He received prophylactic antibiotics [sultamicillin tosilate hydrate (SBTPC)], was discharged 2 weeks after surgery without any evidence of infection, and immediately returned to his job.

However, 2 weeks later (4 weeks after TSS) he was transported to the nearest emergency hospital with consciousness disturbances, neck stiffness, and a high fever. He was diagnosed with SPM due to his clinical symptoms, CSF examination (cell counts: 28,864 μL, protein: 612 mg/dl, glucose: 2 mg/dl), and CSF culture. He was treated intensively with appropriate antibiotics, but he suffered a temporal lobe infarction due to associated encephalitis. At present, this patient is partially disabled and requires assistance with his daily activities.

In this case, anaerobic Gram-positive rods and Gram-positive cocci had been found but *Str. pneumoniae* was not detected via intraoperative BCSM.

The clinical characteristics of these three cases are summarized in Table 1.

Discussion

I. Clinical characteristics and pathogenesis of SPM

Streptococcus species is known to cause meningoencephalitis in both children and adults, especially after sinusitis, middle ear infections, and/or pneumonia by local extension or hematologic dissemination.[5,6] Reported intracranial or systemic complications of SPM include local complications, such as seizure, arterial occlusion, venous thrombosis, arterial vasculitis, arterial spasm, diffuse brain swelling, hydrocephalus, encephalitis, cranial nerve palsies, hearing loss, as well as systemic complications like septic shock, disseminated intravascular coagulation, acute renal failure, and adult respiratory distress syndrome.[1,5–7]

SPM has a rather high mortality rate (20% to 30%) despite recent developments of highly effective antibiotics.[1] As in other reports,[1,5,7] SPM complications in our series were associated with very severe symptoms and a poor prognosis.[1,5] Neurological deficits due to arterial vasculitis or encephalitis remained in all three cases, one patient (Case 2) died due to severe associated brain edema. Similarly, cerebral infarctions in various areas found in our three cases suggest intracranial arterial occlusion due to arterial vasculitis associated with SPM.

To our knowledge, few SPM cases after surgery have been reported in other conditions, including a healthy immunocompetent man 3 months after a cochlear implant,[8] a 9-month-old girl with an underlying frontoethmoidal encephalomeningocele who received facial surgery,[9] and

Table 1 Summary of our three cases of post-TSS SPM

		Case 1	Case 2	Case 3
	Age/gender	4, M	40, M	55, M
	DM	(–)	(–)	(–)
	Surgical approach	Sublabial TSS	Transnasal TSS	Transnasal TSS
	Pathology of tumor	Craniopharyngioma	non-functioning adenoma	GH adenoma
CSF leakage	During surgery	(+)	(–)	(–)
	After surgery	(–)	(–)	(–)
	BCSM	Not exam	*Staphylococcus* species, *Klebshiella pneumonia*	Gram-positive rods, anaerobic Gram-positive rods
	Perioperative antibiotics used	CEZ	CEZ	SBTPC
	Postoperative hormonal replacement	Hydrocortisone, levothyloxine sodium hydrate, DDAVP	(–)	(–)
SPM	Onset after surgery (week)	8 weeks	4 weeks	4 weeks
	Initial symptoms	High fever, headache and unconsciousness with generalized convulsion	High fever, severe headache with unconsciousness	Unconsciousness
CSF data	Cell counts	2530/μL	Not available	28864/μL
	Protein	134 mg/dl		612 mg/dl
	Glucose	12 mg/dl		2 mg/dl
	Outcome	SD	D	SD

BCSM: bacterial culture of sphenoidal sinus mucous membrane, CEZ: cefazoline sodium, CSF: cerebrospinal fluid, D: dead, DM: diabetes mellitus, GH: growth hormone, M: male, SBTPC: sultamicillintonsilate hydrate, SD: severely disabled, SPM: *Streptococcus pneumoniae* meningoencephalitis, TSS: transsphenoidal surgery.

a 5-year-old boy with obstructive sleep apnea who had undergone adenotonsillectomy.[9] Notably SPM after TSS has been reported in only one case in the literature.[1] In this report Bakar and Hakki Tekkok[1] described a 56-year-old man with SPM after TSS who became hyperpyrexic and progressed to confusion and lethargy 2 days after an uneventful surgery. Unlike our cases, these symptoms occurred early after surgery and the patient made an uneventful recovery, although CSF leakage was not observed throughout the course of meningitis as in our other cases. Indeed, postoperative meningitis after TSS is usually associated with postoperative CSF leakage early after surgery,[2,3] suggesting direct infection from the operative field to the intracranial region.

