Hindawi
Advances in Materials Science and Engineering
Volume 2022, Article ID 8015625, 13 pages
https://doi.org/10.1155/2022/8015625

Review Article

Application of Three-Dimensional (3D) Printing in Neurosurgery

Hao Li,[1] **Linyun Lu**,[1] **Ning Li**,[1] **Liu Zi**,[2] **and Qian Wen**[1]

[1]*Department of Integrated Traditional Chinese and Western Medicine, West China Hospital of Sichuan University, Chengdu, China*
[2]*Fujian Provincial Key Laboratory of Neurodegenerative Disease and Aging Research, Institute of Neuroscience, School of Medicine, Xiamen University, Xiamen, China*

Correspondence should be addressed to Qian Wen; wenqian@wchscu.cn

Received 26 November 2021; Accepted 19 September 2022; Published 27 September 2022

Academic Editor: Sezgin Ersoy

Copyright © 2022 Hao Li et al. This is an open access article distributed under the Creative Commons Attribution License, which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Three-dimensional (3D) printing has been increasingly used in various fields of medicine, such as in auxiliary diagnosis and treatment, medical teaching, and regenerative medicine. Most operations performed by neurosurgeons and associated pathological examinations involve complex, microscopic anatomical structures that cannot be observed outside. 3D-printed models can reproduce anatomical structures, pathological tissues, and cells with high accuracy, enhancing our understanding of complex aspects of anatomy and pathology. They can also assist in preoperative planning and simulation, help in surgical or interventional surgery precision medicine, and improve the effectiveness of treatments. This review comprehensively summarizes and discusses its current application progress and problems, including treatments for common diseases (e.g., intracranial tumors, intracranial hemorrhage, intracranial aneurysms, skull repair, and neural prosthetics), clinical training, and preoperative plans. With its widespread applications, 3D printing as an innovative tool will provide new directions for developing imaging, strategies, and interventions in neurosurgical diseases.

1. Introduction

American scientist Chuck Hull first proposed the concept of 3D printing in 1983. 3D printing, also known as additive manufacturing (AM), refers to transforming digital information into physical models [1]. In this process, 3D objects are generated via depositing material in successive layers based on geometric structure parameters collected by computer-aided design (CAD) software or 3D scanners [2]. 3D printing is a fast and relatively economical way to transform a conceptual prototype based on data into a final usable product without the use of expensive molds or tools and can help achieve greater flexibility for creating complex shapes than is possible with the use of traditional manufacturing techniques [3]. This technology has many advantages, including a simple operation method, customizable design, high reliability, high cost-effectiveness, and diversity of compatible materials [4, 5]. In the past 30 years, 3D printing has developed rapidly and has shown considerable advantages in the fields of energy [6, 7], aerospace science and technology [8, 9], and machinery manufacturing [10, 11]. 3D printing technology can freely produce various complex 3D biological structures, such as multilayer tubular structures [12], microfibrous structures [13], cellular structures [14], and internal and external anatomical structures [15, 16]. With the development and progress of materials science, medical imaging, and tissue engineering, 3D printing technology has gradually come to be applied in the medical field, including for auxiliary diagnosis and treatment, medical teaching, and regenerative medicine research [17].

Most surgical operations and related pathological examinations carried out by neurosurgeons involve complex and microscopic anatomical structures, such as the brain, blood vessels, intracranial nerves, the skull, and other structural relationships that cannot be observed externally [18]. The success of surgery largely depends on the neurosurgeon's understanding of the anatomical structure. Advances in imaging technology [19], such as multidetector computed tomography (MDCT), magnetic resonance

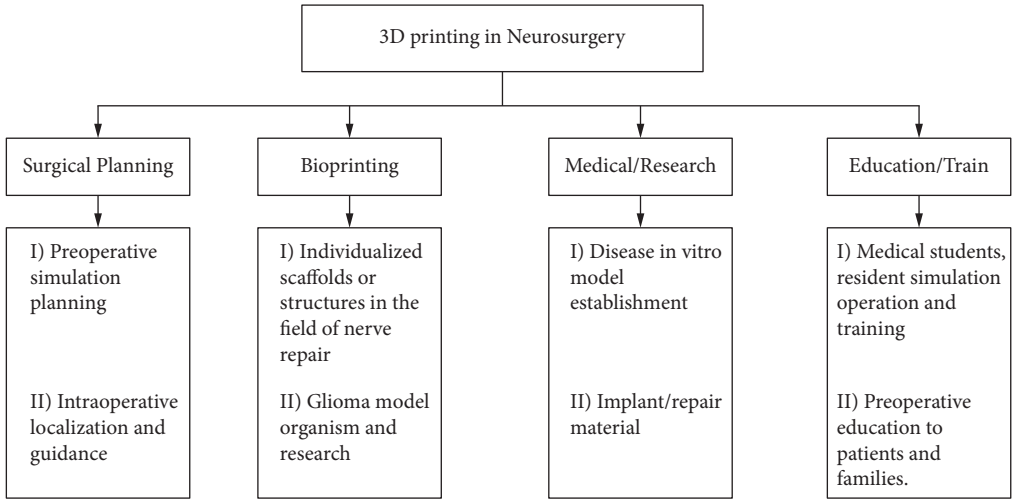


Figure 1: Flowchart of 3D printing applications in neurosurgery.

imaging (MRI), X-rays, and computed tomography (CT), have enabled us to obtain high-resolution two-dimensional images. However, it is difficult to describe complex 3D structures accurately based on the limited 2D data gained through the above tools. 3D printing provides a practical solution to the rules of virtual two-dimensional image analysis [20]. Through 3D printing, anatomical structures can be reconstructed. Then physical models can be created to prepare various surgical models, tumor models, vascular models, neural prostheses, and skull repair materials required by neurosurgeons for clinical practice and surgical simulation training [21–24].

This review aims to provide an overview of 3D-printed models in medical applications, focusing on their value in neurosurgery and highlighting future research directions. Figure 1 shows an abstract of the application of 3D printing in neurosurgery.

2. Overview of 3D Printing

3D printing can be described as an additive manufacturing process by which freeform 3D structures can be formed layer by layer from 3D computer models. Constructing physical 3D models from anatomical imaging data (MRI/CT) takes place in three steps: (1) image acquisition, (2) image data processing, and (3) 3D printing.

The accuracy and repeatability of 3D-printed models depend on the reliability of the images obtained. This can be affected by imaging, tissue segmentation, and any subsequent processing of segmented tissue stored in the STereoLithography (STL) model using computer-aided design software [25]. Additionally, the accuracy of the models produced and processed by different 3D printers can also improve when using the same STL model. A comparative study found that dental tool models could be printed using two printer technologies: continuous-liquid interface production (CLIP) and digital light processing (DLP) printers. Whether the base of the print model is solid or hollow, the CLIP technology printer used to generate the model is closer to that used in reference [26].

Rapid prototyping is a common method used for converting computational data into 3D solid models [27]. Rapid prototyping is a 3D model manufacturing method that uses CT or MRI data sets to create virtual 3D surface models. The virtual model is first decomposed into thin layers. A rapid prototyping machine then builds a solid model layer by layer to produce a complete solid model. In biomedicine, 3D printing techniques such as fused deposition modeling [28], stereolithography [29], polyjet processing [30], selective laser sintering [31], 3D inkjet printing [32], and digital light processing [33] are the most common processes used. The printing method applied for the final physical model may depend on the clinical purposes and requirements, the availability of 3D printers, the printing materials used, and the associated costs. Table 1 summarizes the bioprinting process, comparing different types of bioprinting processes, printing materials, and other features.

3. Applications of 3D Printing in the Neurosurgical Clinic

3D printing has shown excellent prospects for many medical applications. It is widely used and can be varied according to application requirements in terms of the lesion type, location, severity, etc. In neurosurgery, 3D-printed models are mainly applied to guide surgical procedures, including preoperative simulation or planning, intraoperative guidance and positioning [35–37]. 3D bioprinting can also be employed to improve the understanding of tumor biology and investigate new therapeutic approaches [38–41]. It can also apply to the research and application of new nerve and skull repair materials [42–45]. 3D-printed models are also used for simulation training to increase learning and practice opportunities, improve doctor–patient communication, increase the confidence of neurosurgeons in performing complex surgical procedures, and improve surgical skills [46, 47].

Table 1: Characteristics of 3D bioprinting processes.

