*) behaved like an ultrasoft, viscoelastic polymer. With a mechanical stiffness of E = 25.29 ± 2.68 kPa, brain model slices were less than an order of magnitude stiffer than mammalian brain slices with a stiffness of E = 2.64 ± 0.40 kPa.

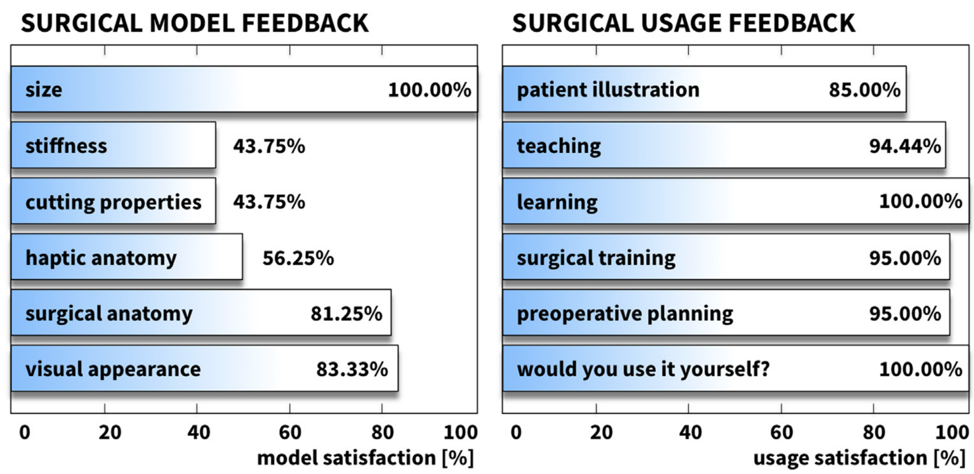

Figure 9. Surgical feedback. Neurosurgeons and residents were surveyed regarding the features of the brain model (*left*) and its usefulness for patient illustration, teaching, learning, surgical training, and preoperative planning (*right*).

scans, and magnetic resonance imaging.[24] With these images, patient-specific devices and anatomical models can be 3D-printed quickly, easily, and cost efficiently.

3D-printed models are gaining popularity rapidly in orthopedic surgery,[9] plastic surgery, and vascular surgery.[10] Although 3D printing seems to have an almost limitless potential in neurosurgery,[14] its current use remains mainly focused on neurovascular applications.[6,25] A major limiting factor is that the material properties of 3D-printed structures are far from those of the human brain: The material stiffness of ABS, one of the most frequently used thermoplastics in 3D printing, is 6 orders of magnitude larger than the stiffness of brain tissue.[22] Materials that can be used by current 3D printers are limited by virtue of the layered deposition process: They must be meltable, injectable, and stiff enough for the object to sustain its own weight as the material hardens. With current 3D printing technologies, is impossible to print structures with stiffnesses in the kilopascal range, especially in the dimensions of the human brain.[15]

In this technical note, we circumvented this limitation by using the 3D printed model as a template for molding and casting. As casting material, we have selected ballistic gelatin,[17] a widely used soft-tissue simulant for physical surrogates of the human body.[23] We characterized the mechanical properties of gelatin slices using nanoindentation and compared them with slices of the mammalian brain.[18] Gelatin was 5 orders of magnitude softer than ABS and less than an order of magnitude stiffer than mammalian brain tissue. The gelatin rheology was unaffected by age; fresh and 3-month-old samples displayed a same mechanical behavior and only moderate stiffness alterations. Although it would be desirable to further decrease the stiffness of the model, our current brain model is easily deformable under mechanical loading and already several orders of magnitude softer than any other anatomically realistic brain model.

