Implication of Human Fetal Ventral Mesencephalon to the Bilateral Caudate Nucleus in Advanced Parkinson’s Disease.

PO Byrne, Y Caglar, A Detta, ER Hitchcock, Birmingham, UK

Twelve patients had bilateral caudal nucleus implantations of late stage fetal mesencephalon as the fourth series of a study of experimental surgery by transplantation for advanced Parkinson’s disease. Patients with an age range of 55–67 years were operated upon in the latter part of 1991. Subsequently they have been systematically followed up in terms of preoperative and postoperative clinical assessment and the results of those available for follow up to date were outlined. The results refer to timed motor performance tests, CAPIT core assessment, Northwestern University disability scores and Schwab and England ratings obtained preoperatively with drug regimens adjusted to maximum efficacy and then at time intervals postoperatively; in addition, non-ductions occurring in individual patients were analysed.

The results of this fourth experimental series were discussed with reference to earlier series and factors important in human fetal cell transplantation for neurodegenerative disorders with their attendant problems were discussed.

Nerve Muscle Pedicle Reinnervation of Skeletal Muscle

WP Gray, TF Buckley, WO Kirwan, Cork, Eire

Direct nerve suture and interposition grafting are compromised by the regenerating neural chaos at each suture line. A technique for transplanting intact nerves into denervated muscle was described.

A neurovascular pedicle of muscle containing motor endplates was harvested, with its motor nerve in continuity, from the donor muscle motor point, and was implanted into the denervated recipient muscle. Thirty-six adult New Zealand White rabbits underwent reinnervation of the left peroneus longus (fast twitch) muscle with a nerve muscle pedicle from the soleus muscle (slow twitch). The right peroneus longus served as a control. Reinnervation was assessed using microstimulatory single fibre electromyography alterations in muscle fibre typing and grouping, and isometric response curves. Neurofilament antibody was used for axonal staining.

Motor endplate jitter was 13 μs preoperatively, 45 μs at two months, 32 μs at four months and 18 μs at six months (p < 0.001). Fibre typing showed progressive conversion to slow twitch fibres with prominent grouping. This was confirmed on measuring isometric twitch responses. Neurofilament staining clearly demonstrated growth of nerve fibres across the pedicle muscle interface.

It is concluded that the nerve muscle pedicle technique achieves reinnervation by growth of new nerve fibres across the pedicle–recipient muscle interface.

Dynamic Oxygen Micropolarography of Peritumoral White Matter: The Influence of Oedema on Tissue Oxygenation

GS Cruickshank, R Rampling, Glasgow, UK

Dynamic oxygen micropolarography of malignant brain tumours has shown that a high proportion have a large hypoxic volume and that this correlates with the relative resistance of these tumours to radiotherapy. The spatial resolution of this technique allows a unique analysis of the factors affecting the oxygen supply at the microenvironmental level rather than other methods which integrate values over a large tissue volume. In this study we have used this technique to examine the oedematous peritumoral white matter to determine the influence of oedema on the local oxygen tension of this area, as this is the logical site for therapeutic intervention after surgery.

Peroperative oxygen tension (pO2) measurements were made in 24 patients undergoing routine craniotomy for tumour decompression. A 300 μm microneurographic probe with a 12 μm oxygen sensitive tip was advanced under computerised step control using ultrasound guidance. A number of static probe measurements were also made to provide pseudostop-flow assessments of relative oxygen consumption (VO2).

Morphometric measurements on tumour and peritumoral biopsies were performed using standard techniques.

pO2 frequency histograms of 192 readings (six probe passes of 32 readings 700 μm apart) were plotted at 2.5 mmHg intervals. There was a surprisingly high incidence of low pO2 values (18% < 2.5 mmHg) by comparison with that reported in normal white matter (< 2% < 2.5 mmHg).2 Median and low pO2 values were correlated with intercapillary distance in peritumoral white matter (r = 0.87) but not so clearly in tumours. Maximum pO2 levels recorded in peritumoral white matter were equivalent or better than that seen in tumours. VO2 values varied between 6 and 12% only, in peritumoral white matter.

High percentages of low pO2 values in the peritumoral region are of clinical and therapeutic significance. Increased intercapillary distance correlates with lower pO2 values but the small variation in VO2 levels suggests that peritumoral hypoxia is more related to impaired capillary patency than altered or increased oxygen uptake in the expanded intercapillary space. Peritumoral oedema and its effects do not seem to be a limiting factor for oxygen supply to tumours, and thus a cause of tumour hypoxia.


Dynamic Magnetic Resonance Imaging for Measurement of Regional Haemodynamics After Transient Cerebral Ischaemia

R Macfarlane, LM Hamberg, E Tasdemiroglu, JW Belliveau, B Rosen, MA Moskowitz. London, UK and Boston, USA

Because alterations in cerebral blood volume (CBV) are not necessarily coupled to those of cerebral blood flow (CBF) under pathological conditions, a noninvasive technique able to measure regional and temporal changes of each parameter simultaneously might aid investigation of perturbed cerebrovascular states.

