Multiple Intraoperative Monitoring-assisted Microneurosurgical Treatment for Anterior Circulation Cerebral Aneurysm

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This study investigated the efficacy of multiple intraoperative monitoring techniques including indocyanine green angiography (ICGA), somatosensory evoked potential (SSEP) and motor evoked potential (MEP) in the clinical outcome of microneurosurgical treatment for anterior circulation cerebral aneurysm. Fifty-two anterior circulation cerebral aneurysms (Hunt and Hess [H&H] grades 0, 1 or 2) from 45 Chinese in-patients were completely clipped. In one patient, ICGA directed neurosurgeons to readjust aneurysmal clips in order to eliminate a residual aneurysm and restore patency of a branching artery. SSEP/MEP directed neurosurgeons to implement intervention measures in 12 patients for recovery of SSEP/MEP changes, and SSEP/MEP changes partially/ totally recovered in 11 of these 12 patients (91.6%). Postoperative motor deficits were observed in three patients, two of which were Glasgow Outcome Scale level 3 (4.4%). In conclusion, for patients with anterior circulation cerebral aneurysm (H&H grade < 3), multiple intraoperative monitoring was beneficial for finding residual aneurysms, detecting ischaemic events in the perforating arteries and reducing severe postoperative motor deficiency.

**KEY WORDS:** Cerebral aneurysm; Microsurgery; Indocyanine green angiography; Somatosensory evoked potential; Motor evoked potential

**Introduction**

Recurrence after surgical treatment and perforating artery blood flow disturbance are two major causes of postoperative complications in cerebral aneurysms. Among patients with cerebral aneurysm, 5.2% have been found to exhibit residual aneurysms and 4.4% experience cerebral infarction because of blood flow disturbance in perforating arteries after microneurosurgical treatment.¹,² To our knowledge, however, only a few studies have examined the methods for direct and rapid detection of residual aneurysms and the prediction of ischaemic events.

The aim of the present retrospective study was to determine the efficacy of indocyanine green angiography (ICGA), somatosensory evoked potential (SSEP) and motor evoked potential (MEP) for the real-time detection of residual aneurysms and prediction of perforating artery ischaemia during microneurosurgical treatment for cerebral aneurysm.
Patients and methods

PATIENT POPULATION
This retrospective study enrolled consecutive patients with an anterior circulation aneurysm who underwent multiple intraoperative monitoring-assisted microneurosurgical treatment at the Department of Neurosurgery, Beijing Tiantan Hospital affiliated to Capital Medical University, Beijing, China, between January and August 2010. All patients were admitted from the Outpatient Department and included cases of subarachnoid haemorrhage (SAH) and cerebral aneurysm space-occupying symptoms (visual decrease, visual field defect, oculomotor palsy, headache), as well as cases revealed during routine examination. On admission, all patients were graded according to the Hunt and Hess (H&H) scale; grade 0, unruptured aneurysm; grade 1, asymptomatic, mild headache, slight nuchal rigidity; grade 2, moderate to severe headache, nuchal rigidity, no neurological deficit other than cranial nerve palsy; grade 3, drowsiness/confusion, mild focal neurological deficit; grade 4, stupor, moderate to severe hemiparesis; and grade 5, coma, decerebrate posturing. To evaluate the general condition of the cerebral tissue and ventricular system, all patients underwent a cranio-cerebral computed tomography (CT) scan on admission. Prior to operation, all patients underwent whole-brain vessel digital subtraction angiography (DSA) to determine the size and location of the aneurysm.

For neurosurgical monitoring, ICGA, SSEP and MEP were approved by the Ethics Committee of Capital Medical University and written consent for ICGA, SSEP and MEP was included in the written authorization for microneurosurgical treatment signed by each patient and their direct relatives.

SURGICAL PROCEDURES
Total vein anaesthesia was used for all patients and muscle relaxant administration was prohibited after intubation. For craniotomy, a pterional approach was used. For patients with multiple cerebral aneurysms, the culprit aneurysm for SAH was treated as the priority. The parent artery was temporarily occluded for dissociating and clipping complex or ruptured aneurysms. Yasargil® aneurysm clips (Aesculap, Tuttinglen, Germany) were selected for clipping the aneurysms.