II. Inoculation routes of *Str. pneumoniae*

There have been no reports of similar types of SPM with a delayed onset in the absence of CSF rhinorrhea after any other intracranial surgery. However, there has been an increase in the number of reported cases of SPM in patients undergoing cochlear implants.[10] Like our cases, meningitis occurred more than 30 days after surgery in 20 of 29 children with SPM after cochlear implantation. Moreover, the inoculation routes of *Str. pneumoniae* in these cases were considered to occur via three different routes: hematogenously or directly through the middle or inner ear after cochlear implantation. Through experiments in rats, Wei et al.[11] demonstrated that greater numbers of *Str. pneumoniae* were localized to postoperatively regenerated bony and fibrous tissue, and that persistence of the pathogens in these areas can reach the central nervous system via perineural and perivascular spaces that develop SPM after cochlear implantation. This finding is consistent with other studies showing a higher risk of late-onset pneumococcal meningitis after temporal bone fracture.[12]

Therefore, it is plausible that the mechanism of late-onset SPM after TSS is similar to that of patients with cochlear implants or temporal bone fracture.[11,12] *Str. pneumoniae* might localize to postoperatively regenerated bony and fibrous tissue around the sellar floor after TSS, and late-onset meningoencephalitis may have occurred without CSF leakage by *Str. pneumoniae* infection, which then spread either hematogenously or directly to the central nervous system. Moreover, it is conceivable that reduced resistance to infection plays a role in the development of meningoencephalitis, and this might have been an associated factor in our three patients.

III. Clinical meaning of bacterial cultures of sphenoidal sinus

Small segments of sphenoid sinus mucous membranes obtained during surgery were cultured in 316 consecutive patients undergoing TSS or extended TSS for pituitary tumors at Toranomon Hospital between January 2006 and July 2007. From these cultures, 31 various types of bacteria were detected. Moreover, bacterial cultures were positive in 276 (87.3%) patients and *Str. pneumoniae* was not found in any of the patients in this series. Postoperative meningitis occurred in only 2/316 patients (0.63%). In these two patients, nasal bacteria were not found in the culture of the sphenoidal sinus mucous membrane obtained during surgery. Similarly, *Str. pneumoniae* was not found in the culture of the sphenoidal sinus membrane in the two SPM patients that we examined, indicating that BCSM performed during surgery is useless for predicting postoperative meningitis after TSS or for the identification of responsible microorganisms.

IV. Prevention of postoperative SPM

Currently, our three cases with late-onset SPM after TSS confirmed that (1) SPM occurs suddenly in 1 or 2 months after an uneventful postoperative course without any pre-existing signs or symptoms and (2) SPM is not associated with CSF leakage. CEZ or SBTPC were administered as postoperative prophylaxis in our three SPM patients. Both CEZ and SBTPC are sensitive for *Str. pneumoniae* and have a wide spectrum. The first and second generations of cephem and beta-lactam antibiotics are recommended for the prevention of postoperative infections.[13] CEZ is the first generation of cephem and SBTPC is a beta-lactam antibiotic, and both are involved in these groups. Therefore, there appears to be no effective prophylaxis against delayed SPM after TSS. The most important lesson to be learned here is that every neurosurgeon dealing with pituitary lesions should know that this type of postoperative meningitis might occur, although it is extremely rare. In addition, we speculate that our three SPM patients had reduced resistance to infection, as the first case was a child, the second case was a man with moderate anemia because of two TSSs within a short span, and the third was a blue-collar worker who returned to his job immediately after discharge.