Types of bioprinters	Biomaterials	Cell viability/ resolution	Bioprinting speed	Cost	Advantages	Disadvantages
Inkjet-based bioprinting	Low-viscosity suspension of living cells; biomolecules; growth factors	~90% 20–100 μm	Fast (<10,000 droplets/s)	Low	Wide availability; low cost; high resolution; high printing speed; ability to introduce concentration gradients in 3D constructs	Poor vertical structure clogging characteristics; thermal and mechanical stress to cells; limited printable materials (liquid only)
Pressure-assisted bioprinting	Hydrogel; melt; cells; proteins and ceramic materials; solutions, pastes, or dispersions of low to high viscosity; poly lactic-co-glycolic acid (PLGA); tricalcium phosphate (TCP); collagen and chitosan; collagen alginate-silica composites coated with HA; and agarose with gelatin	40–80% 200 μm	Slow	Medium	Numerous materials that can be printed with any dimensions; mild conditions (room temperature); use of cellular spheroids; direct incorporation of cells; and homogenous distribution of cells	Limited mechanical stiffness; critical timing of gelation time; specific matching of the densities of the material and the liquid medium to preserve shapes; low resolution and viability
Laser-assisted bioprinting	Hydrogel, media, cells, proteins and ceramic materials of varying viscosity	>95% >20 μm	Medium	High	Nozzle-free, noncontact process; cells are printed with high activity and high resolution; high control of ink droplets and precise delivery	High cost; cumbersome and time consuming; requires a metal film and thus is subject to metallic particle contamination
Stereolithography	Light-sensitive polymer materials; curable acrylics and epoxies	>90% ~1.2–200 μm	Fast (<40,000 mm/s)	Low	Solid freeform and nozzle-free technology; highest fabrication accuracy; compatibility with an increasing number of materials; light-sensitive hydrogels can be printed layer by layer	Applicable to photopolymers only; lack of biocompatible and biodegradable polymers; harmful effects from residual toxic photo-curing reagents; possibility of harm to DNA and human skin by ultraviolet (UV)

Reprinted with permission under open access by Li et al. [34].

3.1. Intracranial Space-Occupying Lesions. Due to the complex structure of the human brain, the location of intracranial space-occupying lesions is closely related to brain nerves and the cerebrovascular system. Therefore, the surgical treatment of intracranial space-occupying lesions is complex and requires accurate preoperative and surgical trajectory planning. Before the surgical treatment of complex intracranial space-occupying lesions can take place, 3D printing can be used to accurately print a model of the intracranial tumor and the blood vessels and nerves around the cancer according to the imaging data. The scope of the resectioning needed can be accurately determined during surgery to reduce the damage to the blood vessels and nerves, improve the accuracy and safety of the surgical treatment, and promote the recovery of postoperative patients [48]. Materials of different colors can also be used to mark the skull, blood vessels, nerves, tumors, and other structures to help ensure the better protection of nerve and blood vessel tissues and the adequate exposure and removal of tumors [49]. Huang et al. [50] used 3D printing technology to assist an endoscopic transnasal approach for the treatment of large adenoma, which reduced vascular and nerve damage, shortened surgical time, and significantly decreased blood loss compared with traditional surgery. The incidence of postoperative complications was relatively low (Figure 2).

Glioma is one of the most common intracranial placeholders, accounting for 81% of all malignant brain tumors [51]. As one of the most common histological gliomas, glioblastoma accounts for about 45% of all gliomas, and the 5-year survival rate is about 5% [52]. Gliomas destroy cortical and subcortical structures with invasive progression [24]. Specific structures surrounding the deep tumor, such as fibers, perforators, and ventricles, need

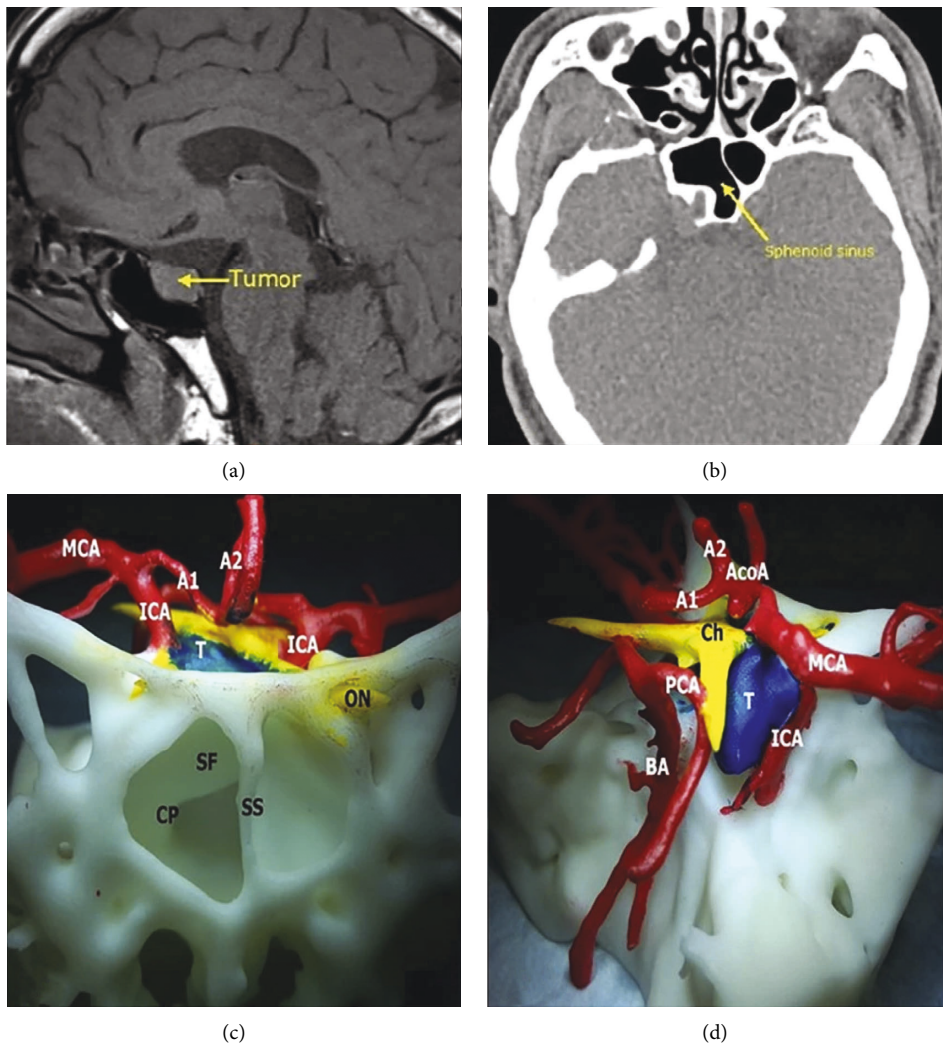


Figure 2: (a) MRI of the sella turcica region showing tumor lesions. The yellow arrow points to the tumor. (b) CT of the sphenoidal sinus. The yellow arrow points to the sphenoidal sinus. (c, d) Frontal and lateral views. SF, sellar floor; SS, sphenoid septation; CP, carotid protuberance; A1, A1 segment of the anterior cerebral artery; BA, basilar artery; PCA, posterior cerebral artery; A2, A2 segment of the anterior cerebral artery; Ch, chiasm; T, tumor; ON, optic nerve; AcoA, anterior communicating artery; MCA, middle cerebral artery; reprinted with permission under open access from Huang et al. [50].

special attention during tumor resection in patients with glioma. 3D printing can intuitively reflect the spatial relationship between the tumor and the adjacent white matter region [53]. The glioma stem cell model can also be printed by 3D bioprinting technology for long-term in vitro culture to simulate the brain tumor microenvironment. The model can not only express its biomarkers but also reveal its potential function when needed. In addition, 3D bioprinted brain tumor models are more resistant to chemotherapy drugs than 2D models. This indicates that 3D bioprinted brain tumor models are of great help to glioma stem cell biology and the study of susceptibility to antitumor drugs [40]. Heinrich et al. [51] used 3D bioprinting technology to print a miniature brain composed of glioblastocytes and macrophages to explore the interaction between the two cell types and the treatment methods needed for such interaction. The strategy proposed by the authors is based on a two-step bioprinting process. In the first step, a smaller brain model of a mouse macrophage line containing a cavity is printed. The second step is to fill the mouse glioblastoma cells embedded with biological ink as well as photocrosslinked constructs. Bricks made from a mixture of 3% W/V gelatin methylacryl and 4% W/V gelatin are then printed at the optimum concentration. In this way, 3D bioprinted miniature brains can be created with two cell types, demonstrating that the inhibition of the interaction between macrophages and tumor cells leads to reduced tumor growth and a greater sensitivity to chemotherapy. This 3D bioprinted tumor model is used to improve the understanding of tumor biology and evaluate new cancer therapies.

3.2. Intracranial Vascular Disease. Intracranial vascular-related surgery is a risky and challenging operation in neurosurgery, with a high disability rate and mortality.

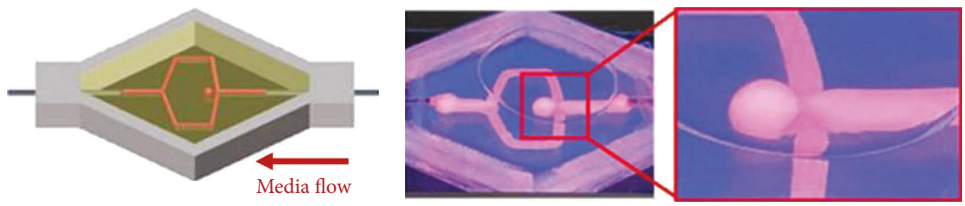
Intracranial blood vessels have highly complex courses. Many branches of basilar arteries and variable traffic branches require doctors to analyze the imaging data thoroughly and have a solid spatial imagination and anatomical foundation [54].

