

Efficacy of Dural Sealant System for Preventing Brain Shift and Improving Accuracy in Deep Brain Stimulation Surgery

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Abstract

The success of deep brain stimulation (DBS) depends heavily on surgical accuracy, and brain shift is recognized as a significant factor influencing accuracy. We investigated the factors associated with surgical accuracy and showed the effectiveness of a dural sealant system for preventing brain shift in 32 consecutive cases receiving DBS. Thirty-two patients receiving DBS between March 2014 and May 2015 were included in this study. We employed conventional burr hole techniques for the first 18 cases (Group I) and a dural sealant system (DuraSeal) for the subsequent 14 cases (Group II). We measured gaps between the actual positions of electrodes and the predetermined target positions. We then retrospectively evaluated the factors involved in surgical accuracy. The average gap between an electrode's actual and target positions was 1.55 ± 0.83 mm in all cases. Postoperative subdural air volume *e*, the only factor associated with surgical accuracy ($r = 0.536$, $P < 0.0001$), was significantly smaller in Group II (Group I: 43.9 ± 27.7 , Group II: 12.1 ± 12.5 ml, $P = 0.0006$). The average electrode position gap was also significantly smaller in Group II (Group I: 1.77 ± 0.91 , Group II: 1.27 ± 0.59 mm, $P = 0.035$). Use of a dural sealant system could significantly reduce intracranial air volume, which should improve surgical accuracy.

Key words: brain shift, deep brain stimulation, dural sealant system, surgical accuracy

Introduction

The success of stereotactic functional surgery depends heavily on the surgical accuracy with which the target structure is defined and reached. It is essential that the electrodes are placed in their intended positions especially in deep brain stimulation (DBS) surgery. Recently, direct targeting based on Magnetic Resonance Imaging (MRI) has been proposed as a replacement for indirect targeting based on atlas or anatomical landmarks, such as the mid-commissural point (MCP) and red nucleus.^{1–3)} Therefore, it is important that brain shift does not occur, so that all brain structures remain where the images show them. In fact, brain shift has been reported to affect surgical accuracy more significantly than age, preoperative ventricular volume,

or surgery time.^{4–7)} Brain shift mainly occurs due to loss of cerebrospinal fluid (CSF). Various techniques for preventing it have been reported, such as intermittent injection of saline to the burr hole, avoiding CSF suction, or sealing dural defects with fibrin glue or a dural sealant system,⁸⁾ but a sufficiently effective technique has not yet been identified.

In this study of 32 consecutive patients, we show that brain shift was the only factor that affected surgical accuracy and demonstrates the effectiveness of a convenient dural sealant system for preventing brain shift.

Materials and Methods

Patient population

This study was approved by the Ethics Committee of Okayama University Hospital (No. 1703-018). This study examined 32 consecutive patients receiving DBS surgery for the first time in our facility between March 2014 and May 2015. Of these patients, 26 suffered

Received: December 13, 2017; Accepted: February 22, 2018

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from Parkinson's disease, four from tremors and two from dystonia. As a target structure, the subthalamic nucleus (STN) was chosen in 19 cases, the internal segment of the globus pallidus (GPi) in eight cases and the nucleus ventralis intermedius of the thalamus (Vim) in five cases. The first 18 patients were treated using the standard burr hole surgical technique (Group I, Parkinson's disease (PD): 12 cases, tremor: four cases, dystonia: two cases). The subsequent 14 patients were treated with the dural sealant system (Group II, PD: 14 cases). We explored the factors involved in surgical accuracy in these cases including target nuclei, unilateral or bilateral operation, number of punctures, age at the time of surgery, Evans index representing ventricle enlargement, surgery time (whole head procedure time), and postoperative subdural air volume.