MULTIPLE INTRAOPERATIVE MONITORING
Pentero® (Carl Zeiss Meditec, Oberkochen, Germany) and Leica OH4 (Leica Microsystems, Wetzlar, Germany) fluorescent microscopes were used for microneurosurgical management. Indocyanine green saline solution (5 mg/ml, 0.5 mg/kg) was injected into the femoral vein by bolus. After the aneurysm was completely exposed, ICGA was performed to examine the aneurysm and assess the basic blood flow status of the parent, branching and perforating arteries. After microneurosurgical management was suspended or finished, ICGA was performed to examine the aneurysm clipping and to re-evaluate the patency of the parent, branching and perforating arteries. If a residual aneurysm was detected, aneurysmal clips were re-adjusted until it was confirmed by repeated ICGA to be eliminated. When decreased arterial patency was detected, aneurysmal clips were re-adjusted and nimodipine solution (0.02 mg/ml) was applied topically until restored arterial patency was confirmed by repeated ICGA.

A Nicolet Endeavor 16 channel desktop intraoperative monitoring system (Nicolet Instruments, Madison, WI, USA) was used for SSEP and MEP monitoring. Standard surface
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electroencephalography electrodes were located according to the international 10–20 electrode placement system. Baseline SSEP and MEP data were obtained before the dura mater was resected. SSEP and MEP changes (amplitude decrease, latency increase or waveform loss) were compared with baseline readings. Intervention measures for SSEP and MEP recovery included suspending aneurysm clipping, dismantling the temporary occlusion of the parent artery and topical application of nimodipine solution for 10 min within the operation field. Once SSEP/MEP changes were detected, microneurosurgical management was suspended within 1.5 min in order to implement instant intervention measures. When the parent artery was temporarily occluded for removing an intra-aneurysmal thrombus, reconstructing the parent artery, clipping a ruptured aneurysm or clipping a disassociating complex aneurysm, delayed intervention measures were implemented for SSEP/MEP recovery after microneurosurgical management was finished. Neurosurgeons resumed microneurosurgical management when SSEP/MEP began to recover or failed to recover within 10 min after implementing the intervention measures. Total recovery of SSEP/MEP was defined as a changed waveform or when latency returned to baseline level after the topical application of nimodipine solution 10 min following completion of microneurosurgical management. Partial recovery of SSEP/MEP was defined as a changed waveform or when latency had begun to recover, yet failed to return to baseline level after the topical application of nimodipine solution 10 min following completion of microneurosurgical management.

POSTOPERATIVE EVALUATION
All patients underwent a craniocerebral CT scan on the first day after operation and on discharge. They also all underwent whole-brain vessel DSA to evaluate the outcome of microneurosurgical treatment and patency of the parent and branching arteries at 1 week after operation. For all patients at discharge, muscle power was evaluated by the Medical Research Council (MRC) Scale for Muscle Strength and clinical outcome was assessed by the Glasgow Outcome Scale (GOS).

STATISTICAL ANALYSES
Statistical analyses were carried out using the SPSS® statistical package, version 13.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Data were analysed using the McNemar test. A P-value < 0.05 was considered to be statistically significant.

Results
PATIENT POPULATION
In total 45 patients with anterior circulation cerebral aneurysms were included in the study (21 males, 24 females; mean ± SD age 48 ± 11 years [range 23 – 69 years]) and underwent multiple intraoperative monitoring-assisted microneurosurgical treatment. There were 21 cases of SAH, four of cerebral aneurysm space-occupying symptoms and 20 cases were identified during routine examination. The H&H scale on admission was grade 0 in 24 cases, grade 1 in 16 cases and grade 2 in five cases.