Intracerebral hemorrhage (ICH) is an acute and severe neurosurgical disease. It is a widespread neurosurgical disease with poor prognosis and outcomes. Hematoma is usually located in the brain parenchyma—for example, near the basal ganglia [55]. In recent years, the use of endoscopic surgery for hematoma evacuation has gradually replaced craniotomy to minimize brain injury [56]. In endoscopic surgery for basal ganglia hemorrhage, the use of 3D-printed head and face model guidance can enable surgeons to safely achieve a higher resection rate than is possible using traditional digital imaging data. This new method is suitable for treating basal ganglia bleeding, which is usually elongated and oval in shape. Path assistance by 3D printing has the advantages of only leading to minor trauma and sound effects. Postoperative imaging results have shown a significant reduction in hematoma volume without recurrent bleeding [57].

The brain stem has long been considered a no-go area in neurosurgery. Despite advances being made in microsurgical techniques, craniotomy can be used to remove the brain stem hematoma. However, the success rate is low, and patients with unstable vital signs cannot tolerate this type of surgery. Craniotomy hematoma removal and puncture drainage are the primary surgical treatment used for brain stem bleeding [58, 59]. Therefore, hematoma puncture and drainage have been increasingly applied for the surgical treatment of intracerebral bleeding due to its minimally invasive nature, low cost, and short operation time [60], especially for patients experiencing severe brainstem hemorrhage. However, the main factors limiting the puncture drainage of brainstem hematoma are localization and navigation problems. These technical problems can be solved using stereotactic technology. This technique is less invasive and takes less time to complete but requires expensive equipment, limiting its use in primary hospitals. Therefore, a puncture positioning tool with a low cost and high precision is needed. However, 3D printing technology can construct navigation models to achieve the personalized and precise puncture and drainage of brainstem hematoma [61]. The purpose of 3D printing navigation mold technology is to improve the precision of puncture positioning and reduce the operation time and cost compared to that of unguided puncture and drainage. The accuracy of this technique is slightly lower than that of the stereotactic course. However, stereotactic equipment is expensive and requires a fixed head frame. As a result, it is risky for severely ill patients to undergo surgery and they will require general anesthesia. In contrast, 3D-printing puncture techniques are inexpensive and do not require a fixed headrest, thereby reducing pain and allowing surgery to be performed under local anesthesia [62].

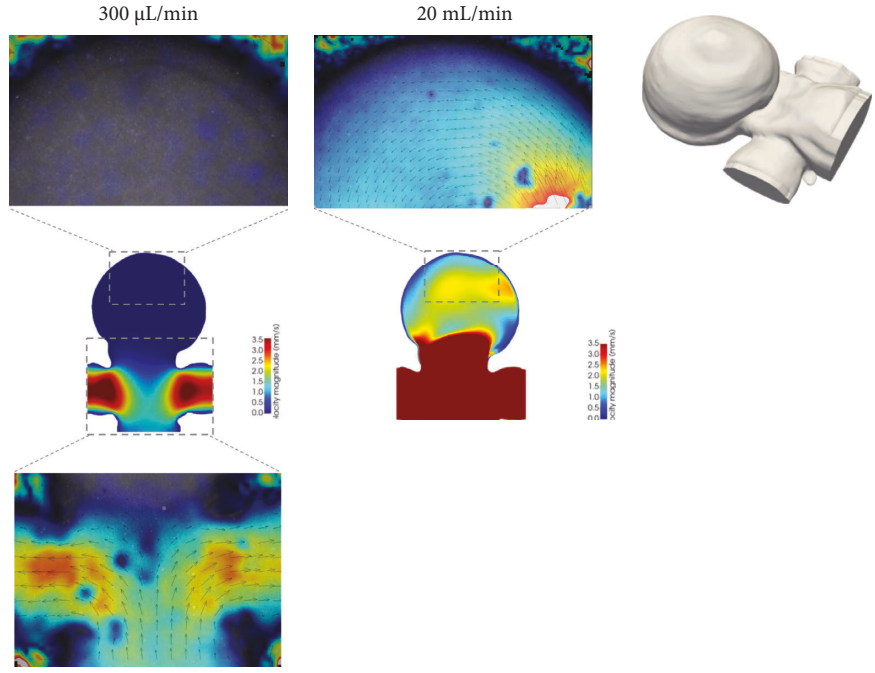
The prevalence of saccular unruptured intracranial aneurysms (UIAs) in the adult population was recorded as 3%, but due to the increase in intracranial imaging quality and inspection frequency they are being found more and more often [63]. Aneurysm location and previous history show that the risk of rupture within five years is 0–50% [64]. At present, the surgical treatments for ruptured intracranial aneurysms can be roughly divided into craniotomy aneurysm clipping and endovascular embolization [65]. 3D-printed model technology has certain advantages in neurovascular and endovascular surgery [66]. Multimode image reconstruction was carried out using 3D printing technology to fabricate a 3D hollow aneurysm model and perform clipping to simulate surgical operation. Many simulated operations were performed under a microscope to gain a more complete understanding of the spatial location of the aneurysm and the adjacent blood vessels and nerves. The surgical injury was significantly reduced in subsequent operations and the operation time was shortened [67]. Color paint can also be used to 3D print aneurysm models to create realistic hemodynamic models or provide the advanced visualization of these vascular lesions [68]. Similarly, 3D printing can assist microcatheter plasticity in performing aneurysm embolization for patients. In this way, intracranial aneurysm embolization is more safe, stable, and effective [69]. Jang [70] et al. carried out the 3D printing of the vascularized tissue structure of aneurysms using gelatin-fibrin hydrogel (Figure 3). In vitro devices can directly measure flow through a particle image velocimeter, thus allowing the direct assessment of vascular flow dynamics through comparison with the 3D computational fluid dynamics model (Figure 4). This in vitro aneurysm model is a promising method for testing the biocompatibility and hemostatic efficiency of embolization devices. Moreover, it can provide hemodynamic information and help to predict aneurysm ruptures.

3.3. Cranioplasty. Clinically, patients with high intracranial pressure and cerebral hernia due to intracerebral hemorrhage, brain trauma, large-scale cerebral infarction, and other diseases often need decompression with bone flap removal, resulting in postoperative local skull loss [71]. Skull defects can usually be repaired with autologous bone or allogeneic bone. However, the size and shape of skull loss in each patient can differ, leading to great difficulties and challenges occurring in skull repair. 3D printing technology can be based on the patient's CT and other imaging data and be carried out according to the patient's specific situation to prepare skull repair materials. The repair material used is generally a biocompatible material, such as polymethyl methacrylate (PMMA) or knitted polypropylene polyester [72–75] (Figures 5 and 6). The 3D modeling technique has several advantages: it can help to develop a specific understanding of bone morphology, accurately and directly plan the preoperative bending of the plate, and improve the accuracy of bone acquisition by using negative imprints of the space that needs to be reconstructed. The use of 3D printing technology to prepare new molds for cranioplasty can significantly lower medical costs without affecting the prognosis of patients [77, 78]. In addition, 3D printing is used to customize heat-cured PMMA, an economical and time-saving solution comparable to patient-specific titanium or PEEK prosthetics [79].



(a) (b)

Figure 3: Flowchart showing 3D printing applications in neurosurgery and the in vitro living cerebral aneurysm. (a) Illustration of the 3D-printed aneurysm bioreactor. (b) The in vitro aneurysm vessel structure perfused with red fluorescent beads, demonstrating the formation of the patent vessel postevacuation of sacrificial ink; reprinted with permission under open access by Jang et al. [70].



(a) (b) (c)

Figure 4: Particle image velocimetry (PIV) analysis and 3D computational flow model simulations. (a) (Above) PIV measurement at the back of the aneurysm dome showing no detectable flow at a 300-μl min^{-1} flow rate. (Middle) A 3D flow simulation of the same geometry and flow rate at $z = -0.66$ mm. (Below) PIV measurements within the parent and daughter vessels captured with a 2 × objective at the same flow rate. (b) (Above) PIV measurement gathered at the back of the aneurysm dome showing circular flow patterns and captured with a 4 × objective at a 20-ml min^{-1} flow rate. (Below) Simulation of the same geometry and flow rate demonstrating that fluid motion only occurs within the dome at high flow rates. (c) High-fidelity geometric reconstruction of the printed living aneurysm constructed from image stacks gathered via confocal microscopy; reprinted with permission under open access by Jang et al. [70].