Gadolinium-DTPA was injected as a bolus into the femoral vein of seven anesthetised cats placed in the bore of a 4.7 T MRI, while rapid sequence images were acquired every 1·3 s. After a baseline study, global cerebral ischaemia was induced for 10 minutes. Further imaging sequences were repeated at intervals after reperfusion. CBV changes were calculated relative to the baseline and, after direct measurement of vascular transit time (VTT), the CBF index (CBFI) was computed.1

Relative CBV (rCBV) and CBFI rose sharply during the early reperfusion period. Both fell to near-basal levels at 45 minutes. Thereafter CBV rose slowly, whereas CBFI continued to fall. At three hours, CBFI was 1·6 times basal (p < 0·05), whereas CBFI had returned to pre-ischaemic values. VTT fell from 4·4 to 1·6 s at 30 minutes, was near-normal at one hour, but increased to 6·7 s at three hours (p < 0·05). CBFI results were comparable with those obtained in previous radionuclide studies.2

It is concluded that dynamic susceptibility–contrast MRI provides a noninvasive, in vivo method for determination of CBFI and rCBV.


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testing; secondly, that clinically, it has performed well up to 18 months postoperatively, even when no bone has been inserted; and finally: that there have been no neurological problems due to sublaminar passage of the cable.

NONOPERATIVE ADMISSIONS TO A REGIONAL NEUROSURGICAL UNIT: ARE THEY JUSTIFIED?

IK Pople, RJ Nelson. Bristol, UK

The aim of this audit was to find out how many patients are discharged from our neurosurgical unit without having an operation and whether these admissions are all clinically justified. During 12 months, 2509 patients were admitted, of whom 1637 (65%) had an operation. A further 530 (21%) patients had an inpatient neuroradiological investigation (CT myelogram, or cerebral angiogram). Of the remaining 342 patients, 119 had a head injury and 223 were admitted and discharged as an inpatient; of these, 217 had an intra-cranial procedure. Secondary investigation of hydrocephalus was adequately treated, and, secondly, that in the distal syringus group without HHB or hydrocephalus, the filling mechanism is likely to be the tethering of the cord without drainage of the syrinx is the preferred treatment in these patients.

SPINAL FIXATION USING A NEW FLEXIBLE CABLE (SOFTWIRE™)

D Peterson, HA Crockard. London, UK

Stainless steel monofilament wire of varying thickness is widely used, but non-conformability, difficulty in reproducing consistent tensioning and, most importantly, neural damage during sublaminar wire passage are major drawbacks. It is against this background that alternatives have been developed. The stainless steel cable (Softwire™) is 60 times more flexible than 20 gauge wire. It has a higher tensile strength (74-4 kg) compared with 20 gauge (35.5 kg) and 18 gauge (49.9 kg) monofilament. The loop's tensile strength and fatigue-life exceeded 20 gauge and 18 gauge monofilament wire.

Fifty-eight patients aged 10-79 years were selected for cable fixation on exactly the same basis as those in the past would have had monofilament wire insertion. All had six monthly follow-up review, most had atlantoaxial rheumatoid disease (32 patients); 12 had spinal tumours. All had preoperative and postoperative radiographs. Spinal stenosis was present in six, and 18 months to detect cable breakage, movement of implant, or signs of bone fusion. To date, 436 cables have been implanted at 233 levels and there have been no broken cables or slippage of a chin cable construct. Fifteen patients have had 12- and four have had 18-month reviews after surgery. Most (54 patients) had occipitocervical instability or cervical stenosis (14 patients). There were no changes in SSEP during the passage of wires and, postoperatively, no patient deteriorated neurologically.

It is concluded that, firstly, the new cable is less likely to be displaced than the monofilament stainless steel wire on biomechanical

Preoperative shunts were performed in 25% of children and 14% of older patients. Subtotal or radical surgical removal was achieved in 50% of patients irrespective of age. Five patients died in the first month after primary surgery and two patients after revision surgery. There was no significant difference in the number of surgical explorations in the three age groups (mean: 1-98, median = 2, range: 1-6). Lasting visual improvement occurred after surgery in 25% of patients. Radiotherapy was given postoperatively in 33%.

At follow-up, 65% of patients in the series are still alive. Thirty-one percent of those with panhypopituitarism, 40% have abnormal function and 53% have frank panhypopituitarism. Forty-two per cent are functionally blind. Children had significantly worse vision post-operatively (p = 0.037). Adjuvant DXT did not significantly improve outcome nor increase the chance of panhypopituitarism or visual loss.

It was concluded that the management of craniopharyngioma still remains a real challenge.

ENDOSCOPIC MANAGEMENT OF PINAL TUMOURS

HB Coakham, IK Pople, DR Sandeman. Bristol, UK

The histological nature of pineal region tumours critically determines optimal treatment. Most authorities argue that all pineal tumours should be biopsied to avoid potentially dangerous tumour spillage which can occasionally be hazardous in the pineal region, or by direct open surgery which may not always be necessary, particularly in cases of undifferentiated germinoma. Many cases of pineal tumour are admitted with acute hydrocephalus as emergencies.

We have developed a management system using transvenous endoscopic biopsy and third ventriculostomy. This one-step procedure is minimally invasive and achieves two goals of safe adequate biopsy and immediate treatment of hydrocephalus while definitive histology and CBF marker studies are awaited. During this period immunohistology and electron microscopy is also performed.

