Application of a three-dimensional printed model to localize a cranial cerebrospinal fluid leak: a case report

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Abstract
Localization of defect sites is a major challenge for surgical repair of cerebrospinal fluid (CSF) leaks. Here, we report a case in which we applied a 3-dimensional (3D) printed model to accurately identify the defect sites and facilitate the successful repair of a cranial CSF leak. A 37-year-old female patient diagnosed with recurrent nasopharyngeal carcinoma suffered CSF rhinorrhea and severe bacterial meningitis. Lumbar drainage and antibiotic administration failed to control the condition. In addition to high resolution computed tomography and magnetic resonance imaging, we applied a 3D printed model of the skull to improve the understanding of the osseous destruction at the skull base and aid in accurately localizing the defect sites of the right middle fossa. Accordingly, a right temporalis pedicled flap combined with an autogenous fascia lata flap was applied to cover the defect sites. The leak stopped postoperatively, and meningitis was relieved by enhanced antibacterial treatment. As a complement to high resolution

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computed tomography and magnetic resonance imaging, a 3D printed model may improve localization of complex defect sites and surgical planning by allowing preoperative visualization of the skull condition.

**Keywords**
Three-dimensional printing, cerebrospinal fluid leak, case report, nasopharyngeal carcinoma, bacterial meningitis, osseous destruction

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**Introduction**
A cranial cerebrospinal fluid (CSF) leak occurs when an osseous and dural defect is present at the skull base, resulting in an abnormal communication between the subarachnoid space and the extracranial space in the paranasal sinuses, nasal cavity, middle ear, or mastoid air cells. Craniofacial trauma, previous surgeries on or around the skull, tumor at the skull base, and congenital abnormalities of the skull base or inner ear are common causes of cranial CSF leaks. Patients with cranial CSF leaks often present with rhinorrhea or otorrhea, low-pressure headaches, and meningitis. Although some CSF leaks may heal with conservative treatments such as bed rest, many CSF leaks require surgical repair. Successful surgical repair depends on the precise localization of the leak sites. High resolution computed tomography (HRCT) is the best initial investigation tool for this purpose. However, some osseous defects detected by HRCT are still difficult to efficiently localize during surgery because HRCT is a two-dimensional (2D) method that limits the presentation of spatial structures.

Three-dimensional (3D) printing technology allows transformation of 2D virtual images into 3D physical models. The highly personalized design of 3D printed models allows medical professionals to produce patient-specific models that can present anatomical structures in detail and facilitate preoperative surgical planning. We previously reported the utility of 3D printed models of skull base meningioma for preoperatively visualizing the skull base condition and improving surgical planning. For CSF leaks caused by osseous defects at the skull base, 3D printing technology may be beneficial for localization of defect sites and surgical repair planning via preoperative visualization of the skull condition.

Here, we report a nasopharyngeal carcinoma patient who suffered from a cranial CSF leak caused by tumor-related and iatrogenic destruction at the skull base. We applied a 3D printed model to accurately identify the osseous defects, which facilitated a successful repair of the CSF leak.

**Case report**
A 37-year-old woman presented with CSF rhinorrhea followed by severe bacterial meningitis. The patient complained of serious headaches and a high fever.

The patient was initially diagnosed with a nasopharyngeal carcinoma (cT2N0M0) and received radiotherapy (72 Gy/41 fractions) in 2002. She was closely followed up
and had an uneventful course until the tumor recurred in the pharyngeal area and external auditory meatus in 2014. An endoscopic nasopharyngectomy was performed at a local hospital without adjuvant chemotherapy or radiotherapy. In April 2015, the patient was referred to our center because of progressive disease (rT4N0M0) (Figure 1). Radiotherapy (56 Gy/28 fractions) with concomitant chemotherapy (5-fluorouracil + nedaplatin) followed by seven courses of maintenance chemotherapy (5-fluorouracil + nedaplatin) was suggested. The tumor had decreased in October 2015. In June 2016, the patient started to suffer from headaches and dysphagia. Tumor progression accompanied by considerable nasopharyngeal necrosis adjacent to the right carotid artery was noted on contrast-enhanced magnetic resonance imaging (MRI). Therefore, occlusion of the right carotid artery was performed to prevent lethal hemorrhage caused by potential tumor invasion and tissue necrosis.