3.4. Neural Prosthetics. Peripheral nerve injury is a widespread nervous system disease. It is usually caused by trauma, surgical injuries, sports injuries, accidents, and violence [80, 81]. It seriously affects the quality of daily life, such as sensory and motor dysfunction, nerve palsy pain, and muscle atrophy [82]. The ability of peripheral nerves to repair themselves depends on the patient's age and the mechanism of injury. When the peripheral nerve ruptures, the two distal extremities retract apart, and lose the nutritional supply to the neuron's cell body, causing synapses and myelin sheaths to degenerate and eventually disappear altogether. At present, the clinical treatment for nerve fracture less than 1 cm is fine surgical suture through tension-free neural tube suture, which helps promote axis regeneration and restore nerve function [83]. However, if the length exceeds 5 mm, suture repair cannot be performed. In such cases, autologous nerve transplantation is the most commonly used method. But this method requires the transplantation of healthy nerves, which can damage the donor site and may lead to the formation of neuroma [84]. With the development of 3D printing technology, multiple bioprinted catheters for peripheral nerves become an available approach to promote the healing of broken nerves. A study using cell-free artificial implants of electrospun fibers for sciatic nerve injury showed a significant increase in functional nerve recovery when the 3D collagen tubes were filled

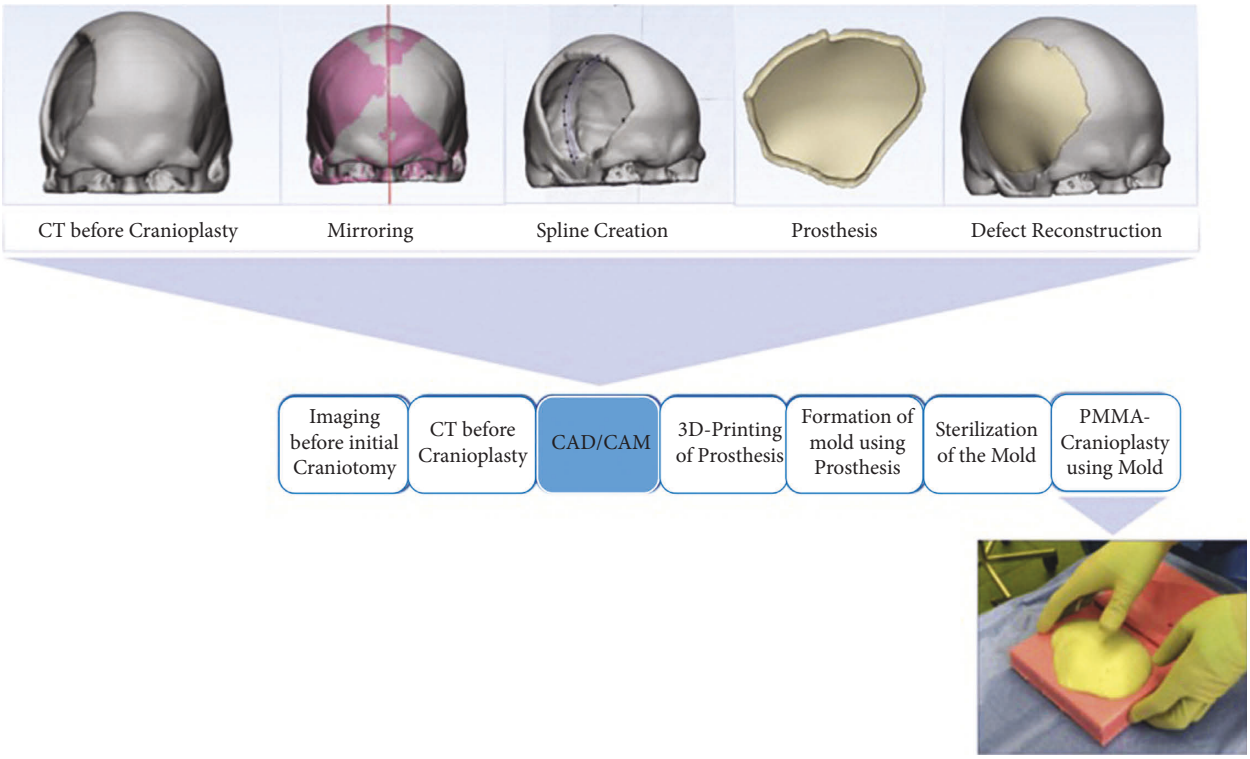


Figure 5: Workflow of the production of implantable patient-specific PMMA implants. The upper row shows the CAD/CAM (computer-assisted design/computer-assisted manufacturing) of the prosthesis that is printed out using a 3D printer. The prosthesis is then used to form the heat-resistant silicone mold, which is sterilized and intraoperatively used to form the patient-specific PMMA implant. 3D, three-dimensional; CT, computed tomography; PMMA, polymethyl methacrylate; reprinted with permission under open access by Schön et al. [76].

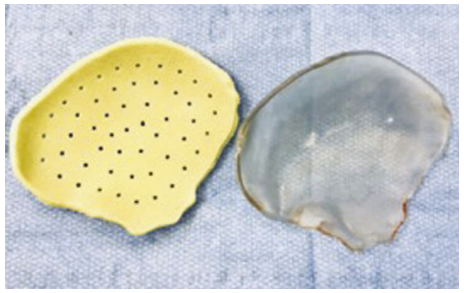


Figure 6: (Left) Ready-to-implant sterile PMMA implant after removal from the silicone mold. (Right) Biocompatible and sterilized 3D-printed template (Med610) used to reconstruct the patient's bone defect; reprinted with permission by Schön et al. [76].

with biodegradable poly-ε-caprolactone (PCL) and/PCL (c/PCL) blends containing collagen [85]. It is also possible to print catheters that contain neurotrophic or other factors. They construct the directionally aligned chitosan nanofiber hydrogel grafted with RGI/KLT peptide mixture (ACG-RGI/KLT). ACG-RGI/KLT targets Schwann cells and promotes their proliferation and secretion of neurotrophic factors (Figure 7). In the early stage of injury, ACG-RGI/KLT promotes nerve regeneration and vascular penetration. After 12 weeks, ACG-RGI/KLT promotes nerve regeneration and functional recovery in rats [86].

3.5. Clinical Training and Preoperative Planning. The brain is the most complex and precise organ in the human body. Its internal lesions are diverse and complicated, causing great difficulties and challenges in the clinical treatment of neurosurgery. Surgical training is traditionally conducted through the apprenticeship model, in which trainees perform operations in surgical theatres under the supervision of experts. Still, neurosurgery remains complex and risky [87], meaning there are few opportunities for young surgeons to practice [88]. Therefore, establishing a mature and effective simulation training system will be conducive to improving the success rate of surgery and reducing surgical injuries [89]. At present, animal models, cadaver specimens, and simulators account for most of surgeons' training. Still, cadaver specimens without blood flow and animal models that have significant differences in anatomical structure cannot provide a natural operation simulation environment [90]. At present, 3D printing technology is widely used in clinical training and is able to overcome the above shortcomings [91–93].

3D printing offers a unique method of replication for patients with specific pathological structures. It can identify anatomical variations and quickly generate trainable 3D models for trainees and experienced neurosurgeons, allowing them to perform preoperative simulate surgery [94, 95]. Computed tomography (CT) and magnetic resonance imaging (MRI) image data can be transformed into