A *Str. pneumoniae* vaccine has recently been proven effective in preventing severe pneumonia and meningitis due to this organism.[14,15] Therefore, the preoperative use of a vaccine should be recommended for patients who will require TSS, especially in pediatric patients younger than 5 years, in patients older than 65 years, and in immune-compromised patients. Although there is no definitive evidence that this vaccine can prevent SPM following surgery, this should be taken into account give the seriousness of this condition and the poor prognosis of postoperative SPM.

Conflicts of Interest Disclosure

The authors have no personal, financial, or institutional interest in any of the drugs, or devices in the article. All authors who are members of The Japan Neurosurgical Society (JNS) have registered online Self-reported COI Disclosure Statement Forms through the website for JNS members.

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Address reprint requests to: Nobuyuki Kobayashi, MD, Department of Neurosurgery, Yuuai Memorial Hospital, Higashi-Ushigaya 707, Koga, Ibaraki 306-0232, Japan.
e-mail: nobukb@yomogi.ne.jp

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ORIGINAL ARTICLE

A handmade eye movement monitor using a piezoelectric device during transsphenoidal surgery

Kenichi Oyama · Fusae Kawana · Kazue Suenaga · Noriaki Fukuhara · Shozo Yamada

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Abstract We describe a handmade eye movement monitor featuring a piezoelectric device for use during transsphenoidal surgery (TSS). The sensor consists of a piezoelectric device, condensers, resistors, and several inexpensive parts. Eyeball movements elicited by surgical manipulations during TSS for cavernous sinus tumor are detected by small disc-shaped sensors taped to the eyelids. The responses could be monitored as sharp waves on an electroencephalograph. After we started using this monitor, both the incidence and the severity of cranial nerve injuries during TSS for cavernous sinus tumor decreased. Our device is especially useful at operations to remove functioning pituitary adenomas invading the cavernous sinus and contributes to their favorable endocrine outcomes. None of our patients manifested the postoperative swelling of the eyelids or conjunctival congestion generally seen in patients subjected to the insertion of needle sensors for the acquisition of electromyograms of the extraocular muscles, which is widely used during surgery to identify the cranial nerves responsible for eye movement. Our monitor is less expensive and easier to use than any commercially available sensor devices. As our method does not require the insertion of needle sensors, it is less invasive than electromyography of the extraocular muscles.

Keywords Cavernous sinus · Piezoelectric device · Pituitary adenoma · Transsphenoidal surgery

K. Oyama · N. Fukuhara · S. Yamada
Department of Hypothalamic and Pituitary Surgery, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo 1058470, Japan

F. Kawana
Division of Clinical Physiology, Toranomon Hospital, 2-2-2 Toranomon, Minato-ku, Tokyo 1058470, Japan

S. Yamada
Okinaka Memorial Institute for Medical Research, 2-2-2 Toranomon, Minato-ku, Tokyo 1058470, Japan

K. Suenaga
Japan Sleep Total Health Checkup Association, 6-27-49, Shinjuku, Shinjuku-ku, Tokyo 1600022, Japan

K. Oyama (✉)
Department of Neurological Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 1138603, Japan
e-mail: ko-neuro@nms.ac.jp

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Introduction

Some pituitary adenomas and other sellar and parasellar tumors involve the cavernous sinus, which harbors cranial nerves such as oculomortor, trochlear, and abducens nerves. Consequently, one of the major complications during transsphenoidal surgery (TSS) for cavernous sinus tumors is cranial nerve damage [2, 3]. Electromyograms of extraocular muscles, which are generally used during surgery to identify the cranial nerves responsible for eye movement, are traditionally obtained by needle sensors inserted into the muscles [4]. However, the procedure is cumbersome [1] and may result in postoperative swelling of the eyelids, conjunctival congestion, and inflammation. In addition, needle insertion into the superior oblique muscle innervated by a trochlear nerve is complex. As the earlier monitoring system that used a small, easily applied disc-shaped pressure sensor [3, 5] is no longer available, we developed a small pressure sensor monitor using a piezoelectric device by ourselves.