Surgical procedure for deep brain stimulation

Gadolinium-enhanced axial T₁- and T₂-weighted images in three directions obtained before surgery by 3-T MRI (GE; Fairfield, CT, USA) were usually used for planning. As a general rule, the target for each operation (STN, GPi, or Vim) was located based on direct visualization of that brain structure using surgical planning computer software (*Framelink* software; Medtronic-Sofamor-Danek, MI, USA). These locations corresponded approximately to the following coordinates from the MCP: STN: 11–12 mm lateral, 2–3 mm posterior, and 4 mm inferior; GPi: 20–22 mm lateral, 3–5 mm anterior, and 2–4 mm inferior; Vim: 13–14 mm lateral, 3–5 mm posterior, and 0 mm inferior. Our routine procedure was as follows: the stereotactic frame (Leksell G model, Elekta; Stockholm, Sweden) was placed under local anesthesia with propofol (1 mg/kg). A CT scan was then performed after the localizer was attached to the frame. After that, the surgery was started with the patient's head elevated about 30 degrees so that the patient does not feel comfortable. The entry point was approximately 2 cm anterior and 4 cm lateral from the bregma to ensure that the trajectory would avoid the cortical veins, sulcus and lateral ventricle. After a 4 cm curvilinear skin incision was made at the entry point, the burr hole was made. The stereotactic arc and a customized long cannula and manipulator (YMF Yamashita Factory; Saitama) were fixed. The patient was then X-rayed with the attached device (ASAHI ROENTGEN, Kyoto) in the A–P and lateral directions in order to make fine adjustments to the targeting, and finally, the dura mater was opened. 5 mm diameter hole was made in the dura mater in order to prevent the CSF from flowing out just prior to electrode insertion. We used single track microelectrode recording (MER)

to search for neuronal activity except in the case of Vim-DBS. We also performed test stimulation to confirm the improvement of motor symptoms. After the microelectrode was placed, the DBS electrodes were stabilized with a Stimloc anchoring device and burr hole cover (Medtronic). Finally, an implantable programmable generator (IPG) was embedded subcutaneously on both sides of the anterior chest under general anesthesia.

Conventional burr hole technique (Group I)

After creating the 5 mm diameter hole in the dura mater and cauterizing the cortical surface, we immediately started MER examination. We tried not to suction outflowing CSF or fill empty space with saline.

Burr hole technique with dural sealant system (Group II)

After cauterizing the dura mater and setting the microelectrode, the 5 mm diameter hole was created in the dura mater without damaging the arachnoid or the pia mater, as in Group I. Subsequently, just after the cortical surface by 4 mm diameter was cauterized in preparation for the re-puncture, it was covered with Duraseal (1 ml, INTEGRA Life-Sciences, Plainsboro, NJ, USA) (Figs. 1A and 1B). The needle electrode for MER was then inserted. When re-puncture was needed, the first application of Duraseal was not removed.

Measurement of postoperative intracranial air volume

Computed tomography performed on the day after surgery was used to analyze intracranial air volume. The bilateral air volume was measured by iPlan (Brainlab AG; Feldkirchen, Germany).⁹⁾

Measurement of the gap between electrode and predetermined optimal target

For this measurement, we used a fusion image of preoperative MRI and postoperative CT obtained 3 months after the surgery. The location of each electrode was identified from MCP which was determined at the time of surgery. The gap between each electrode and its predetermined optimal target was measured in the lateral, A–P and vertical directions as well as directly. We used a calculation formula $(\Delta X^2 + \Delta Y^2 + \Delta Z^2)^{1/2}$ which derive the distance of two points on a 3D plane to measure true gap.

Statistical analysis

The relations between true gap and postoperative subdural air volume, age at the time of surgery, Evans index, and surgery time were analyzed with Pearson's correlation. Comparisons between two groups were analyzed with Student's *t*-test.