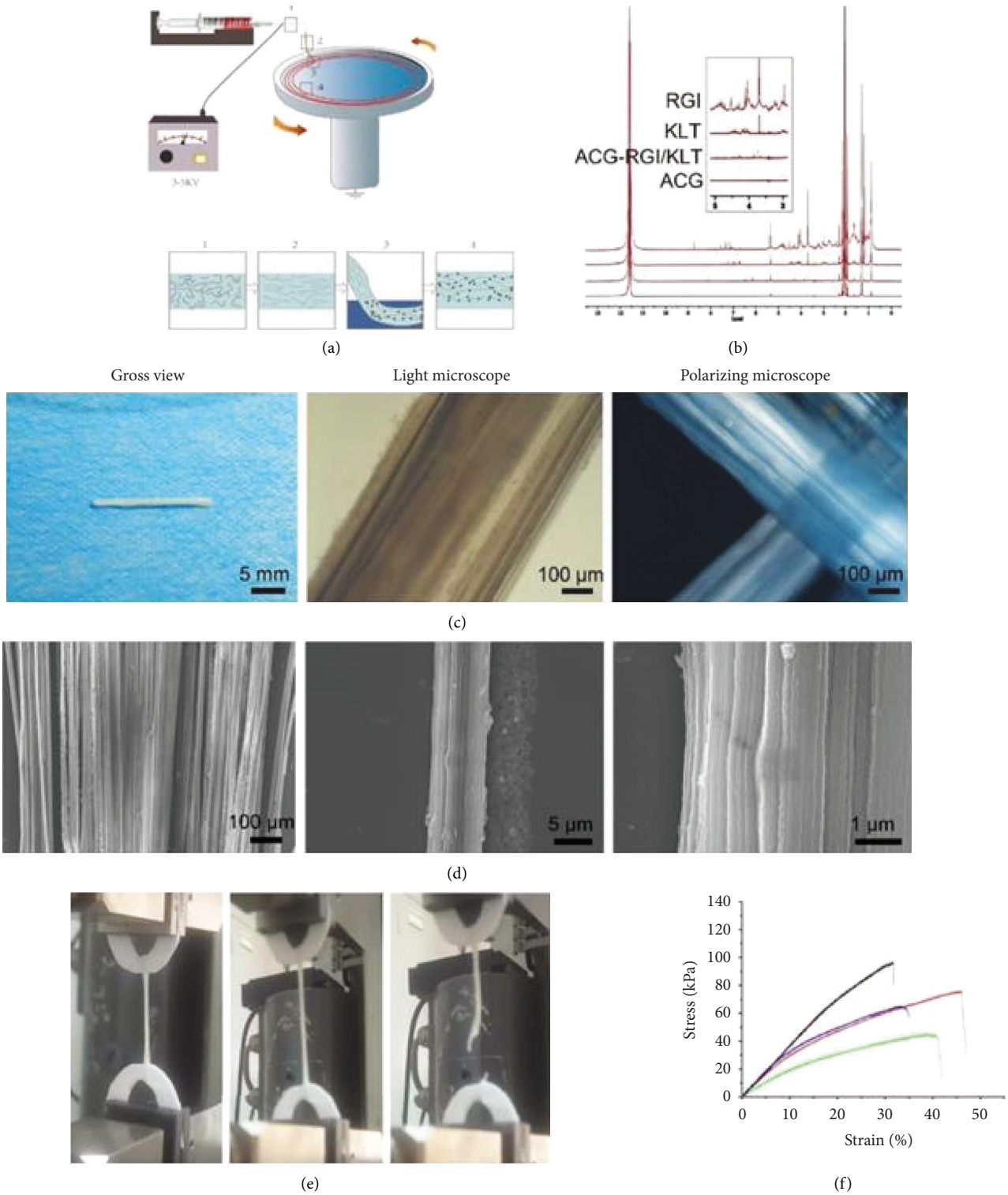


Figure 7: Preparation and characteristics of aligned chitosan fiber hydrogel. (a) Illustration of the electrospinning and mechanical stretching setup. A voltage of 3–5 kV was applied between the spinning solution and collector. Chitosan polymer chains became increasingly aligned as the chitosan hydrogel was extruded from the needle (box 1) and stretched during entry (box 2) into a rotating bath. As the chitosan hydrogel entered the rotating bath (box 3) containing sodium tripolyphosphate (STPP; black dots) under mechanical stretching, chitosan chains were further aligned and crosslinked by STPP in the bath (box 4), thus forming a stable chitosan nanofiber hydrogel. (b) Proton nuclear magnetic resonance (NMR) spectroscopy of RGI and KLT. (c) Gross view and light microscopic images of an aligned chitosan hydrogel bundle. Polarized light microscopic images show optical extinction in the crossover region of two chitosan fiber bundles. (d) Scanning electron microscopy (SEM) images of aligned chitosan fiber hydrogel (ACG) showing hierarchically aligned structures under different magnifications. (e) Test of the mechanical properties of aligned chitosan hydrogels. (f) Elastic modulus of aligned chitosan hydrogels; reprinted with permission under open access by Rao et al. [79].

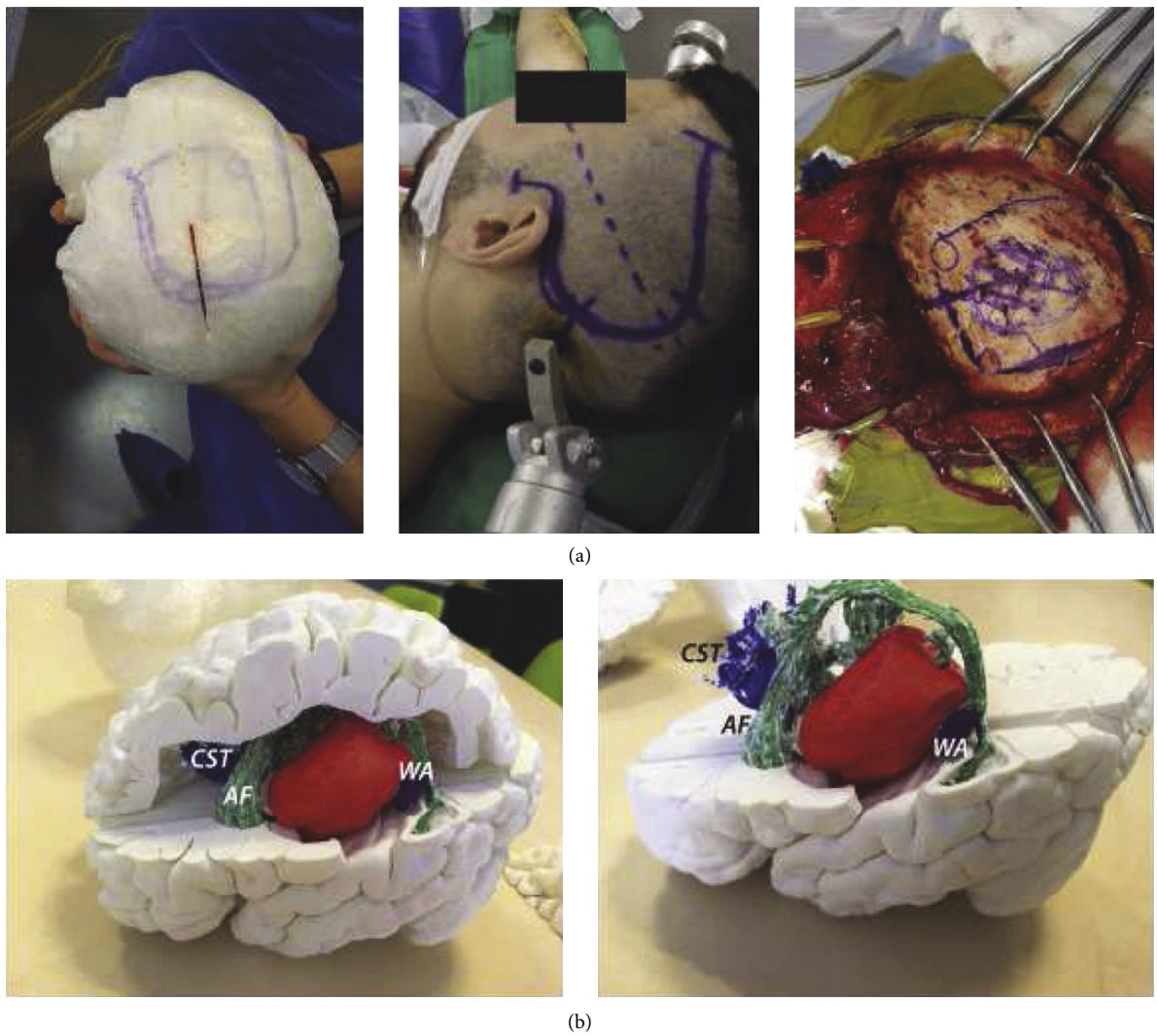


Figure 8: Three-dimensional (3D)-printed model. (a) The printed model of the skull was employed to plan the surgical approach for this patient. (b) 3D-printed model of the intracranial structures of interest: glioma (in red), the corticospinal tract (CST) (in blue), the arcuate fasciculus (AF) (in green), and Wernicke volume of activation (WA) (in purple); reproduced with permission by Gomez-Feria et al. [53] (copyright 2020, Elsevier Ltd.).

3D printing information and printed out in a structural model of the skull that is as close to the human body as possible. The ventricle and the lesions in the ventricle system can also be reconstructed and printed in 3D, providing an ideal model for endoscopic intraventricular operation training [46, 96–98]. Zhu et al. [99] used 3D printing technology to make skull models and simulated endoscopy and the endoscopic removal of intracerebral hematoma (ICH) with tubular retractors. With the increase in training times, operation proficiency and assessment scores have been significantly improved. Gomez-feria et al. [53] reported a case of a 42-year-old woman who was a bilingual Spanish and English teacher with aphasia that affected both languages simultaneously. MRI showed a large lesion in the right temoral insula, suggesting the presence of low-grade astrocytoma. Neurosurgical planning using fMRI language mapping identified two functional areas in the right hemisphere's frontal lobe and temporal cortex in both languages, located 8.8 mm and 2.2 mm from the glioma, respectively. A DTI study revealed the partial invasion of the right inferior longitudinal tract (Figure 8). Awake craniotomy was recommended, but the patient was reluctant to undergo this treatment. As a result, she was placed under general anesthesia and did not undergo cortical mapping during the surgery. Neurosurgeons used 3D-printed models to perform adequate preoperative simulations to complete the surgery. The patient recovered well after the surgery without her use of language and other functions being affected.

4. Conclusion and Future Perspectives

The use of 3D printing technology is a new and promising development in the field of neurosurgery. The application of 3D printing technology has shown promising prospects in neurosurgery. However, the use of 3D printing in clinical

practice still has some limitations. Firstly, the resolution and accuracy of CT, MRI, and other types of images have somewhat hindered the development of 3D printing technologies. Compared to other techniques such as MRI, multislice spiral CT can provide high-contrast images. However, patients will also be exposed to ionizing radiation. Therefore, inventing or finding an imaging method that can reduce radiation exposure and improve image resolution would be of great value. Secondly, the high cost of this technology is another issue that needs to be addressed before 3D printing can be incorporated into routine clinical practice. It is believed that 3D printing will become a technology that will be acceptable to both patients and clinicians as the cost of 3D printers and printing materials decreases [100]. Thirdly, despite the high accuracy and quality of 3D-printed models, most are static at present. Even when polychromatic materials are used, they do not fully represent the actual characteristics of normal tissue. Although 3D printing technology has made significant progress, the use of 3D printing to create soft tissue structures still needs to be further explored. Few attempts have been made to capture the mechanical properties of soft tissue and high-resolution anatomical details. In addition, in the field of neurosurgery, a combination of hard and soft materials must be used to simulate the skull and underlying brain tissue accurately. This combination approach could be helpful in other areas of surgery as well. The wetting properties of hydrogels can increase the realism of the feel of biological tissue in printed models, making them excellent for use in soft-tissue surgery simulations. Although 3D-printed hydrogel materials are widely used in tissue engineering at present [101, 102], these technologies have not yet been applied to the manufacture of surgical simulation anatomical models. Surgeons may also encounter conditions such as bleeding during surgery that cannot be simulated by models made from ordinary materials. With the development of 3D printing technology and materials, the next generation of surgical simulations will be more realistic, significantly improving surgical training and preoperative planning and thus increasing surgical success rates.