Materials and methods

Our sensor consists of a piezoelectric device, condensers (0.022 F, 1 F), plastic film, tape, coated wires, small pieces of rubber, and a distributing base; the resistances are 100 kΩ, 1, 1.5, and 5 MΩ. All components are inexpensive and readily available; they are arranged on the distributing base as shown in Fig. 1a. Our prototype (Fig. 1b) detected eye movements induced by manipulation during surgery for cavernous sinus tumors; however, as we found it to be somewhat fragile, we made improvements to render it more durable for frequent use (Fig. 1c).

We maintain total anesthesia by intravenously administering propofol and fentanyl; muscle relaxants are used only for anesthesia induction. A disc-shaped monitor sensor is taped on each eyelid, and two reference electrodes are placed on the forehead and shoulders (Fig. 1d). Eye movements are recorded on an electroencephalograph. The electrical conditions for measurements were the following: amplifier, sensitivity 200 μV/div, high-cut filter 20 Hz, and low-cut filter 0.5 Hz; acquisition, sampling time 500 μs; monitor time 0.5 s/div; and analysis time 0.2 s/div.

Results

Eye movements induced by mechanical stimulation of cranial nerves in the cavernous sinus are detected only by the monitor on the side of surgical manipulation; they manifest as sharp spike waves on the monitor (Fig. 2a). As our monitor detects only eye movements, it is difficult to identify the cranial nerve inducing the movement. Other movements elicited by, for example, touching of the patient, can be differentiated from eye movements because they are picked up by both sensors and exhibited as several similar waves on bilateral recordings (Fig. 2b). We can also detect eye movements induced by electrical stimulation (intensity, 1–2 mA; duration, 0.1 ms) using a monopolar stimulator to distinguish cranial nerves from surrounding fibrous tissues in the cavernous sinus.

After we started using this monitor, the incidence and severity of cranial nerve injuries during TSS for cavernous sinus tumor decreased. Our device is especially useful at operations to remove functioning pituitary adenomas invading the cavernous sinus. Elsewhere [6, 7], we reported the favorable endocrine outcomes without major cranial nerve injuries in patients operated for functioning tumors.

None of the patients in whom we used our monitor experienced the postoperative swelling of the eyelids or conjunctival congestion that is generally observed in patients subjected to needle sensor insertion for electromyography of extraocular muscles. We also used our monitor in two craniotomies via the combined transpetrosal approach to address huge skull base tumors invading around nerves III–VI. In