Problems 3 mm, rigid solid lens endoscope (Storz) is introduced via a right frontal burr hole, passed through the foramen of Monro for biopsy of the tumour under direct vision, avoiding obvious blood vessels. This is followed by endoscopic third ventriculostomy carried out with diathermy fenestration and more recently Fogarty balloon catheter dilatation. Alternatively an Ommaya reservoir is placed in the burr hole and may be revised to a VP shunt if necessary.

Tumour types we have successfully managed by this technique are pineoblastoma, pineocytoma, germinoma, teratoma, astrocytoma, and carcinoma (15 cases in total). The more recent five cases have received third ventriculostomies. According to current management protocols and depending on histology, tumours were then treated by either resection via the parasellar transtentorial approach or by radiation or chemotherapy. There were no significant complications, and long term follow up data was presented.
CLINICOPATHOLOGICAL EXPERIENCE OVER 30 YEARS WITH PINERAL REGION TUMOURS IN NORTHERN IRELAND

B Mathew, B Herron, B Clements, M Mirakhor, T Fannin. Belfast, U.K.

Pinear region tumours constitute only 0.4-1.1% of intracranial tumours. In Northern Ireland there are 1-6 million people served by one neuroscience unit and 26 patients with pineal region tumours have been identified and carefully followed up.

The purpose of the present retrospective review was to establish a clinicopathological correlation of survival with histology and type of tumour. The paraffin blocks had been stored and were re-studied using H&E, immunocytochemistry and electron microscopy. Tumour typing was performed according to the 1990 WHO classification.

There were a total of 24 pineal region tumours and two suprasellar germinomas which are frequently classified with pineal region tumours because of their common germ cell origin. There were 22 men and four women. The mean age was 27.5 (range 6-62 years). All 24 pineal region tumours had symptoms/signs of raised intracranial pressure and required initial shunting. The two patients with suprasellar germinomas presented with visual loss.

In 22 patients a tissue diagnosis was obtained, 16 by craniotomy, three by stereotaxy, one by cytology and two by post-mortem examination. Open biopsies were performed in the prone position by the suboccipital transtentorial approach. On six occasions biopsies via the open approach was abandoned because of difficulty with retraction. There was minimal operative morbidity but two patients died postoperatively (one stereotactic biopsy causing haemorrhage from a hypernephroma secondary to a transtentorial approach). All patients except one with a teratoma received radiotherapy. The table shows histology and three-year survival (where available).

<table>
<thead>
<tr>
<th>Tumour Type</th>
<th>No (%)</th>
<th>3-year survival</th>
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<tbody>
<tr>
<td>Pineal parenchymal</td>
<td>11 (50)</td>
<td>71 (n = 7)</td>
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<tr>
<td>Pineoblastoma</td>
<td>6 (27)</td>
<td>60 (n = 5)</td>
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<tr>
<td>Pineocytoma</td>
<td>4 (18)</td>
<td>100 (n = 1)</td>
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<td>Pineoblastoma (pure)</td>
<td>1 (5)</td>
<td>100 (n = 1)</td>
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<tr>
<td>Germ cell tumours</td>
<td>7 (32)</td>
<td>40 (n = 5)</td>
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<tr>
<td>Germioma</td>
<td>4 (18)</td>
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<tr>
<td>Teratoma</td>
<td>3 (14)</td>
<td>100 (one)</td>
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<tr>
<td>Astrocytoma</td>
<td>2 (9)</td>
<td>50 (n = 2)</td>
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<tr>
<td>Ependymoma</td>
<td>2 (9)</td>
<td>50 (n = 2)</td>
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<tr>
<td>Metastatic</td>
<td>(hypernephroma)</td>
<td>1 (5)</td>
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<tr>
<td>No histology</td>
<td>4 (18)</td>
<td>25 (n = 4)</td>
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</table>

n = Number with three year follow up.

The low incidence of germinoma and the longer survival for pineal parenchymal tumours note. The management of patients by 'blind' irradiation without a histological diagnosis needs to be questioned.

MENINGIOMAS OF THE CEREBELLOPOPTINE ANGLE: A REPORT OF 41 CASES


Meningiomas of the cerebellopontine angle (CPA) are rare. This retrospective study presents 41 cases from a total of 625 tumours operated upon by one surgeon with the survival and the tumours based upon their anatomical distribution and correlating this with outcome.

Tumours were divided into six groups: lateral, internal auditory meatal, midpetrosal, inferior, Meckel's, and petroclival. Four different approaches were used either singly or in combination. Twenty-five patients had a total removal, 10 subtotal, and three were treated conservatively. There were no operative deaths. A good result (return to normal life) occurred in 30 cases, a fair outcome in seven, and a poor outcome in five. There were two deaths from late recurrence. Median follow up was 8-5 years.

Most tumours lateral to the internal auditory meatus had a complete removal, with a good outcome. Case removal and cranial nerve deficits were more common with medial tumours but incomplete removal did not correlate with early recurrence. Poor outcome was associated with cranial nerve deficits and brainstem damage.