Figure 1. Cranial contrast-enhanced magnetic resonance imaging (MRI) showed changes in nasopharyngeal lesions from April 2015 to June 2016. Tumor recurrence (arrow) was noted in the right nasopharyngeal area in April 2015, but the tumor decreased (arrow) after chemoradiotherapy in October 2015. Tumor progression (arrow) accompanied by considerable nasopharyngeal necrosis was noted on contrast-enhanced MRI in June 2016.
In November 2016, the patient developed a cranial CSF leak with apparent clinical symptoms including nasal dripping and swallowing of sweet-tasting fluid. Shortly, serious headaches and a high fever developed, and CSF tests confirmed severe bacterial meningitis. Lumbar drainage and antibiotic administration failed to control the condition. Cranial MRI and computed tomography (CT) revealed extensive osteoradionecrosis of the skull base and obvious pneumocephalus (Figure 2a–d).

We then utilized the HRCT data and 3D printing technology to produce a 3D printed model of the skull base. The detailed 3D printing protocol was described in our previous study. Briefly, cranial CT images with a thickness of 1 mm were used for 3D volume rendering using Mimics software (Materialise, Leuven, Belgium). Then, the DICOM file was converted to an STL file followed by printing of a 1:1 scale physical model with a fused deposition modeling (FDM) 3D printer and ivory-colored acrylonitrile butadiene styrene.

The 3D printed model provided a more realistic view of the local condition and aided in identification of the potential defect sites. As shown on the model, the osseous defects near the foramen and ovale were considered responsible for the CSF leak (Figure 2e–g). Therefore, the flap designed for repair covered the right middle cranial fossa. Considering the extensive osseous defects and limited vascularized nasal flaps, a lateral craniotomy, instead of an endonasal endoscopic approach, was planned for the leak repair.

Accordingly, a right frontotemporal craniotomy was performed (Figure 3a).

Figure 2. Cranial contrast-enhanced magnetic resonance imaging (MRI) revealed extensive osteoradionecrosis (circle) of the right middle skull base (a–c), with obvious pneumocephalus (arrow) (d). The three-dimensional (3D)-printed model demonstrated that the osseous defects (arrow) were near the right lacerum and foramen ovale (e–g).
An autogenous fascia lata flap combined with a right temporalis pedicle flap was applied to cover the leaks using a subdural method (Figure 3b–c). The surgical procedures are summarized in Figure 4.

Postoperatively, the patient developed slight right facial numbness without visual deficits. The clinical symptoms of nasal dripping and swallowing of sweet-tasting fluid disappeared, and the pneumocephalus was absorbed (Figure 5a). Meningitis was relieved by enhanced antibacterial treatment. A neovascularized flap was noted on contrast-enhanced MRI at 2 months postoperatively (Figure 5b–c). Although the patient was satisfied with the successful CSF leak repair, she unfortunately died of tumor progression in November 2017.

The reporting of this study conforms to the CARE guidelines. Verbal informed consent was obtained from the patient. The study was approved by the Institutional Review Board of Sun Yat-sen University Cancer Center (Guangzhou, Guangdong, China) (No. B2020-118-01) and adhered to the tenets of the Declaration of Helsinki.

**Discussion**

In this case, we utilized 3D printing technology in addition to HRCT and MRI to precisely localize a CSF leak at the skull base, which showed extensive tumor-related and iatrogenic destruction.

Accurate localization of defect sites is critical for successful repair of a CSF leak. The sensitivity and specificity of HRCT in localizing a CSF leak range from 44% to 100% and from 45% to 100%, respectively. In cases in which the leak sites are unidentified on HRCT, CT or MRI cisternography with intrathecal contrast material is indicated. Studies have reported that the accuracy, sensitivity, and specificity of MRI cisternography are 89%, 87%, and 100%, respectively. CT and MRI cisternography require the leak to be active at the time of scanning. Moreover, potential complications include those related to lumbar puncture and adverse reactions to contrast material, including anaphylactoid reactions and seizures. Intrathecal injection of fluorescein is used to locate the CSF fistula during an endonasal endoscopic procedure, but this method was inappropriate for craniotomy in this patient.