LOCATION AND SIZE OF ANEURYSMS
In total 52 aneurysms were identified and these were located in the middle cerebral artery (MCA) in 20 cases, the anterior communicating artery (ACoA) in 10 cases, the internal carotid artery (ICA) bifurcation in seven cases, the posterior communicating artery (PCoA) in six cases, the carotid-ophthalmic artery (COA) in six cases, the
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antior choroidal artery in two cases and the anterior cerebral artery (ACA) in one case. The sizes of aneurysms, defined by preoperative whole-brain vessel DSA were: giant (diameter ≥ 25 mm) in seven cases; large (diameter 10 – 25 mm) in 10 cases; and small (diameter ≤ 10 mm) in 35 cases. The mean ± SD diameter of the 52 cerebral aneurysms was 11.5 ± 8.1 mm.

MICRONEUROSURGICAL RESULTS

All 52 aneurysms were clipped in 45 operations (one operation per patient). Sixteen patients underwent temporary occlusion of the parent artery during microneurosurgical treatment, with a mean ± SD occlusion time of 5.3 ± 3.3 min (range 1 – 10 min). Postoperative whole-brain vessel DSA confirmed that the 52 aneurysms had been completely clipped and that all parent and branching arteries were patent.

MULTIPLE INTRAOPERATIVE MONITORING AND CLINICAL OUTCOME

In one patient with a COA aneurysm, ICGA found a residual aneurysm and directed the neurosurgeon to eliminate this (Fig. 1); no postoperative neural deficiency was observed. ICGA confirmed complete clipping of aneurysms in the other 44 cases studied. Changes in SSEP/MEP during microneurosurgery directed neurosurgeons to implement instant intervention in seven patients and postoperative motor deficiencies were observed in two patients (Table 1). SSEP/MEP changes directed implementation of delayed intervention in four patients and no postoperative motor deficiencies were found in these cases (Table 2). In another patient with a COA aneurysm, ICGA detected a blood flow decrease in the MCA branches and directed the neurosurgeon to restore their patency (Fig. 2), while SSEP/MEP detected ensuing decreased SSEP/MEP and directed the neurosurgeon to implement delayed intervention measures (Fig. 3); no postoperative neural deficiency was observed. The other 32 patients showed no abnormal discoveries using multiple intraoperative monitoring; among these patients there was one case of postoperative contralateral motor deficiency (grade 4 on the MRC Scale for Muscle Strength5,6 – active movement against gravity and resistance).

COMPARATIVE EFFECTIVENESS OF ICGA AND SSEP/MEP

Comparison between ICGA and SSEP/MEP revealed that SSEP/MEP was significantly more effective than ICGA in detecting ischaemic events in patients undergoing microneurosurgical treatment for anterior circulation cerebral aneurysm (P < 0.001; McNemar test; Table 3).

Discussion

Residual aneurysm accounts for recurrent cerebral aneurysm in 2.9% of patients with cerebral aneurysm receiving neurosurgical management,7,8 and can result in compression effects and recurrent SAH with fatal consequences.9,10 For perforating arteries, once occluded or injured, their lumen might fail to expand after removal of the aneurysmal clip or recanalization of the parent artery and even a small reduction in blood flow in a large major artery might result in severe ischaemia in the peripheral territory of perforating arteries.11,12 Stenosis of the parent artery as a result of aneurysm clipping, temporary occlusion of the parent artery and direct injury are the most common causes of impaired blood flow in perforating arteries during neurosurgical treatment for cerebral aneurysm.2 Furthermore, cerebral vasospasm affecting the complete arterial system of the Willis...
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circle has been shown to impair autoregulatory vasodilation and minimize the luminal calibre of intraparenchymal vessels during cerebral ischaemia.\textsuperscript{13,14} Accordingly, a considerable number of cases are accompanied by cerebral infarction because of perforating artery blood flow disturbance. Thus, complete clipping of the cerebral aneurysm and preservation of perforating artery blood flow are two critical tasks in the microneurosurgical management of cerebral aneurysm.