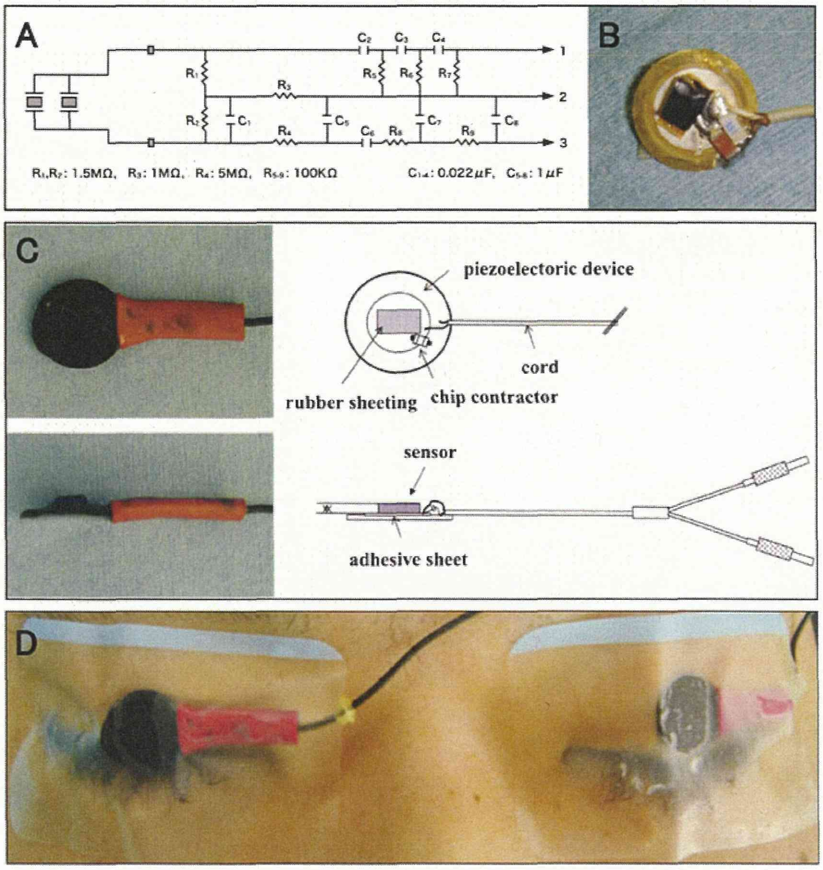


Fig. 1 **a** The sensor consists of a piezoelectric device, plastic film, tape, coated wires, small pieces of rubber, a distributing base, and condensers (0.022 F, 1 F). The resistances are 100 kΩ, 1, 1.5, and 5 MΩ. **b** Prototype of our handmade eye movement monitor. **c** The improved version of our sensor features a plastic cover to increase its durability. **d** Two disc-shaped monitor sensors are taped to the eyelids

Fig. 2 A 37-year-old woman with bitemporal hemianopsia. Her pituitary adenoma invaded the left cavernous sinus. Two recordings were obtained using our eye movement monitor during TSS. **a** Eye movements induced by mechanical stimulation of the cranial nerves in the left cavernous sinus were detected only with the sensor on the *left*. They appear as sharp spike waves on the left (L)-side recording. **b** Large movements elicited by intraoperative actions, e.g., touching of the patient by the surgeon, could be differentiated from eye movements because they were picked up by both sensors and manifested as several similar waves on both right- (R) and left (L)-side recordings

those cases, we were unable to detect eye movements induced by surgical manipulations and both patients suffered postoperative cranial nerve dysfunction.

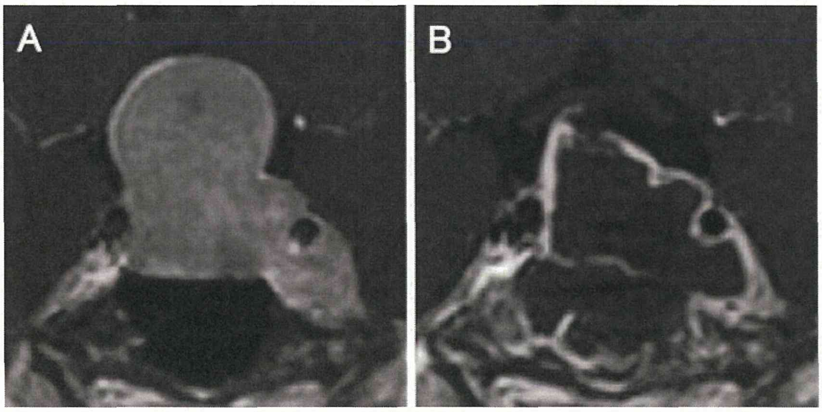
Case presentation

This 37-year-old woman was referred to our hospital with bitemporal hemianopsia. Magnetic resonance imaging (MRI) showed a pituitary macroadenoma invading the left cavernous sinus (Fig. 3a). Using our eye movement monitor, we performed microscopic extended TSS. We opened the anterior–inferior wall of the cavernous sinus to remove the tumor. Upon manipulation of the left cavernous sinus tumor, the monitor displayed spike waves only on the left-side recording (Fig. 2a). As we could identify the abducens nerve on the lateral cavernous sinus wall during the procedure, we were able to preserve it. Postoperative MRI confirmed complete removal of the tumor (Fig. 3b). The patient suffered neither postoperative cranial nerve dysfunction nor eyelid swelling.

Discussion

Intraoperative electromyography, used to identify the cranial nerves responsible for eye movement, requires the insertion or suturing of needle electrodes into extraocular muscles [3, 4]. This cumbersome procedure may result in postoperative swelling of the eyelids, conjunctival congestion, and inflammation. The monitoring system that used a small, easily applied disc-shaped pressure sensor for detecting facial movement induced by surgical manipulation around facial nerves [5] and eyeball movement during cavernous sinus manipulation at TSS [3] is no longer available. Therefore, we developed a small pressure sensor monitor using a piezoelectric device. The highly sensitive pressure sensor makes use of the piezoelectric effect, a phenomenon of ratable polarization induced by pressure. It can detect very weak body vibrations induced by snoring, and at our hospital, it is used to monitor patients with sleep apnea syndrome. We developed a pressure sensor that incorporates an inexpensive piezoelectric device and uses an available electroencephalograph; consequently, it is less costly than any commercially available sensor devices.