Conflicts of Interest

The authors declare no conflicts of interest.

Authors' Contributions

HL and LL equally contributed to this work. HL wrote the paper and LL revised the style. NL and ZL supervised the paper structure and revised the contents. QW provided the conception of the manuscript. All authors contributed to the article and approved the submitted version. Hao Li and Linyun Lu are contributed equally to this work and share first authorship.

References

[1] S. M. Peltola, F. P. W. Melchels, D. W. Grijpma, and M. Kellomaki, "A review of rapid prototyping techniques for tissue engineering purposes," *Annals of Medicine*, vol. 40, no. 4, pp. 268–280, 2008.

[2] B. Berman, "3-D printing: the new industrial revolution," *Business Horizons*, vol. 55, no. 2, pp. 155–162, 2012.

[3] Q. Yan, H. Dong, J. Su et al., "A review of 3D printing technology for medical applications," *Engineering*, vol. 4, no. 5, pp. 729–742, 2018.

[4] S. Derakhshanfar, R. Mbeleck, K. Xu, X. Zhang, W. Zhong, and M. Xing, "3D bioprinting for biomedical devices and tissue engineering: a review of recent trends and advances," *Bioactive Materials*, vol. 3, no. 2, pp. 144–156, 2018.

[5] J. Jang, J. Y. Park, G. Gao, and D. W. Cho, "Biomaterials-based 3D cell printing for next-generation therapeutics and diagnostics," *Biomaterials*, vol. 156, pp. 88–106, 2018.

[6] K. Fu, Y. Yao, J. Dai, and L. Hu, "Progress in 3D printing of carbon materials for energy-related applications," *Adv Mater*, vol. 29, no. 9, Article ID 1603486, 2017.

[7] V. Egorov, U. Gulzar, Y. Zhang, S. Breen, and C. O'Dwyer, "Evolution of 3D printing methods and materials for electrochemical energy storage," *Adv Mater*, vol. 32, no. 29, Article ID e2000556, 2020.

[8] J. E. Snyder, D. Walsh, P. A. Carr, and L. J. Rothschild, "A makerspace for life support systems in space," *Trends in Biotechnology*, vol. 37, no. 11, pp. 1164–1174, 2019.

[9] N. Cubo-Mateo, S. Podhajsky, D. Knickmann, K. Slenzka, T. Ghidini, and M. Gelinsky, "Can 3D bioprinting be a key for exploratory missions and human settlements on the Moon and Mars?" *Biofabrication*, vol. 12, no. 4, Article ID 043001, 2020.

[10] M. Mahmoudi, S. R. Burlison, S. Moreno, and M. Minary-Jolandan, "Additive-free and support-free 3D printing of thermosetting polymers with isotropic mechanical properties," *ACS Appl Mater Interfaces*, vol. 13, no. 4, pp. 5529–5538, 2021.

[11] B. Elder, R. Neupane, E. Tokita, U. Ghosh, S. Hales, and Y. L. Kong, "Nanomaterial patterning in 3D printing," *Adv Mater*, vol. 32, no. 17, Article ID e1907142, 2020.

[12] H. Nam, H. J. Jeong, Y. Jo et al., "Multi-layered free-form 3D cell-printed tubular construct with decellularized inner and outer esophageal tissue-derived bioinks," *Scientific Reports*, vol. 10, no. 1, p. 7255, 2020.

[13] Y. S. Zhang, A. Arneri, S. Bersini et al., "Bioprinting 3D microfibrous scaffolds for engineering endothelialized myocardium and heart-on-a-chip," *Biomaterials*, vol. 110, pp. 45–59, 2016.

[14] B. S. Kim, Y. W. Kwon, J. S. Kong et al., "3D cell printing of in vitro stabilized skin model and in vivo pre-vascularized skin patch using tissue-specific extracellular matrix bioink: a step towards advanced skin tissue engineering," *Biomaterials*, vol. 168, pp. 38–53, 2018.

[15] R. Chae, J. D. Sharon, I. Kournoutas et al., "Replicating skull base anatomy with 3D technologies: a comparative study using 3D-scanned and 3D-printed models of the temporal bone," *Otology & Neurotology*, vol. 41, no. 3, pp. e392–e403, 2020.

[16] J. Witowski, N. Wake, A. Grochowska et al., "Investigating accuracy of 3D printed liver models with computed tomography," *Quantitative Imaging in Medicine and Surgery*, vol. 9, no. 1, pp. 43–52, 2019.

[17] N. Shahrubudin, T. C. Lee, and R. Ramlan, "An overview on 3D printing technology: technological, materials, and applications," *Procedia Manufacturing*, vol. 35, pp. 1286–1296, 2019.

[18] S. Mohammadi and N. Weiskopf, "Computational neuroanatomy and microstructure imaging using magnetic resonance imaging," *Nervenarzt, Der*, vol. 88, no. 8, pp. 839–849, 2017.

[19] J. P. Lerch, A. J. W. van der Kouwe, A. Raznahan et al., "Studying neuroanatomy using MRI," *Nature Neuroscience*, vol. 20, no. 3, pp. 314–326, 2017.

[20] T. M. Bücking, E. R. Hill, J. L. Robertson, E. Maneas, A. A. Plumb, and D. I. Nikitichev, "From medical imaging data to 3D printed anatomical models," *PLoS One*, vol. 12, no. 5, Article ID e0178540, 2017.

[21] J. S. Naftulin, E. Y. Kimchi, and S. S. Cash, "Streamlined, inexpensive 3D printing of the brain and skull," *PLoS One*, vol. 10, no. 8, Article ID e0136198, 2015.

[22] J. Thawani, M. Randazzo, J. Pisapia, and N. Singh, "3D printing in neurosurgery: a systematic review," *Surgical Neurology International*, vol. 7, no. 34, pp. S801–S809, 2016.

[23] V. Waran, V. Narayanan, R. Karrupiah, and C. Y. Cham, "3D printing in neurosurgery," *3D Printing in Medicine*, pp. 51–58, 2017.

[24] S. Konakondla, C. J. Brimley, J. M. Sublett et al., "Multimodality 3D superposition and automated whole brain tractography: comprehensive printing of the functional brain," *Cureus*, vol. 9, no. 9, Article ID e1731, 2017.

[25] E. George, P. Liacouras, F. J. Rybicki, and D. Mitsouras, "Measuring and establishing the accuracy and reproducibility of 3D printed medical models," *RadioGraphics*, vol. 37, no. 5, pp. 1424–1450, 2017.

[26] O. Rungrojwittayakul, J. Y. Kan, K. Shiozaki et al., "Accuracy of 3D printed models created by two technologies of printers with different designs of model base," *Journal of Prosthodontics*, vol. 29, no. 2, pp. 124–128, 2020.

[27] H. W. Kang, S. J. Lee, I. K. Ko, C. Kengla, J. J. Yoo, and A. Atala, "A 3D bioprinting system to produce human-scale tissue constructs with structural integrity," *Nature Biotechnology*, vol. 34, no. 3, pp. 312–319, 2016.

[28] K. S. Boparai, R. Singh, and H. Singh, "Development of rapid tooling using fused deposition modeling: a review[J]," *Rapid Prototyping Journal*, vol. 22, 2016.

[29] A. Bhargav, V. Sanjairaj, V. Rosa, L. W. Feng, and J. Fuh Yh, "Applications of additive manufacturing in dentistry: a review," *Journal of Biomedical Materials Research Part B: Applied Biomaterials*, vol. 106, no. 5, pp. 2058–2064, 2018.

[30] C. N. Ionita, M. Mokin, N. Varble et al., "Challenges and limitations of patient-specific vascular phantom fabrication using 3D Polyjet printing," *Proceedings of SPIE-The International Society for Optical Engineering*, vol. 9038, Article ID 90380m, 2014.

[31] E. O. Olakanmi, R. F. Cochrane, and K. W. Dalgarno, "A review on selective laser sintering/melting (SLS/SLM) of aluminium alloy powders: processing, microstructure, and properties," *Progress in Materials Science*, vol. 74, pp. 401–477, 2015.

[32] M. Nakamura, A. Kobayashi, F. Takagi et al., "Biocompatible inkjet printing technique for designed seeding of individual living cells," *Tissue Engineering*, vol. 11, no. 11-12, pp. 1658–1666, 2005.

[33] F. Da and S. Gai, "Flexible three-dimensional measurement technique based on a digital light processing projector," *Applied Optics*, vol. 47, no. 3, pp. 377–385, 2008.