For the detection of residual cerebral aneurysm and blood flow disturbances in branching and perforating arteries during the neurosurgical management of cerebral

FIGURE 1: Role of indocyanine green angiography (ICGA) in directing the neurosurgeon to eliminate a residual aneurysmal neck by readjusting aneurysmal clips. (A) Left-side carotid-ophthalmic artery (COA) aneurysm shown by whole-brain vessel digital subtraction angiography (DSA). (B) Left-side COA aneurysm exposed. (C) Aneurysmal neck revealed by ICGA. (D) Placement of aneurysmal clip. (E) Residual aneurysmal neck revealed by ICGA. (F) Fibrous tissue of the aneurysm removed. (G) Placement of another aneurysmal clip. (H) Repeat ICGA showing that the residual aneurysmal neck had been eliminated. (I) Postoperative whole-brain vessel DSA showing that the aneurysm was completely clipped and the parent/branching arteries were patent.
# TABLE 1:
Clinical outcome of patients receiving instant intervention measures after changes in somatosensory evoked potential (SSEP) / motor evoked potential (MEP) during microneurosurgical treatment for anterior circulation cerebral aneurysm

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years), sex</th>
<th>Aneurysm location</th>
<th>Temporary occlusion</th>
<th>SSEP changes/ recovery</th>
<th>MEP changes/ recovery</th>
<th>Postoperative contralateral muscle strength</th>
<th>Postoperative cerebral infarction</th>
<th>Glasgow Outcome Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>53, male</td>
<td>Left MCA</td>
<td>–</td>
<td>Left decrease/–</td>
<td>–</td>
<td>0</td>
<td>Left basal ganglia</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>36, female</td>
<td>Left MCA</td>
<td>(Left MCA) 3 min</td>
<td>Left decrease/–</td>
<td>Right loss/partial</td>
<td>1</td>
<td>Left frontal lobe &amp; left basal ganglia</td>
<td>3</td>
</tr>
<tr>
<td>3</td>
<td>47, female</td>
<td>Left ACoA</td>
<td>–</td>
<td>Left decrease/ complete</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>38, male</td>
<td>Right ICA</td>
<td>–</td>
<td>Left decrease/ complete</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>5</td>
<td>47, female</td>
<td>Left MCA</td>
<td>(Left MCA) 2.5 min/1.5 min</td>
<td>Right decrease/partial</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>6</td>
<td>56, female</td>
<td>Right MCA</td>
<td>(Right MCA) 2 min</td>
<td>Left decrease/ complete</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>7</td>
<td>42, female</td>
<td>Right ACoA</td>
<td>(Right ACA) 3 min/7 min/10 min</td>
<td>Left decrease/ complete</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
</tbody>
</table>

*Medical Research Council Scale for Muscle Strength. MCA, middle cerebral artery; ACoA, anterior communicating artery; ICA, internal carotid artery; ACA, anterior cerebral artery.
### TABLE 2:
Clinical outcome of patients receiving delayed intervention measures after changes in somatosensory evoked potential (SSEP) / motor evoked potential (MEP) during microneurosurgical treatment for anterior circulation cerebral aneurysm

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years), sex</th>
<th>Aneurysm location</th>
<th>Temporary occlusion</th>
<th>SSEP changes / recovery</th>
<th>MEP changes / recovery</th>
<th>Postoperative contralateral muscle strength</th>
<th>Postoperative cerebral infarction</th>
<th>Glasgow Outcome Scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32, female</td>
<td>Right MCA</td>
<td>(Right MCA) 10 min</td>
<td>–</td>
<td>Left loss / complete</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>2</td>
<td>62, female</td>
<td>Right ACoA</td>
<td>(Right ACA) 5 min</td>
<td>Left decrease / complete</td>
<td>Left decrease / complete</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>3</td>
<td>48, male</td>
<td>Right ACoA and Right MCA</td>
<td>(Bilateral ACA) 9 min</td>
<td>Right decrease / complete</td>
<td>–</td>
<td>V</td>
<td>–</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>24, male</td>
<td>Left MCA</td>
<td>(Left MCA) 10 min</td>
<td>–</td>
<td>Right loss / complete</td>
<td>V</td>
<td>Multiple lacunar infarctions</td>
<td>5</td>
</tr>
</tbody>
</table>

*Medical Research Council Scale for Muscle Strength.5,6
MCA, middle cerebral artery; ACoA, anterior communicating artery; ACA, anterior cerebral artery.
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Compared with intraoperative DSA, ICGA is safe and feasible for intraoperative monitoring because no radioactivity is involved, it is non-invasive and has a lower cost. Furthermore, ICGA has been shown to provide visualization of the silhouette of residual aneurysms and is able to direct neurosurgeons to eliminate them accurately.