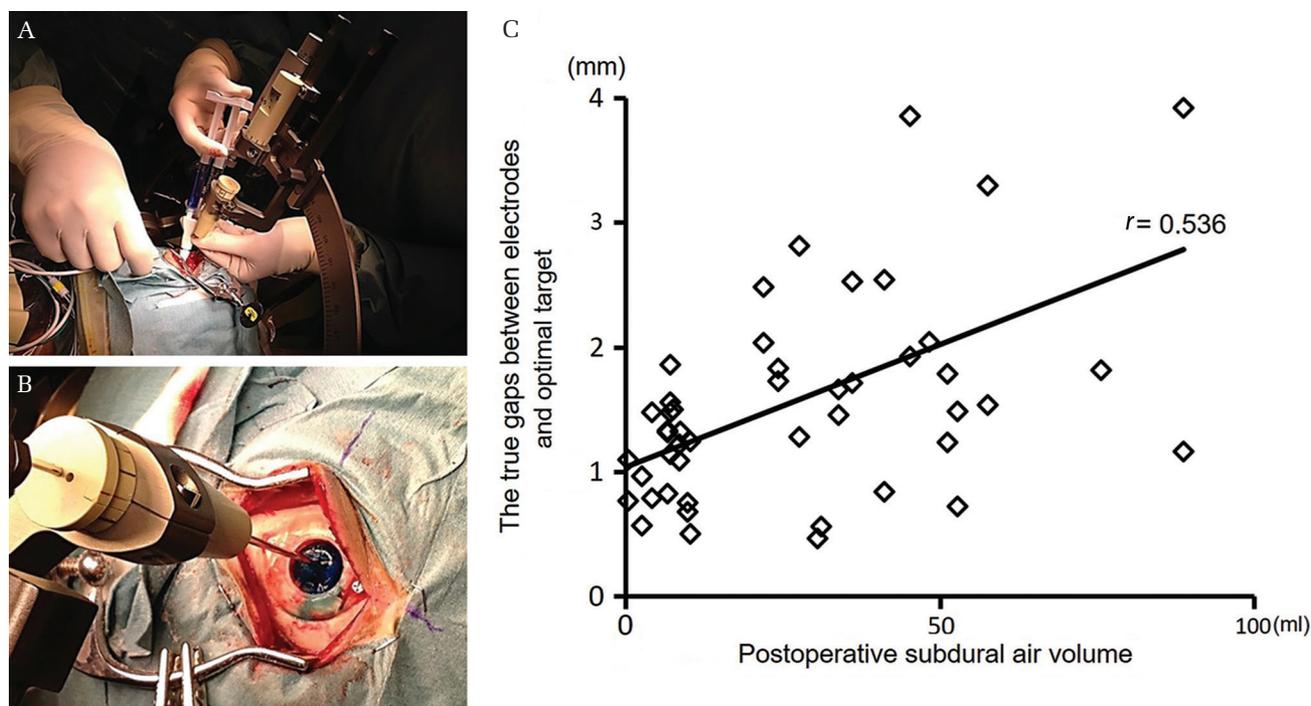


Fig. 1 (A) Typical method of dural sealant system (DuraSeal) application: DuraSeal was sprayed into the burr hole after the dura mater was opened. Later, the blue gel-like (B) DuraSeal was packed into the burr hole. (C) Correlation of surgical accuracy with postoperative subdural air volume. A positive correlation between surgical accuracy and postoperative subdural air volume was observed (correlation coefficient: $r = 0.536$, contribution ratio: $r^2 = 0.28$, $P < 0.0001$).

Comparisons among three groups were analyzed with one-factor ANOVA. P values less than 0.05 were considered to be significant. Mean values are presented \pm standard deviation (SD).

Results

Postoperative subdural air volume was the sole factor associated with surgical accuracy

The average true gap between electrodes and optimal targets was 1.27 ± 0.59 mm in all cases. The postoperative subdural air volume was the sole factor associated with surgical accuracy (correlation coefficient: $r = 0.536$, contribution ratio: $r^2 = 0.28$, $P < 0.0001$, Fig. 1C). There was no correlation with target nucleus ($P = 0.14$), bilateral operation ($P = 0.27$), number of puncture trial ($P = 0.34$), age at the time of surgery ($P = 0.37$), Evans index ($P = 0.56$), or surgery time ($P = 0.09$) (Table 1).

Dural sealant system decreased postoperative subdural air volume

The postoperative subdural air volume was significantly smaller in Group I (12.1 ± 12.5 and 43.9 ± 27.7 ml in Groups I and II, respectively, Student's t -test: $P = 0.0006$, Fig. 2). There were no significant

differences between the two groups with respect to target nucleus (Group I, STN: 10, GPi: 4, Vim: 4; Group II, STN: 9, GPi: 4, Vim: 1, $P = 0.50$), unilateral or bilateral operation (Group I, both sides: 12, one side: 6; Group II, both sides: 11, one side: 3, $P = 0.46$), number of punctures (Group I, single puncture: 27, two or more: 3; Group II, single puncture: 23, two or more: 2, $P = 0.80$), age at time of surgery (Group I: 65.7 ± 8.9 , Group II: 60.9 ± 9.6 , $P = 0.16$), Evans index (Group I: 0.27 ± 0.03 , Group II: 0.27 ± 0.02 , $P = 0.73$) or surgery time (Group I: 222 ± 60 , Group II: 238 ± 56 min, $P = 0.45$) (Table 2).