[34] J. Li, M. Chen, X. Fan, and H. Zhou, "Recent advances in bioprinting techniques: approaches, applications and future prospects," *Journal of Translational Medicine*, vol. 14, no. 1, p. 271, 2016.

[35] P. Gargiulo, Í. Árnadóttir, M. Gíslason, K. Edmunds, and I. Olafsson, "New directions in 3D medical modeling: 3D-printing anatomy and functions in neurosurgical planning," *Journal of Healthcare Engineering*, vol. 2017, pp. 1–8, 2017.

[36] M. Oishi, M. Fukuda, N. Yajima et al., "Interactive presurgical simulation applying advanced 3D imaging and modeling techniques for skull base and deep tumors," *Journal of Neurosurgery*, vol. 119, no. 1, pp. 94–105, 2013.

[37] J. W. Bae, D. Y. Lee, C. H. Pang et al., "Clinical application of 3D virtual and printed models for cerebrovascular diseases," *Clinical Neurology and Neurosurgery*, vol. 206, Article ID 106719, 2021.

[38] C. Parra-Cantu, W. Li, A. Quiñones-Hinojosa, and Y. S. Zhang, "3D bioprinting of glioblastoma models," *J 3D Print Med*, vol. 4, no. 2, pp. 113–125, 2020.

[39] M. A. Hermida, J. D. Kumar, D. Schwarz et al., "Three dimensional in vitro models of cancer: bioprinting multilineage glioblastoma models," *Advances in Biological Regulation*, vol. 75, Article ID 100658, 2020.

[40] X. Dai, C. Ma, Q. Lan, and T. Xu, "3D bioprinted glioma stem cells for brain tumor model and applications of drug susceptibility," *Biofabrication*, vol. 8, no. 4, Article ID 045005, 2016.

[41] X. Wang, X. Li, J. Ding et al., "3D bioprinted glioma microenvironment for glioma vascularization," *Journal of Biomedical Materials Research Part A*, vol. 109, no. 6, pp. 915–925, 2021.

[42] L. Zhang, G. Yang, B. N. Johnson, and X. Jia, "Three-dimensional (3D) printed scaffold and material selection for bone repair," *Acta Biomaterialia*, vol. 84, pp. 16–33, 2019.

[43] C. E. Stewart, C. F. K. Kan, B. R. Stewart et al., "Machine intelligence for nerve conduit design and production," *Journal of Biological Engineering*, vol. 14, no. 1, p. 25, 2020.

[44] X. Y. Chen, S. Zhang, J. P. Jiang et al., "Three-dimensional bioprinting collagen/silk fibroin scaffold combined with neural stem cells promotes nerve regeneration after spinal cord injury," *Neural Regen Res*, vol. 15, no. 5, pp. 959–968, 2020.

[45] D. Joung, V. Truong, C. C. Neitzke et al., "3D printed stem-cell derived neural progenitors generate spinal cord scaffolds," *Adv Funct Mater*, vol. 28, no. 39, Article ID 1801850, 2018.

[46] J. Zhu, J. Yang, C. Tang, Z. Cong, X. Cai, and C. Ma, "Design and validation of a 3D-printed simulator for endoscopic third ventriculostomy," *Childs Nerv Syst*, vol. 36, no. 4, pp. 743–748, 2020.

[47] A. S. Grosch, T. Schröder, T. Schröder, J. Onken, and T. Picht, "Development and initial evaluation of a novel simulation model for comprehensive brain tumor surgery training," *Acta Neurochirurgica*, vol. 162, no. 8, pp. 1957–1965, 2020.

[48] M. Kosterhon, M. Neufurth, and A. Neulen, "Multicolor 3D printing of complex intracranial tumors in neurosurgery[J]," *Journal of Visualized Experiments*, vol. 2020, no. 155.

[49] X. Y. Guo, Z. Q. He, H. Duan et al., "The utility of 3-dimensional-printed models for skull base meningioma surgery," *Annals of Translational Medicine*, vol. 8, no. 6, p. 370, 2020.

[50] X. Huang, Z. Liu, X. Wang et al., "A small 3D-printing model of macroadenomas for endoscopic endonasal surgery," *Pituitary*, vol. 22, no. 1, pp. 46–53, 2019.

[51] M. A. Heinrich, R. Bansal, T. Lammers, Y. S. Zhang, R. Michel Schiffelers, and J. Prakash, "3D-Bioprinted mini-brain: a glioblastoma model to study cellular interactions and

therapeutics," *Adv Mater*, vol. 31, no. 14, Article ID e1806590, 2019.

[52] Q. T. Ostrom, L. Bauchet, F. G. Davis et al., "The epidemiology of glioma in adults: a state of the science review," *Neuro-Oncology*, vol. 16, no. 7, pp. 896–913, 2014.

[53] J. Gomez-Feria, J. L. Narros, G. G. Ciriza et al., "3D printing of diffuse low-grade gliomas involving eloquent cortical areas and subcortical functional pathways: technical note," *World Neurosurgery*, vol. 147, pp. 164–171.e4, 2021.

[54] R. D. Brown Jr. and J. P. Broderick, "Unruptured intracranial aneurysms: epidemiology, natural history, management options, and familial screening," *The Lancet Neurology*, vol. 13, no. 4, pp. 393–404, 2014.

[55] A. Meretoja, D. Strbian, J. Putaala et al., "SMASH-U: a proposal for etiologic classification of intracerebral hemorrhage[J]," *Stroke*, vol. 43, no. 10, pp. 2592–2597, 2012.

[56] Y. Wu, S. Zhang, Y. Dong et al., "Therapeutic effect of electronic endoscopic hematoma removal on hypertensive basal ganglia cerebral hemorrhage based on smart medical technology," *Journal of Healthcare Engineering*, vol. 2021, pp. 1–10, 2021.

[57] J. Zhang, H. Cheng, S. Zhou et al., "3D-printed model-guided endoscopic evacuation for basal ganglia hemorrhage," *Scientific Reports*, vol. 10, no. 1, p. 5196, 2020.

[58] L. H. Chen, F. J. Li, H. T. Zhang, W. J. Chen, K. Sun, and R. X. Xu, "The microsurgical treatment for primary hypertensive brainstem hemorrhage: experience with 52 patients," *Asian Journal of Surgery*, vol. 44, no. 1, pp. 123–130, 2021.

[59] K. Li, X. Ding, Q. Wang et al., "Low-cost, accurate, effective treatment of hypertensive cerebral hemorrhage with three-dimensional printing technology," *Frontiers in Neurology*, vol. 12, no. 110, Article ID 608403, 2021.

[60] B. Barnes, D. F. Hanley, and J. R. Carhuapoma, "Minimally invasive surgery for intracerebral haemorrhage," *Current Opinion in Critical Care*, vol. 20, no. 2, pp. 148–152, 2014.

[61] Y. Li, H. Cheng, Z. Li et al., "Clinical value of 3D-printed navigation technology combined with neuroendoscopy for intracerebral hemorrhage," *Transl Stroke Res*, vol. 12, no. 6, pp. 1035–1044, 2021.

[62] Q. Wang, W. Guo, Y. Liu et al., "Application of a 3D-printed navigation mold in puncture drainage for brainstem hemorrhage," *Journal of Surgical Research*, vol. 245, pp. 99–106, 2020.

[63] N. Etminan and G. J. Rinkel, "Unruptured intracranial aneurysms: development, rupture and preventive management," *Nature Reviews Neurology*, vol. 12, no. 12, pp. 699–713, 2016.

[64] D. O. Wiebers, J. P. Whisnant, and J. Huston 3rd, "Unruptured intracranial aneurysms: natural history, clinical outcome, and risks of surgical and endovascular treatment," *The Lancet*, vol. 362, no. 9378, pp. 103–110, 2003.

[65] A. J. Molyneux, R. S. Kerr, L. M. Yu et al., "International subarachnoid aneurysm trial (ISAT) of neurosurgical clipping versus endovascular coiling in 2143 patients with ruptured intracranial aneurysms: a randomised comparison of effects on survival, dependency, seizures, rebleeding, subgroups, and aneurysm occlusion," *The Lancet*, vol. 366, no. 9488, pp. 809–817, 2005.

[66] L. S. Mcguire, A. Fuentes, and A. Alaraj, "Three-dimensional modeling in training, simulation, and surgical planning in open vascular and endovascular neurosurgery: a systematic review of the literature," *World Neurosurgery*, vol. 154, pp. 53–63, 2021.

[67] M. A. Tomcik, N. R. Gerig, and J. A. Prahlow, "Sudden death from ruptured intracranial vascular malformation," *Forensic Science, Medicine and Pathology*, vol. 7, no. 2, pp. 185–191, 2011.

[68] J. R. Anderson, W. L. Thompson, A. K. Alkattan et al., "Three-dimensional printing of anatomically accurate, patient specific intracranial aneurysm models," *Journal of Neurointerventional Surgery*, vol. 8, no. 5, pp. 517–520, 2016.

[69] Y. Xu, W. Tian, Z. Wei et al., "Microcatheter shaping using three-dimensional printed models for intracranial aneurysm coiling," *Journal of Neurointerventional Surgery*, vol. 12, no. 3, pp. 308–310, 2020.