In the present study, ICGA directed neurosurgeons to eliminate a residual aneurysm in one case and confirmed complete clipping of aneurysms in the other 44 cases studied. Postoperative DSA confirmed that all aneurysms were completely clipped; thus, ICGA was effective in eliminating the risks of residual aneurysm.

With respect to the preservation of blood flow, ICGA could detect minor decreases in blood flow of the exposed parent and

FIGURE 2: Role of indocyanine green angiography (ICGA) in directing the neurosurgeon to restore the patency of branching arteries by readjusting aneurysmal clips. (A) Right-side carotid-ophthalmic artery aneurysm exposed. (B) Intra-aneurysmal thrombus revealed by ICGA. (C) Gradual removal of the thrombosis. (D) Placement of aneurysmal clips. (E) Decreased patency of middle cerebral artery (MCA) branches revealed by ICGA. (F) Readjustment of aneurysmal clips. (G) Repeat ICGA showed that MCA branches were patent.
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perforating arteries in the focal operation field in real time. Thus, ICGA was able to direct neurosurgeons to implement intervention measures in real time to prevent iatrogenic ischaemic events in the focal operation field. In the present study, ICGA directed neurosurgeons to restore patency of branching arteries at the focal operation field in one patient, and prevented a decrease in blood flow of branching and perforating arteries at the focal operation field in the other 44 patients. Thus, ICGA contributed to the restoration and preservation of patency of parent and branching arteries at the focal operation field, thereby preventing related ischaemic events.

It was not possible, however, to use ICGA to evaluate cerebral blood flow supply based upon neural function or to detect blood flow changes beyond the focal operative area. In the present study, SSEP/MEP detected changes after decreased patency of branching arteries at the focal operation field were restored in one patient. Furthermore, comparison of ICGA and evoked potentials in detecting ischaemic events indicated significant differences;

FIGURE 3: Role of somatosensory evoked potential (SSEP) and motor evoked potential (MEP) in directing the neurosurgeon to reverse ischaemic events by implementing intervention measures. SSEP: (A, left) P15–N20–P25 complex of the left upper extremity decreased (9) and returned to baseline level (35) after intervention measures were implemented; (A, right) N35–P40–N55 complex of the left lower extremity decreased (19) and returned to baseline level (21) after intervention measures were implemented. MEP: (B, left) P1–N1 complex of the left upper extremity decreased (13:54:26) and recovered partially (13:57:59) after intervention measures were implemented. (B, right) P2–N2 complex of the left lower extremity decreased (13:54:26) and returned to baseline level (13:57:59) after intervention measures were implemented.
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Accordingly, evoked potentials were more efficient in detecting ischaemic events. SSEP in the upper and lower limbs has been reported to reflect blood flow in the MCA and the ACA, respectively.\textsuperscript{19–21} SSEP changes in the territory of a target cerebral artery during its temporary occlusion may help the neurosurgeon to alter neurosurgical strategy and avoid ischaemic damage.\textsuperscript{22} Collateral circulation pathways consisting of proximal anastomoses at the Willis circle and leptomeningeal vessels that are also involved in cerebral blood supply have been reported to be outside the detection range of ICGA.\textsuperscript{23} Furthermore, deep perforating arteries, such as the lenticulostriate arteries, are not supplied by collateral vessels during MCA occlusion, and lacunar infarcts usually follow occlusion of a terminal or side branch of the lenticulostriate arteries.\textsuperscript{24,25} MEP has been shown to be superior to SSEP in detecting blood flow disturbances in perforating arteries, particularly during subcortical ischaemia because of the lenticulostriate arteries and anterior choroidal artery.\textsuperscript{26,27} MEP changes are accepted as signs of ischaemic events at the pyramidal tract, and detection of MEP changes and adjustment of surgical strategy contribute to prevent irreversible pyramidal tract damage.\textsuperscript{28} By contrast, intraoperative loss of MEP reliably predicts both severe and permanent postoperative motor deficits.\textsuperscript{29}