Fig. 3 **a** MRI showed a pituitary macroadenoma invading into the left cavernous sinus, and **b** postoperative MRI confirmed a complete removal of the tumor



The original, now unavailable nerve monitor introduced by Shibuya et al. [5] changed the eye movement signal into a sound signal audible by the surgeon. As our monitor does not yet provide this feature, it requires visual monitoring.

The surgical indication for pituitary adenomas invading the cavernous sinus remains controversial. Two major surgical complications of removing cavernous sinus tumor are carotid injury and cranial nerve injuries [2, 3]. As the former is a fatal complication, the option to remove tumors inside the cavernous sinus must be considered very carefully in view of the patient's age and physiological condition, and the biological behavior of the adenoma.

Several nonsurgical options are available for managing pituitary adenomas invading the cavernous sinus, e.g., monitoring the clinical course, medical therapy, radiotherapy, and combinations thereof. In patients, especially with functioning adenomas as seen in Cushing's disease and acromegaly, whose tumors are refractory to nonsurgical treatment, we may choose to remove the cavernous tumor. During its removal, we use a micro-Doppler probe to identify the internal carotid artery and our eye movement monitor to avoid cranial nerve injuries. In the 4-year period from January 2006 to December 2009, we performed 1,252 TSSs for sellar and parasellar lesions. We encountered two carotid injuries (0.16 %), both were in patients with a pituitary adenoma who had undergone earlier surgery at another institution. As we have never experienced carotid injury in patients undergoing their first operation, we stress the importance of exercising the great care when removing residual or recurrent pituitary adenomas invading the cavernous sinus.

Although we found our monitor useful at TSS, this was not the case in operations to treat huge tumors via a combined transpetrosal approach. We think that the sensor moved away from the eyeball when the skin flap was rolled away and consequently could not detect eye movement induced by surgical manipulations. On the other hand, our eye movement monitor may be useful at temporal craniotomies that involve manipulations around the III, IV, and VI nerves when the skin flap is away from the eyelid.

Conclusion

Our eye movement monitor is useful for avoiding cranial nerve injuries associated with cavernous sinus manipulation especially during TSS. It is inexpensive, easy to use, and less invasive than electromyographic monitoring with needle electrodes.

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Comments

William T. Couldwell, Salt Lake City, USA

The authors have developed a piezoelectric device to measure eye movements invoked by nerve irritation during surgery for removal of tumors with cavernous sinus invasion. This is an interesting innovation, and the authors should be congratulated for developing this technique. It avoids using EMG electrodes placed in the ocular musculature.

I believe that this method introduces a practical and inexpensive mechanism to monitor cranial nerve function during TSS or direct intracranial cavernous surgery. I would encourage the authors to follow up with more clinical experience to develop parameters, which would be useful for predicting immediate and long-term outcome of cranial nerve function following manipulation at surgery.

Kalmon D. Post, New York, USA

As endoscopic TSS has become more widespread, so also has removal of intracavernous sinus tumors become more aggressive. Attention has been directed toward the carotid artery and the usage of micro-doppler probes, and stereotactic directed resections have been very helpful in preventing injury. I still strongly believe that even one carotid injury in one hundred patients would be unacceptable.

The authors in this presentation have addressed the other issue of protecting the extraocular movements by protecting the third, fourth, and sixth cranial nerves during cavernous sinus dissections. The device seems effective and relatively inexpensive compared to other choices. It is also less invasive. As more experience is acquired, we shall see whether this type of surgery can be done safely enough to become more widespread. This piezoelectric device for eye movement monitoring may significantly help. However, as I noted above, injury to the carotid artery is completely unacceptable and may increase as surgery through the transsphenoidal route moves lateral to the carotid artery.