LATERAL APPROACHES TO FORAMEN MAGNUM TUMOURS

B George, G.L. Paris, France

Foramen magnum tumours are operated on via three main approaches: anterior (transoral), posterior (medial posterior and lateral) and approaches (anterolateral and posterolateral approaches). The anterolateral approach is also used to expose the vertebral artery in the internal jugular, the accessory nerve is dissected free, and the vertebral artery is exposed above C1 and between C1 and C2. After opening the transverse foramen of C1, the vertebral artery is displaced medially, giving access to the condyle, C1 lateral mass, and C1-C2 joint.

The postero-lateral approach is a lateral enlargement of the standard posterior opening, allowing the control of the vertebral artery in its C1 groove, which provides access to the condyle and C1 lateral mass. The anterolateral approach was mainly reserved for osseous (n = 18) and extradural nonosseous (n = 14) tumours. The postero-lateral approach was used for intradural tumours (n = 42).

The benefits of the lateral approaches were discussed from a series of 230 foramen magnum cases.

ACUTE INTRAOPERATIVE BRAIN HERNIATION COMPLICATING ELECTIVE NEUROSURGERY; NEURORADIOLOGICAL FINDINGS, PATHOPHYSIOLOGICAL MECHANISMS AND MANAGEMENT CONSIDERATIONS

R Viswanathan, J. Whitley, Edinburgh, U.K.

Profound and acute intraoperative brain herniation is most commonly seen following evacuation of a post-traumatic acute subdural haemato ma. The pathophysiological mechanisms probably relate to dysautoregulation of cerebral blood flow and hydrostatic brain oedema and the outcome in such cases is invariably death. Acute intraoperative brain swelling through an elective craniotomy is, however, a much rarer event. The aim of this report, which describes seven such cases, is to describe mechanisms and how and what brain herniation during elective surgery, recommend some management guidelines, and describe the postoperative complications encountered.

Preoperatively four patients with anterior circulation aneurysms were WFNS grade I or II; two patients with tumours (pineoblastoma and astroblastoma) had, despite preoperative steroids, fixed focal deficits, but no impairment of conscious state; one patient with cerebellar AHS (with minimal mass effect) had a WFNS score of 15 but general psychomotor slowing. Intraoperative monitoring of multiple parameters, by a consultant neuroanaesthetist, was unremarkable before open brain herniation. Herniation occurred following intraoperative aneurysmal rupture, before arachnoidal dissection (three patients) and during clip placement (one patient), following placement of a postoperative, very vascular hemispheric astroblastoma; after resection of the pineal tumour, and after an uncomplicated AIDS lesion biopsy. In all cases, the open procedures were abandoned, and the patients transferred to the intensive care unit for elective ventilation and monitoring.

Postoperative CT scans revealed intraventricular and subarachnoid haematoma with paradoxically minimal or no intraparenchymal haematoma, acute brain swelling, or midline shift. Intracranial pressure monitoring was generally unremarkable. All patients recovered from the acute ictus. One patient with an aneurysm rebleed and died three days later. Three had successful aneurysm clipping with two patients resuming their prior employment. The other three patients all recovered, although one had a field defect from occipital lobe damage. Two patients required a second procedure ( duroplasty and closure of pseudoaneurysm of the middle meningeal artery). Overall outcome was remarkably good considering the dramatic and apparently catastrophic nature of the open brain herniation. It is postulated that closure of the scalp to limit brain herniation and prevent pial rupture together with optimal postoperative control of intracranial pressure minimised postoperative morbidity. It would appear that there are fundamental differences in pathophysiological mechanisms, neuroradiological findings, and outcome between open brain herniation occurring in posttraumatic and elective neurosurgical patients.

SHORT-COURSE ANTIBIOTIC THERAPY FOR BRAIN ABSCESS AND SUBDURAL EMPYEMA


It is widely (and empirically) recommended that patients with intracranial sepsis (brain abscess and subdural empyema) should receive antibiotics for eight weeks or longer. Although there is no theoretical, experimental, or clinical evidence to justify these prolonged courses, neither have there been reliable, objective criteria that enable the patient’s response to be monitored and which indicate when treatment should be discontinued. We report the results of a controlled study (CRP) and the patient’s clinical response for this purpose; when the fever resolves and CRP falls to within the normal range, the antibiotic therapy is stopped. In the study patients, 12 with brain abscess and nine with subdural empyema (one with both),
have been treated according to these criteria; all underwent neurological procedures. Of the 19 patients who were evaluable, the median duration of treatment was 14 days (range 11-75 days); the follow-up period ranged from 18-54 months, during which time three patients died. One patient died from a massive pulmonary embolism before completing the course of treatment and in three patients, therapy was prolonged because of undiagnosed deep vein thrombosis (one patient), failure to eradicate the underlying aural pathology (one) and intercurrent infection (one). It was concluded that patients with intracranial sepsis can be treated successfully with courses of antiseptics which are administered for significantly shorter periods than those currently recommended.