Combined SSEP and MEP monitoring is superior to SSEP monitoring alone in predicting ischaemic events caused by blood flow disturbance of perforating arteries in the ICA and MCA areas.\textsuperscript{22,27,30,31} Monitoring of SSEP and MEP has also been applied together to predict intraoperative ischaemic events for cerebral aneurysm.\textsuperscript{32,33} Accordingly, combined use of ICGA, SSEP and MEP can provide optimal detection of ischaemic events arising from blood flow disturbance in perforating arteries during microneurosurgical management of cerebral aneurysm.

Topical application of nimodipine has been reported to be effective in improving focal cerebral blood flow,\textsuperscript{34} and intra-arterial nimodipine has been found to be more effective in dilating perforating arteries than angiographically visible larger arteries.\textsuperscript{35} In the present study, once changes in SSEP/MEP were detected, suspending microneurosurgical management was the preferred option for reversing cerebral blood flow disturbance. After intervention measures were implemented, the SSEP/MEP changes reversed partially or totally in 10 out of 11 patients. In one patient with changes in ICGA, SSEP and MEP, the decreased SSEP

| TABLE 3: Comparison of indocyanine green angiography (ICGA) and changes in somatosensory evoked potential (SSEP) / motor evoked potential (MEP) for detecting ischaemic events in patients undergoing microneurosurgical treatment for anterior circulation cerebral aneurysm |
|---------------------------------|---------------------------------|----------------|
| **ICGA**                       | **SSEP/MEP**                    | **Total**     |
| Ischaemic event                | 1                               | 1***          |
| No ischaemic event             | 11                              | 33            |
| Total                          | 12*                             | 44            |

Data presented as numbers of patients.

***SSEP/MEP was significantly more powerful than ICGA in detecting ischaemic events (P < 0.001; McNemar test).
recovered completely and the decreased MEP recovered partially after intervention measures were implemented. This indicates that the intervention measures contributed to reversing cerebral blood flow disturbances in perforating arteries.

Among the seven patients receiving instant intervention measures after detection of SSEP/MEP changes, severe postoperative motor deficiency was found in patients with a sustained SSEP decrease or incomplete recovery of transient MEP loss, while no motor deficiency was found in patients with a partial/total recovery of the decrease in SSEP. For all the four patients who received delayed intervention measures, partial/total recovery of the decrease in SSEP/MEP or total recovery of the transient loss in MEP were observed and no postoperative motor deficiency was found. For the patient with changes in ICGA, SSEP and MEP, no postoperative neural deficiency was found as the decreased SSEP recovered completely and the decreased MEP recovered partially. Accordingly, in cases involving intervention measures, partial/total recovery of the decrease in SSEP/MEP and total recovery of the transient loss of MEP indicated a decreased risk of postoperative motor deficiency, while sustained SSEP decrease and partial recovery of the transient loss of MEP indicated an increased risk. Thus, SSEP and MEP are specific and effective methods for detecting blood flow disturbance in perforating arteries at distal areas, directing neurosurgeons to implement intervention measures in real time and predicting risks of severe postoperative motor deficiency.

In summary, for patients with an anterior circulation cerebral aneurysm of H&H scale < 3, multiple intraoperative monitoring including ICGA, SSEP and MEP enables detection of residual aneurysms and ischaemic events, providing direction for neurosurgeons to alter their microneurosurgical strategy and reduce the risks of residual aneurysms and severe postoperative motor deficiency because of blood flow disturbance in perforating arteries.

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Conflicts of interest
The authors had no conflicts of interest to declare in relation to this article.


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