Dural sealant system reduced the gaps between electrodes and optimal targets

The gaps between electrodes and predetermined optimal targets in all cases were 0.59 ± 0.38 mm in the lateral direction, 0.84 ± 0.50 mm in A-P, and 0.41 ± 0.29 mm in vertical. The gap was significantly smaller in Group I than in Group II (lateral: 0.80 ± 0.68 and 0.59 ± 0.37 mm, A-P: 1.13 ± 0.83 and 0.83 ± 0.49 mm, vertical: 0.81 ± 0.53 and 0.41 ± 0.29 mm, and true gap: 1.77 ± 0.91 and 1.27 ± 0.59 mm in Groups I and II, respectively, Student's t -test: $P = 0.21$, 0.15, 0.0036, and 0.034 in lateral, A-P, vertical, and true gap, respectively, Fig. 3).

Table 1 Clinical profiles of 32 patients and correlation of factors associated with surgical accuracy

	Results (32 cases, 55 sides)	<i>P</i>	<i>r</i>
Target nuclei	STN: 1.81 ± 0.84 (19 cases) GPI: 1.58 ± 0.89 (8 cases) Vim: 0.84 ± 0.46 mm (5 cases)	0.14	
Sides	Both sides: 1.60 ± 0.85 (23 cases) Single side: 1.20 ± 0.60 mm (9 cases)	0.27	
Number of punctures	Single puncture: 1.52 ± 0.84 (43 sides) Two or more punctures: 1.91 ± 0.96 mm (5 sides)	0.34	
Age (years)	63.6 ± 9.5	0.37	0.13
Evans index	0.27 ± 0.02	0.56	-0.085
Surgery time (min)	229 ± 59	0.09	0.24
Postoperative air volume (ml)	30.1 ± 27	<0.0001	0.54

Surgical accuracy was assessed by measuring the true gaps between electrodes and predetermined optimal target. GPI: globus pallidus, *r*: correlation coefficient, STN: Subthalamic nucleus, Vim: ventralis intermedius.