ANTIMICROBIAL PROPHYLAXIS IN NEUROSURGERY AND FOLLOWING HEAD INJURY


Antibiotics are extensively used within neurosurgical practice in an effort to reduce the rate of postoperative infection. Unquestionable support for the efficacy of prophylactic antibiotics does not exist. This is not because there have been too few attempts to resolve the issue, but because virtually all of the many clinical trials suffer from flaws in design or execution, the most important of these being the failure to achieve statistical significance. Against this background, the benefits of prophylactic antibiotic use in neurosurgery need to be assessed. The Working Party, comprising members of the Society of British Neurological Surgeons and the British Society for Antimicrobial Therapy, reviewed the extensive literature on the use of prophylactic antibiotics in three areas of neurosurgery: (a) clean non-implant procedures; (b) CSF shunt surgery; and (c) skull fracture. Our conclusions and recommendations are as follows: (1) The weight of evidence suggests that antibiotics exert a protective effect in clean nonimplant surgery; a single dose of a first or second generation cephalosporin is an appropriate regimen. (2) For CSF shunt surgery not even a tentative recommendation can be made regarding the use of prophylactic antibiotics. (3) There is no conclusive evidence in the literature to support antibiotic prophylaxis in patients with skull fracture and CSF leak. The risk of CNS infection due to resistant organisms led to the conclusion that antibiotic prophylaxis should be withheld in this situation.

THE EFFECT OF CSF PROTEINS UPON BACTERIAL ADHESION TO SHUNT MATERIAL

HL Brydson, R Hayward, W Harkness, R Bayston. London, UK

The role that proteins play in bacterial adhesion to prosthetic materials has not been proven. For each paper that states that certain proteins promote bacterial adhesion, there is another that draws the opposite conclusion. All of this work has been performed using plasma proteins, however, and the effect of CSF upon neurological prosthetic infections has not been studied. There is some evidence that the concentration of the protein may alter the result, therefore a correlation between work on plasma and CSF cannot be assumed. In this study the effect of individual protein solutions (CSF concentrations) and patient's own CSF upon adhesion to silicone rubber catheters was analysed.

Lengths of sterile catheter were incubated with CSF, protein, or a control solution and were then exposed to a standardised suspension of radiolabelled staphylococci. The adherent organisms were dissolved and the activity measured by scintillation counting. The results indicate that all of the protein solutions and CSF inhibit bacterial adhesion to shunts, with the effect being greater with CSF than for the individual proteins. CSF from children with intraventricular haemorrhage was also compared with that from idiopathic and tumour hydrocephalus and no difference between them could be detected.

AN ANALYSIS OF OUR EXPERIENCE WITH THE VARIABLE PRESSURE SOPHY VALVE SYSTEM AND PROPHYLAXIS AGAINST THE DIRECTION OF BLOOD FLOW

G O'Reilly, B Williams. Birmingham, UK

A selected series of 22 patients with hydrocephalus were treated by a shunt system incorporating a variable pressure Sophy valve or by ventriculoguajal shunting against the direction of blood flow using the El-Shafei system. One patient had sequential insertion of two Sophy valves and an El-Shafei conduit. Patient selection was reserved to those whose hydrocephalus was such that shunting with conventional unipressure or two-stage valves was deemed hazardous. None of the eight patients who had ventriculoguajal shunting by the El-Shafei method demonstrated clinical or radiological improvement subsequent to shunt insertion. Of the 16 Sophy devices inserted only seven resulted in a satisfactory clinical outcome. It was suggested that the value of the Sophy and El-Shafei shunt systems in treating difficult cases of hydrocephalus remains to be proven.

UNITED KINGDOM CSF SHUNT REGISTRY AND SHUNT EVALUATION UNIT

JD Pickard, RD Ashpole, H Whitehouse, M Czosnyka. Cambridge, UK

Approximately 3000 shunt operations are performed in the United Kingdom per year (1500 new, 1500 revisions) at a total cost of over £6 million. Some 80% of shunts fail by 12 years. Most failures are reported in vitro do not behave consistently nor according to the manufacturer’s own specifications. If liability for product failure is to fall on the manufacturer, strict record keeping is crucial under the Consumer Protection Act.

On behalf of the Council of the Society of British Neurological Surgeons, the Executive Committee of the British Association of Paediatric Surgeons, the United Kingdom Hydrocephalus Group and the Association of Spina Bifida and Hydrocephalus, funding has been secured from the Department of Health and the East Anglian Regional Audit Committee to establish the following. (1) The United Kingdom CSF Shunt Registry, equivalent to the United Kingdom Heart Valve Registry, based on completion of a simple card at the time of operation for entry into the Dendrite Patient Analysis and Tracking System. (2) The United Kingdom CSF Shunt Evaluation Unit, which will prepare detailed evaluation reports of the hydrodynamic properties for every type of shunt valve currently available and also has has the facilities for the testing of explanted valves with appropriate safety precautions.

The way in which each initiative will function was outlined to encourage feedback by the Society.

RECURRENT CRANIOSYNOSTOSIS

AD Hockley, M Briggs. Birmingham and Oxford, UK

After an apparently successful correction for craniosynostosis, a small but significant number of patients later develop recurrent deformity needing reoperation. Analysis of 219 cases treated in the Birmingham and Oxford craniofacial units since 1979 demonstrates a higher re-operation rate in syndromal or unilateral coronal synostosis treated below the age of six months. Of the total of 15 patients who underwent repeat fronto-orbital advancement for single suture involvement the re-operation rate was 3% and for multiple it was 8%. In Apert's syndrome the re-operation rate was 16%. With initial surgery performed in the first three months of life there is a significantly higher re-operation rate of 23% falling to 17-9% for surgery between ages three and six months. After six months of age the rate did not exceed 5%.