Although HRCT and MRI cisternography can be used to effectively identify the leak sites, they are 2D methods, which limits their advantage in surgical planning and intraoperative localization. Recent studies have reported application of 3D printed technology in neurosurgery,
1. The patient was placed in a supine position, and the head was fixed using a Mayfield head frame, turned 20° to the left, and tilted back 10°.

2. A straight incision was made in the lateral right thigh, and a fascia lata flap was removed and wrapped in gauze.

3. A right frontotemporal arc incision was made, a right frontotemporal bone window approximately 10 × 8 cm was created, the sphenoid ridge was cut, and the frontal and temporal lobes were retracted.

4. An inflammatory thickening of the arachnoid mater was observed in the operative area. Under the guidance of the 3D printed model, several meningeal defects were identified in the right petrous apex area. The leak was approximately 2 to 3 mm in diameter.

5. The inflammatory tissue was removed, the leaks were covered with the autogenous fascia lata flap, and an ipsilateral temporal muscle flap was placed on the fascia lata flap.

6. The dura mater was repaired with artificial meninges, an indwelling epidural drainage tube was placed, the skull base was fixed with a titanium sheet and nails, and the galea aponeurosis and scalp were sutured.

**Figure 4.** Flowchart of the surgical procedures.

![Flowchart of the surgical procedures](image)

**Figure 5.** The pneumocephalus was absorbed postoperatively (a). A neovascularized flap (arrows) was noted on contrast-enhanced magnetic resonance imaging at 2 months postoperatively (b–c).

including anatomical learning. \(^7,^{16,17}\)

The advantage of 3D printing technology in 2D to 3D transformation makes it potentially complementary to HRCT and MRI cisternography for CSF leak localization. Indeed, 3D volume rendering using reconstructed cranial CT images has previously been used to stereoscopically show osseous defects at the skull base. Compared with 3D volume rendering,
a 3D printed model can further facilitate anatomical orientation during surgery. In this case, the anatomical structures near the osseous defects were previously destroyed by the tumor, chemoradiotherapy, surgery, and inflammation, which significantly increased the intraoperative difficulties in seeking and identifying the defect sites. Because a physical model can present the anatomical landmarks in a more realistic and straightforward manner than 3D volume rendering on a screen, we printed a 1:1 scale physical model for this patient and used it in the operation room. With the real-time guidance of the 3D printed model, we accurately and efficiently localized the defect sites.

3D printing techniques vary, depending on the material chosen. We use FDM technology to produce a 3D printed model that is affordable for most patients. FDM is an extrusion-based 3D printing technology and is currently the most commonly used and most inexpensive 3D printing process. An entry level FDM printer can cost less than 200 USD. Meanwhile, we used ivory-colored acrylonitrile butadiene styrene, which is often used, readily available, and inexpensive. The cost of the 3D printed model in the present study was only approximately 10 USD on the Chinese market, and the actual print time was 6 hours.

Although our 3D printed model precisely showed the osseous defects, room for improvement still exists. Osseous defects at the skull base are usually close to the cranial nerves and large blood vessels. A 3D printed model comprising normal structures, such as the cranial nerves, blood vessels, and muscles around the osseous defect, would enhance the practicability and pertinency of surgical planning, thereby reducing the risks of operation.

Conclusions

This case report describes the successful application of a 3D printed model for accurate repair of a cranial CSF leak. As a complement to HRCT and MRI, 3D printed models may improve localization of complex defect sites and surgical planning via preoperative visualization of the skull condition. Future studies are warranted to confirm the advantages of 3D printing technology in surgical repair of CSF leaks.

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Author contributions

Duan H, Jiang XB, and Mou YG contributed to the study design, and Chen MY, Zhang B, Zhao QY, and Huang YY participated in the treatment of this patient. Duan H and Jiang XB participated in the drafting of this manuscript. Duan H, Jiang XB, and Li C revised the manuscript.

Declaration of conflicting interest

The authors declare that they have no conflict of interest.

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