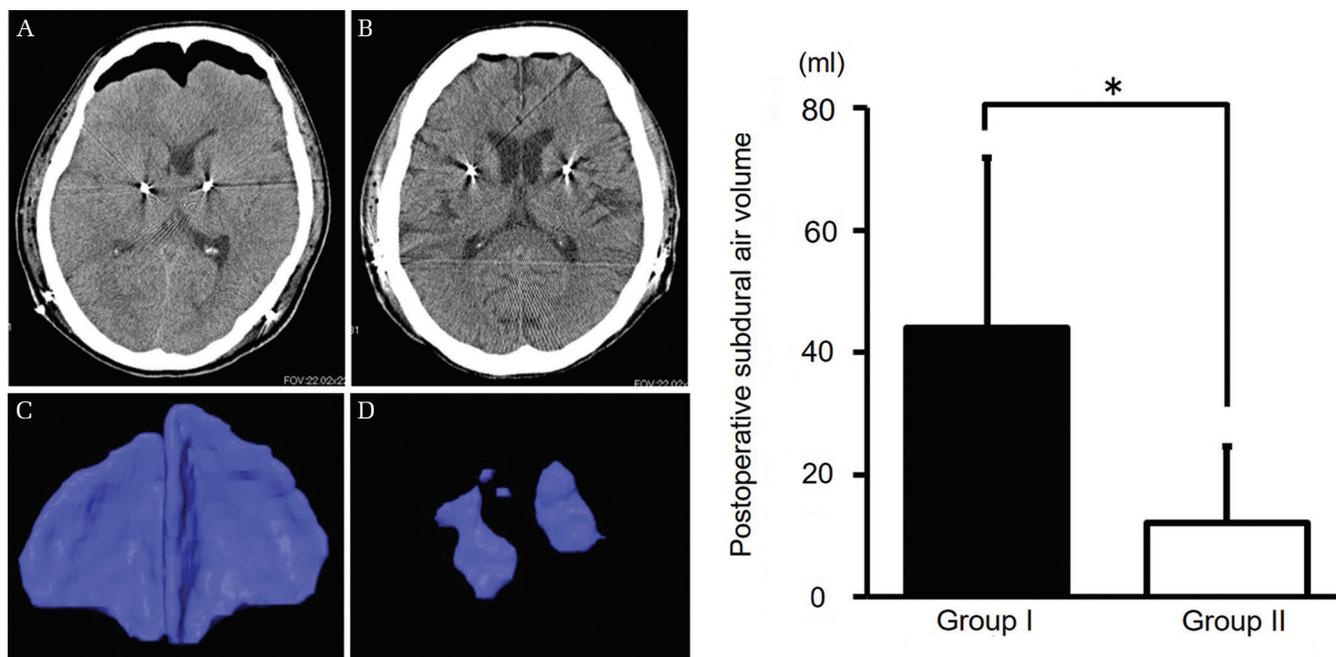


Fig. 2 Comparison of postoperative subdural air volume between the two treatment groups. Based on postoperative CT (A, B), air volume was three-dimensionally modeled using iPlan (C, D) (left: Group I, right: Group II). The postoperative subdural air volume was significantly smaller in Group I (12.1 ± 12.5 and 43.9 ± 27.7 ml in Groups I and II, respectively, Student's *t*-test; **P* = 0.0006).

Discussion

Brain shift as the greatest factor involved in surgical accuracy

In this study, we explored the factors that influenced the accuracy of DBS surgery and showed

that the brain shift was the sole significant factor, as a previous study also demonstrated.^{4-6,10,11} Postoperative intracranial air volume was significantly correlated with shift of the anterior commissure.⁶ The contralateral shift of the anterior and posterior commissures (AC-PC) line in the unilateral surgery

Table 2 Patient characteristics

	Group I (18 cases, 30 sides)	Group II (14 cases, 25 sides)	<i>P</i>
Target nuclei	STN: 10 GPi: 4 Vim: 4	STN: 9, GPi: 4, Vim: 1	0.50
Sides	Both sides: 12, Single side: 6	Both sides: 11, Single side: 3	0.46
Number of punctures	Single puncture: 27 Two or more punctures: 3	Single puncture: 23 Two or more: 2	0.80
Age (years)	65.7 ± 8.9	60.9 ± 9.6	0.16
Evans Index	0.27 ± 0.03	0.27 ± 0.02	0.73
Surgery time (min)	222 ± 60	238 ± 56	0.45

GPi: globus pallidus, STN: Subthalamic nucleus, Vim: ventralis intermedius.

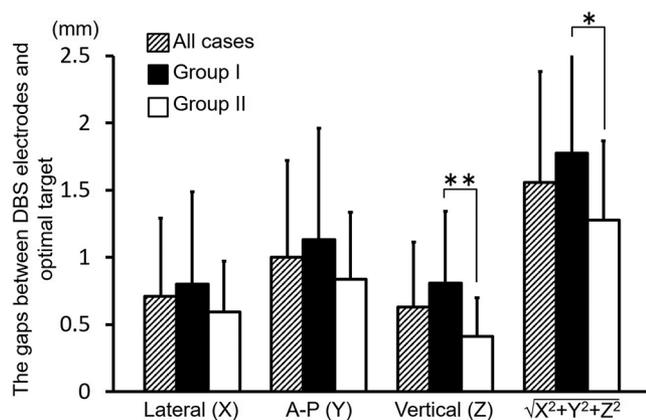


Fig. 3 Gaps between the deep brain stimulation (DBS) electrodes and their predetermined optimal targets. The graph shows the gaps between DBS electrodes and their predetermined optimal targets in the lateral, A-P, vertical and true gaps. The gaps were significantly smaller in Group II than in Group I in terms of true gap and the Z-direction (* $P < 0.05$, ** $P < 0.01$).

and the posterior shift of the AC–PC line in bilateral surgery have been described as developing due to intracranial air invasion.⁴⁾ The DBS electrodes moved on average 3.3 ± 2.5 mm upward along the trajectory with the disappearance of the subdural air. The degree of this displacement was significantly correlated with the amount of post-operative subdural air.⁵⁾ Our result was consistent with those of previous reports. Once the brain had shifted, electrode placement at the intended position became difficult. There have been few reports of concrete solutions for this issue. To counteract observed upward lead displacement, some surgeons have implanted DBS electrodes one contact deeper

than the most ventral point with good response to test stimulation.⁵⁾ In case of significant brain shift, multiple trajectories may be necessary to target the STN accurately.¹¹⁾ Yet multiple trajectories could increase risks such as bleeding, and compensatory adjustments are not necessarily effective in all cases. Therefore, it is primarily important to prevent CSF outflow and brain shift.