Unless there is major raised intracranial pressure or exorbitism, it is recommended that fronto-orbital advancement is deferred to after 6 months of age and in the presence of raised pressure, a preliminary posterior skull release can be helpful in allowing a planned anterior correction later with less risk of recurrent deformity.

AETIOLOGY OF HERNIATION OF THE HINDBRAIN IN CRANIOSYNOSTOSIS: PRELIMINARY OBSERVATIONS

DNP Thompson, RD Hayward, WJ Harkness, BM Jones. London, UK

Herniation of the hindbrain is recognised in association with craniosynostosis. Moreover the concept of acquired hindbrain herniation is reported and has been observed in our practice. This retrospective study aimed to identify some of the aetiological factors responsible for this deformity.

The results of MRI and continuous intraparenchymal intracranial pressure monitoring were reviewed in a total of 33 patients. Two groups were identified; group 1 (n = 21) where there had been no previous vault surgery and group 2 (n = 12) where vault expansion surgery had been performed. Hindbrain herniation was identified in eight (38%) of patients in the unoperated group—all of whom had abnormal intracranial pressure. Among the operated group hindbrain herniation was identified in eight cases (87%), six of whom had abnormal intracranial pressure.

Hydrocephalus, defined in this series as the need for shunt placement for 6 months or more, occurred in one patient in group 1 and in seven patients in group 2; furthermore, herniation of the hindbrain was an invariable accompaniment to all these cases of hydrocephalus.

An index of posterior fossa size relative to
the rest of the cranial vault was developed using the distance from the foramen magnum to the torcular expressed as a percentage of the distance from the foramen magnum to the nasion assessed on midline sagittal MRI scans.

In group 1 the posterior fossa size was 13·1% in cases with herniation of the hindbrain compared with 16·1% in those without. In group 2 the values were 12·4% and 14·2% respectively.

The results confirm the high incidence of hindbrain herniation in craniosynostosis. Furthermore they suggest the incidence may be equal in children who have undergone vault expansion surgery. The anatomical constraints imposed by posterior fossa size, raised intracranial tension, and impaired cerebrospinal fluid circulation all appear to predispose toward herniation of the hindbrain. Potential underlying mechanisms were discussed.

INITIAL STUDIES CHARACTERISING A CLINICALLY RELEVANT RODENT MODEL OF DIFFUSE HINDBRAIN HERNIATION

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Using an experimental model of closed head injury, this study aims to characterise the baseline status of cerebral blood flow (CBF) and neuropathology during the first six hours after injury.

Anaesthetised Sprague-Dawley rats (n = 26), were subjected to either sham or global closed head injury using an "impact acceleration" model. A 450 g weight was dropped from a height of either 1 m (moderate injury) or 2 m (severe injury) onto the intact skull which is protected by a metal plate to prevent skull fracture. The head was free to move on a foam cushion providing the acceleration and deceleration components of the injury. Mean arterial pressure (MAP) was measured continuously and blood gas samples were taken at intervals through a femoral cannula. The hydrogen clearance technique was used for repeated half-hourly CBF measurements at eight time points from 90 to 300 minutes after injury. After six hours animals were perfusion-fixed for neuropathological investigation.

With severe injury, MAP dropped from a mean (SD) of 100 (20) to 48 (4) mmHg recovering to a plateau level of 91 (21) mmHg with a recovery time of 12 (3) minutes after injury. Moderate injury also produced hypotension but with a significantly shorter recovery period of 4 (2) minutes (p < 0·001). By 2·5 hours and continuing through to five hours after injury, hyperaemia was present with CBF significantly higher (p < 0·05) than control levels for both the moderate and severe injury. Using H&E staining techniques, no major cell loss was found in any brain region, although suble ischaemic/hypoxic cell damage was found in the mid-dorsal hippocampus at six hours after injury. Using histochemical markers for cytoskeletal proteins ubiquitin and the 68 kDa neurofilament subunit, no major reactive axonal change could be detected by six hours after injury. Future studies will address the significance of superimposed secondary insults and therapeutic intervention on both the development of post-traumatic reactive axonal swelling and ischaemic cell damage.

CONTINUOUS ASSESSMENT OF GLOBAL CEREBRAL BLOOD FLOW USING LASER DOPPLER FLOURESCOPY IN PATIENTS WITH HEAD INJURY

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The pathophysiological events affecting global cerebral blood flow (CBF) during the acute stages after severe head injury are dynamic and can fluctuate rapidly. To recognise and act on such events a reliable real time assessment of CBF is needed. Using laser Doppler flowmetry (LDF, Moor's Instruments model MBF-3B), we continuously monitored cortical red cell flux (CRCF) during the period of ventilation in 14 patients with severe head injury. Our pooled data demonstrated a consistent CRCF for cerebral perfusion pressure (CPP) above 75 mmHg, a small rise in CRCF at a CPP between 59 and 74 mmHg, and a continuing fall in CRCF as CPP fell below 58 mmHg (fig). The method was also used to monitor the cerebral haemodynamic responses to rheological agents. A consistent increase in CRCF (10%; p < 0·04) occurred following 200 ml bolus of 20% mannitol with a fall in cerebrovascular resistance of 5% (p < 0·04) that was independent of systemic arterial blood pressure. It was concluded that LDF provides a means of detecting spontaneous events that affect CBF globally, and allows accurate monitoring of the cerebral circulation during potential therapeutic intervention.