[70] L. Jang, J. Alvarado, and M. Pepona, "Three-dimensional bioprinting of aneurysm-bearing tissue structure for endovascular deployment of embolization coils[J]," *Biofabrication*, vol. 16, 2020.

[71] A. L. Jardini, M. A. Larosa, M. F. Macedo et al., "Improvement in cranioplasty: advanced prosthesis biomanufacturing," *Procedia CIRP*, vol. 49, pp. 203–208, 2016.

[72] J. Kwarcinski, P. Boughton, J. Gelder, O. Damodaran, A. Doolan, and A. Ruys, "Clinical evaluation of rapid 3D p rint-formed implants for surgical reconstruction of large cranial defects," *ANZ Journal of Surgery*, vol. 91, no. 6, pp. 1226–1232, 2021.

[73] E. T. W. Tan, J. M. Ling, and S. K. Dinesh, "The feasibility of producing patient-specific acrylic cranioplasty implants with a low-cost 3D printer," *Journal of Neurosurgery*, vol. 124, no. 5, pp. 1531–1537, 2016.

[74] R. Chrzan, A. Urbanik, K. Karbowski, M. Moskala, J. Polak, and M. Pyrich, "Cranioplasty prosthesis manufacturing based on reverse engineering technology," *Medical Science Monitor*, vol. 18, no. 1, pp. Mt1–6, 2012.

[75] C.-H. Cheng, H.-Y. Chuang, H.-L. Lin, C. L. Liu, and C. H. Yao, "Surgical results of cranioplasty using three-dimensional printing technology," *Clinical Neurology and Neurosurgery*, vol. 168, pp. 118–123, 2018.

[76] S. N. Schon, N. Skalicky, and N. Sharma, "3D-Printer-Assisted patient-specific polymethyl methacrylate cranioplasty:a case series of 16 consecutive patients[J]," *World Neurosurg*, vol. 148, pp. e356–e362, Article ID 101016, 2021.

[77] M. Lannon, A. Algird, W. Alsunbul, and B. H. Wang, "Cost-effective cranioplasty utilizing 3D printed molds: a Canadian single-center experience," *The Canadian Journal of Neurological Sciences*, vol. 49, no. 2, pp. 196–202, 2021.

[78] E. B. Da Silva Júnior, A. H. De Aragão, M. De Paula Loureiro et al., "Cranioplasty with three-dimensional customised mould for polymethylmethacrylate implant: a series of 16 consecutive patients with cost-effectiveness consideration," *3D Print Med*, vol. 7, no. 1, p. 4, 2021.

[79] B. Lal, M. Ghosh, B. Agarwal, D. Gupta, and A. Roychoudhury, "A novel economically viable solution for 3D printing-assisted cranioplast fabrication," *British Journal of Neurosurgery*, vol. 34, no. 3, pp. 280–283, 2020.

[80] K. Suzuki, H. Tanaka, M. Ebara et al., "Electrospun nanofiber sheets incorporating methylcobalamin promote nerve regeneration and functional recovery in a rat sciatic nerve crush injury model," *Acta Biomaterialia*, vol. 53, pp. 250–259, 2017.

[81] A. Faroni, S. A. Mobasseri, P. J. Kingham, and A. J. Reid, "Peripheral nerve regeneration: e," *Advanced Drug Delivery Reviews*, vol. 82-83, pp. 160–167, 2015.

[82] S. A. Holmes, N. Barakat, M. Bhasin et al., "Biological and behavioral markers of pain following nerve injury in

humans," *Neurobiology of Pain*, vol. 7, Article ID 100038, 2020.

[83] M. T. Houdek and A. Y. Shin, "Management and complications of traumatic peripheral nerve injuries," *Hand Clinics*, vol. 31, no. 2, pp. 151–163, 2015.

[84] E. O. Johnson, A. B. Zoubos, and P. N. Soucacos, "Regeneration and repair of peripheral nerves," *Injury*, vol. 36, no. 4, pp. S24–S29, 2005.

[85] A. Kriebel, D. Hodde, T. Kuenzel, J. Engels, G. Brook, and J. Mey, "Cell-free artificial implants of electrospun fibres in a three-dimensional gelatin matrix support sciatic nerve regeneration *in vivo*," *J Tissue Eng Regen Med*, vol. 11, no. 12, pp. 3289–3304, 2017.

[86] F. Rao, Y. Wang, D. Zhang et al., "Aligned chitosan nanofiber hydrogel grafted with peptides mimicking bioactive brain-derived neurotrophic factor and vascular endothelial growth factor repair long-distance sciatic nerve defects in rats," *Theranostics*, vol. 10, no. 4, pp. 1590–1603, 2020.

[87] J. H. Chi, "Neurosurgery tops malpractice risk," *Neurosurgery*, vol. 69, no. 6, pp. N18–N20, 2011.

[88] W. Clifton, A. Damon, E. Nottmeier, and M. Pichelmann, "The importance of teaching clinical anatomy in surgical skills education: s," *Clinical Anatomy*, vol. 33, no. 1, pp. 124–127, 2020.

[89] A. Suri, D. P. Patra, and R. K. Meena, "Simulation in neurosurgery: past, present, and future," *Neurology India*, vol. 64, no. 3, pp. 387–395, 2016.

[90] R. K. Reznick and H. Macrae, "Teaching surgical skills — changes in the wind," *New England Journal of Medicine*, vol. 355, no. 25, pp. 2664–2669, 2006.

[91] A. Ganguli, G. J. Pagan-Diaz, L. Grant et al., "3D printing for preoperative planning and surgical training: a review," *Biomedical Microdevices*, vol. 20, no. 3, p. 65, 2018.

[92] J. U. Pucci, B. R. Christophe, J. A. Sisti, and E. S. Connolly, "Three-dimensional printing: technologies, applications, and limitations in neurosurgery," *Biotechnology Advances*, vol. 35, no. 5, pp. 521–529, 2017.

[93] T. Martín-Noguerol, F. Paulano-Godino, R. F. Riascos, J. Calabia-del-Campo, J. Marquez-Rivas, and A. Luna, "Hybrid computed tomography and magnetic resonance imaging 3D printed models for neurosurgery planning," *Annals of Translational Medicine*, vol. 7, no. 22, p. 684, 2019.

[94] V. Waran, V. Narayanan, R. Karuppiah, S. L. F. Owen, and T. Aziz, "Utility of multimaterial 3D printers in creating models with pathological entities to enhance the training experience of neurosurgeons," *Journal of Neurosurgery*, vol. 120, no. 2, pp. 489–492, 2014.

[95] P. Weinstock, R. Rehder, S. P. Prabhu, P. W. Forbes, C. J. Roussin, and A. R. Cohen, "Creation of a novel simulator for minimally invasive neurosurgery: fusion of 3D printing and special effects," *Journal of Neurosurgery: Pediatrics*, vol. 20, no. 1, pp. 1–9, 2017.

[96] D. Inoue, K. Yoshimoto, M. Uemura et al., "Three-dimensional high-definition neuroendoscopic surgery: a controlled comparative laboratory study with two-dimensional endoscopy and clinical application," *Journal of Neurological Surgery Part A: Central European Neurosurgery*, vol. 74, no. 06, pp. 357–365, 2013.

[97] V. Waran, V. Narayanan, R. Karuppiah et al., "Neurosurgical endoscopic training via a realistic 3-dimensional model with pathology," *Simulation in Healthcare: The Journal of the Society for Simulation in Healthcare*, vol. 10, no. 1, pp. 43–48, 2015.

[98] M. Licci, F. M. Thieringer, R. Guzman, and J. Soleman, "Development and validation of a synthetic 3D-printed simulator for training in neuroendoscopic ventricular lesion removal," *Neurosurgical Focus*, vol. 48, no. 3, p. E18, 2020.

[99] J. Zhu, G. Wen, C. Tang, C. Zhong, J. Yang, and C. Ma, "A practical 3D-printed model for training of endoscopic and exoscopic intracerebral hematoma surgery with a tubular retractor," *Journal of Neurological Surgery Part A: Central European Neurosurgery*, vol. 81, no. 05, pp. 404–411, 2020.

[100] D. H. Ballard, P. Mills, R. Duszak Jr, J. A. Weisman, F. J. Rybicki, and P. K. Woodard, "Medical 3D printing cost-savings in orthopedic and maxillofacial surgery: cost analysis of operating room time saved with 3D printed anatomic models and surgical guides," *Academic Radiology*, vol. 27, no. 8, pp. 1103–1113, 2020.

[101] T. Anada, C. C. Pan, A. M. Stahl et al., "Vascularized bone-mimetic hydrogel constructs by 3D bioprinting to promote osteogenesis and angiogenesis," *International Journal of Molecular Sciences*, vol. 20, no. 5, p. 1096, 2019.

[102] P. Abdollahiyan, F. Oroojalian, A. Mokhtarzadeh, and M. Guardia, "Hydrogel-based 3D bioprinting for bone and cartilage tissue engineering," *Biotechnology Journal*, vol. 15, no. 12, Article ID e2000095, 2020.