Prevention of CSF outflow and brain shift

Brain shift may be caused by CSF outflow and intracranial air invasion following postural movement of brain structure under the influence of gravity. Cerebrospinal fluid flows out when the dura mater and pia mater are opened due to the difference between intracranial pressure and outside air pressure. Additionally, any increase in intracranial pressure due to physiological phenomena such as coughing can encourage the outflow of CSF. Many studies have reported experimental methods of preventing the outflow of CSF and subsequent brain shift. Cerebrospinal fluid outflow is conventionally decreased by minimizing defects in the dura mater and surgery time, maintaining constant saline irrigation of the burr hole,¹⁾ avoiding CSF suction,¹²⁾ and placing patients in a semi-sitting position during surgery.⁵⁾ Burr hole size does not appear to alter the severity of brain shift.⁹⁾ Many PD patients have postural abnormalities and taking an ideal surgical position is often difficult. Shortening surgery time is also important and it might not be short in this study. During the test stimulation, the improvement of rigidity or akinesia of each joint is evaluated in cases with PD. Additionally, the suppression of tremor at writing and at rest is also evaluated in cases with tremor. It takes about an hour to capture the microelectrode

recording, perform the test stimulation and replace the DBS electrodes carefully after opening the dura mater. Even with extreme caution, it is difficult to completely eliminate brain shift using these classical burr hole techniques alone. In our opinion, physically sealing the dural mater defects is the most effective method. In another study, subcortical brain shift was limited by an image-guided approach and a surgical technique involving a radiofrequency probe and fibrin glue,¹³⁾ but MER was not used in that study, whereas we routinely used and rely heavily on the results of intraoperative physiological testing with MER or test stimulation. Another group also showed the efficacy of sealing dural defects using saline-soaked collagen pieces and fibrin sealant.¹⁴⁾

The usefulness of Duraseal: In our experience using a dural sealant system, dramatically reduced both CSF outflow and brain shift and improve surgical accuracy. The gaps between electrodes and their optimal targets were significantly smaller in both the Z-direction and the true gap measurement than those seen after using conventional burr hole techniques. This result is particularly striking given that the patients' heads were elevated to some extent during surgery, and under these conditions the brain might be expected to shift in the Y- or Z-direction due to the influence of gravity. It was similar to the previous report that MCP shifted mainly in the posterior direction after DBS surgery whereas the comparison target are different.⁷⁾ This dural sealant system has been used in craniotomy and spinal surgery for watertight dural repair. The safety and efficacy of Duraseal has already been shown.^{15–19)} In burr hole surgery, it is possible to reduce the postoperative air volume to 1.3 ± 1.5 ml using Duraseal in STN-DBS.⁸⁾ The burr hole technique used in that study was substantially the same as our technique, though the position of the electrodes was not evaluated afterward. Furthermore, re-puncture, which may increase the risk of CSF outflow, can be performed without brain shift using this system. Additionally, it is very important that this simple technique with dural sealant system enables to perform MER and test stimulation in detail without worrying about the brain shift. There are some limitations in this retrospective study. The overall number of patients in this study was small. Furthermore, improvements in clinical symptoms could not be compared because the underlying diseases varied among patients. Nevertheless, as the study was conducted over a short period of time with consecutive patients and the same surgical procedure excepting the use or nonuse of the dural sealant system, the results are

undoubtedly reliable and the dural sealant system can be recommended with confidence.

Conclusions

In this patient series, brain shift was the only factor that affected surgical accuracy. The dural sealant system appears to be essential for the reduction of CSF outflow. Our simple technique using the dural sealant system is expected to significantly reduce intracranial air volume in DBS surgery, enabling improved surgical accuracy.

Acknowledgments

TS, TA, KK, IK, MO, SS, and AS performed the study. TS, TA, MK, and TY designed the work. TS analyzed the data. TS, TA, MK, TY and ID wrote the paper.

Conflicts of Interest Disclosure

All authors have no conflicts of interest.

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