ACCU RATE 3D COMBINATION AND DISPLAY OF MRCT AND MRA IMAGES FOR SURGICAL PLANNING


Magnetic resonance (MR), x-ray CT, and angiographic images respectively depict soft tissues, bone, and blood vessels. None on its own is sufficient for the preparative assessment of skull base lesions. We have developed and evaluated a computational technique for the 3D combination and display of multimodality images for planning skull base surgery.

Sixteen patients (seven with acoustic neuromas, one with a plasmacoma, one with a cholesterol cyst, six with meningiomas (five subfrontal and suprasellar), one petrous apex) and one with a glomus jugulare tumour underwent MR, CT, and, where appropriate, MR angiography (MRA). The images were displayed using anatomical landmarks rather than an external frame. Two techniques were used for displaying the resulting images: (a) multiple slices of overlaid bone from CT and soft tissue from MR; (b) pseudo-3D movie sequences showing bone from CT, lesions, and optic nerves from MR, and blood vessels from MRA. Possible advantages of the combined images compared with conventional viewing were investigated. For the first eight patients, the overlaid slices were evaluated retrospectively by independent observers. For the second eight, overlaid slices and 3D rendered displays were assessed prospectively, both by the operating and by independent surgeons, and the results validated with operative findings.

In the first eight patients there was an improvement in clarity of the image information and hence in the surgeons' confidence. A more rigorous assessment of the second eight showed a significant improvement in the depiction of tumour-bone relationships (overlaid slices) and of tumour-vasculature relationships (3D rendered displays), both at p < 0·05. The operative findings confirmed this.

The combined images provide a clearer representation of anatomical structures, further indices need to be devised for an objective assessment of the impact of this.
ICP for all patients is presented in the top figure. AMP increases with mean ICP until 45 mmHg, above this breakpoint it starts to decrease significantly (p < 0.05). The patients were divided into three groups according to Glasgow outcome score: GOS 1 and 2 (26 patients), GOS 3 (16 patients), GOS 4 and 5 (10 patients). The AMP/pressure relationship in these groups are presented in the lower figure. The positions of the upper breakpoints differ significantly (p < 0.01). The groups with worse outcomes have upper breakpoints at lower ICPs.

It was concluded that the upper breakpoint of the amplitude-pressure relationship correlates with outcome in patients with head injury.


**THERAPEUTIC WINDOW FOR INTRAVENOUS CALCITONIN GENE-RELATED PEPTIDE IN A RAT MODEL OF FOCAL CEREBRAL ISCHAEMIA**

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We set out to determine the therapeutic window for an intravenous infusion (100 ng/kg per minute) of calcitonin gene-related peptide (CGRP) in a rat model of focal cerebral ischaemia. Ischaemic cerebral blood flow (CBF) was measured using hydrogen clearance and the volume of ischaemic neuronal injury was quantified using conventional histological techniques. When initiated 4 hours before the ischaemic insult, CGRP maintains local CBF at higher levels (35-6 SD 1-9) ml/100 g per minute compared with 13-3 (SD 1-8) ml/100 g per minute in untreated animals) and reduces the volume of ischaemic neuronal injury by 57%. When started one hour after the onset of ischaemia, CBF increased significantly to 27-6 (SD 2-1) ml/100 g per minute and ischaemic neuronal injury was reduced by 40%. When the CGRP infusion was begun two hours after the onset of ischaemia, however, although CBF improved to 23-9 (SD 3-3) ml/100 g per minute, there was no significant improvement in the volume of ischaemic neuronal injury.

These findings confirm the efficacy of an intravenous infusion of the peptide provided it is given within one hour of the onset of a focal cerebral ischaemic event.

**EFFICACY OF TREATMENT OF DELAYED CEREBRAL ISCHAEMIA IN ANEURYSMAL SUBARACHNOID HAEMORRHAGE WITH PROSTACYCLIN DERIVATIVE (ILYPROST)**

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One of the complications of aneurysmal subarachnoid haemorrhage is the associated syndrome of delayed cerebral ischaemia (DCI) in which patients deteriorate neurologically after an interval and may die or be left seriously disabled. Cerebral angiography frequently shows focal arterial narrowing ("vasospasm") and cerebral blood flow studies demonstrate an ischaemic brain. Numerous drugs have been used to attempt to reverse the vasospasm and improve the cerebral ischaemia. None have been shown to have any effect on either, although nimodipine, a calcium antagonist, has been shown to improve the clinical outcome.

The prostanoids are a relatively new series of drugs with vasoactive properties.

One of the family, prostacyclin, is a very potent vasodilator. A pilot study using iloprost, a stable derivative of prostacyclin, was described assessing results clinically and with isotope cerebral blood flow measurements. Eleven patients were treated. There were no deaths. Clinical deterioration was reversed in eight or halved in three patients. In one patient a focal weakness became worse. Cerebral blood flow studies all showed a focal deficit before treatment excluding one who did not have a pretreatment scan. All improved; three returned to normal, two showed hyperperfusion. Improvement in cerebral blood flow has never been previously reported.