A critical element of neurosurgical training is the understanding of neuroanatomy and the ability to safely and precisely navigate surgical instruments through restrictive corridors without causing collateral damage to the surrounding tissue.[3,26] Studying textbooks of neuroanatomy is an important first step in surgical training, but textbook images only provide 2D, static snapshots of the real 3D anatomy. Cadaver dissection provides useful insight into neuroanatomy, but lacks the haptic feedback and dynamic properties of real living tissue.[8] Live animal surgeries offer realistic dynamics, but the animal anatomy might differ significantly from the anatomy of the human brain.[3] With the advance of novel manufacturing technologies,[14] surgical models are progressively recognized as powerful, cost-efficient alternatives that allow errors without cadaver or animal involvement and procedure rehearsal without limitations of cycles.[27] Practicing procedures with personalized, deformable brain models with realistic physiological and anatomical features could help increase the confidence of the trainee.[5] Of course, surgical models should not be used as stand-alone tools: They lack the dynamics of living tissue, they do not mimic pulsing organs, they cannot capture effects of bleeding, and they provide no direct feedback to the user. As such, 3D anatomic brain models should be understood as complements to established surgical training tools and, ideally, be used in combination with critical feedback from experienced senior surgeons.

With this in mind, our brain model was thoroughly examined by 10 neurosurgeons and surgical residents from the United Kingdom and the United States. Their feedback was broadly positive: The stiffness and cutting properties were perceived as the least satisfactory features of the model; yet, model size, visual appearance, and surgical anatomy were perceived as very realistic. Surgeons and residents unanimously rated the model as very useful, and stated that they would actively use it themselves for learning, teaching, patient illustration, surgical training, and preoperative planning. They unanimously expressed the strong need for personalized brain models with anatomically, physiologically, and tactilely realistic properties.

The surgical survey identified aneurysm treatment, tumor removal, Sylvian fissure dissection, and electrode placement as procedures, which could benefit most closely from the proposed model. Future work will therefore focus on adding the cerebral vasculature,[25] the ventricles, the brainstem, and the meninges,[7] ideally printed in a different color and with a different material stiffness. Because gelatin is insoluble at room temperature,[17] it would also be straightforward to emerge the model in a liquid environment to mimic its interaction with the cerebrospinal fluid. This would open additional opportunities, for example, as a training tool for accurate external ventricular drain placement, a common neurosurgical procedure to drain cerebrospinal fluid,[28] for monitoring intracranial pressure,[15] or for brain retraction in craniotomy.[27] Another potential area of application is neurosurgical endoscopy, where 3D-printed models have recently been adopted as training tools in endoscopic third ventriculostomy.[11] To enhance the surgical training experience, it would be desirable to embed the brain model into a closed skull and surround it with a membrane to mimic the dura.

To individualize the model for patient-specific treatment planning in neuro-oncology, we could identify tumors from clinical images and personalize the model by adding tumors of different color and stiffness at their anatomically exact locations.[29] Even if the tissue properties cannot be reproduced exactly yet, model personalization with brain tumors and their surrounding structures could already help surgeons to explain the procedure to the patient and prepare for highly customized procedures on a case-by-case basis,[4] This is an area in which this technology has particular importance. Knowing the precise anatomy of a lesion, and overlying functioning brain, will enable a more specific surgical plan to be made, before the operation. This allows smaller, more precise approaches through the brain and minimizes potential injury to particularly eloquent regions. Currently, this is a technique that crucially relies on experience, and inexperienced surgeons of all grades frequently take a route to a lesion that is less than ideal. This model allows such a surgeon to plan the approach, identify potential issues, and discuss with a more experienced surgeon in the preoperative stage. It can be expected that this will lead to less morbidity to patients.

As 3D printing technologies continue to improve, the manufacturing process for surgical models will become faster, easier, cheaper, and more accurate.[12] We envision that the rapid advances in 3D printing will soon allow us to circumvent one of the 3manufacturing steps and print the silicone mold directly from medical images. Of course, the ultimate vision would be to directly print an anatomically, physiologically, and tactilely realistic surgical model. Although this goal seems feasible for many other organs including bone, the vasculature, or the heart, it seems currently out of reach for ultrasoft organs like the brain. Yet, in the meantime, 3D printing already allows us to create graspable, personalized models of a patient's own brain to educate patients, teach medical students, and train surgical residents.

CONCLUSIONS

3D printing enables the creation of personalized, deformable brain models with realistic physiological and anatomical features, which improve patient education, neurosurgical training, and preoperative planning.

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