**EXPRESSION OF INTERLEUKIN 1ß AND ACTIVATION OF INFLAMMATORY CELLS DURING FOCAL CEREBRAL ISCHAEMIA IN RATS**

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Interleukin 1ß (IL-1ß) plays a central role in inflammation by causing activation of inflammatory cells. This study was designed to determine whether IL-1ß is involved in the response of the brain to ischaemia. Rats were anaesthetized with halothane, the middle cerebral artery was occluded, and animals were sacrificed 0-5, 4, 24, 48, and 72 hours later. IL-1ß was measured in tissue extracts using an enzyme-amplified immunometric assay that was specific for rat IL-1ß. In separate animals, the brains were perfusion fixed and inflammatory cells were identified using immunostaining with ED-1 for microglia and ED-2 for perivascular cells. The IL-1ß content of brains from sham-operated controls was 63 (SD 4) pg/ml protein. Tuber cells of activated microglia and approximately 15 perivascular cells per section. In cortical tissue surrounding the ischaemic core, IL-1ß showed an initial peak of 195 (SD 35) pg/ml protein at 0-5 hour and a second peak of 114 (SD 7) at 48 hours (n = four each). Perivascular cells increased to 50-60 by four hours and remained at this level. ED-1 positive microglia were first detected at 24 hours and increased to 200-300 by 72 hours. Thus, IL-1ß is expressed in cerebral tissue where progressive ischaemic damage is known to occur. Its presence before the appearance of increased perivascular cells or inflammation suggests that it could play a role in activating these inflammatory cells.

**INDUCTION OF IL-1 ß IN HUMAN CEREBRAL CORTEX FOLLOWING ANEURYSMAL SUBARACHNOID HAEMORRHAGE**

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Activation of the immune system may occur in patients with delayed ischaemic neurological deficit (DIND) after aneurysmal subarachnoid haemorrhage.1 Astrocyte proliferation is promoted by interleukin-1 (IL-1); macrophage class II human leuкоyte (HLA) antigens are also involved. Protein kinase C is activated during subarachnoid haemorrhage and it induces macrophage secretion of IL-1.2 Therefore patients with subarachnoid haemorrhage were tested for intracerebral HLA Class II antigens and local formation of IL-1α (a subtype of IL-1). Peripherally or postmortem brain biopsies from eight patients with subarachnoid haemorrhage were used. Consecutive tissue sections were stained using antibodies to HLA DR (class II HLA), IL-1α and the astrocyte marker glial fibrillary acidic protein (GFAP). In situ hybridisation with probes for the IL-1α gene identified IL-1α messenger RNA, thus localising enzymatic activity production. In two patients, areas rich in HLA Class II antigens and astrocytes were identified. IL-1α (messenger RNA and protein) was also detected in these two patients. Findings were compared with clinical outcome; one patient died after onset of DIND and the other after a recurrent haemorrhage. IL-1α messenger RNA was...
detected in a third patient who had a good outcome. These preliminary findings demonstrate intracerebral IL-1α production in some patients after subarachnoid haemorrhage which may account for the astrocyte proliferation sometimes observed.


RADIOSURGERY FOR ARTERIOVENOUS MALFORMATIONS: A HEMODYNAMIC FOLLOW UP STUDY

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This study had two objectives: (a) haemodynamic assessment of cerebral arteriovenous malformations (AVM); (b) to predict the response of an AVM to treatment with stereotactic radiosurgery (SRS). Seventy patients with AVMs were studied, 37 (3:3 ± 5:6 years) with a cerebral AVM, had dynamic cerebral blood flow measurements using radio-labelled human serum albumin (37C-T-HSA; 500 MBq, iv; SA:1G Bq/mI; QC:0-95). Aneurysm (M) and transit (T) times were measured in real time. Patients were assessed before SRS (LINAC) and at three to six months intervals thereafter, for a period of 18 (SD 7) months at a rate of 3-2 (SD 1:3) studies per patient. Response to SRS was indicated by changes in the "steal index" and "cerebral reserve" as functions of appearance (M) and transit (T) times respectively.

Two types of AVM were identified: (a) Fast Flow AVM (61% with affected to non-affected flow ratio of 1-31 (SD 0-04) and a mean transit time ratio of 0-85 ± 0-03, (p < 0-001); and (b) Slow Flow AVM (39%) with a flow ratio of 0-92 (SD 0-06) and a mean transit time ratio of 1-13 ± 0-03, (p < 0-001). Fast flow AVMS showed a better response according to the steal and reserve indices compared to the slow AVMS. It concluded that slow flow AVMS are less responsive to SRS. A haemodynamic follow up of cerebral AVM can be of value in predicting the response to stereotactic radiosurgery.

INTRAOPERATIVE CONFIRMATION OF FUNCTIONAL MRI OF MOTOR CORTEX

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The extent of surgical removal of lesions in or adjacent to the motor cortex is usually restricted by concerns to limit the potential postoperative functional deficit. Intraoperative functional mapping using cortical stimulation under either general or local anaesthesia is one answer to this.1 Methods for identifying the location of the motor cortex in relation to the lesion preoperatively have, until now, been unavailable. Two cases were reported in which preoperative functional MRI was carried out using a Siemens 1-5 T system.1 Imaging was performed using a flash sequence with data being obtained in the resting state and during motor activation. Activation images were obtained by subtracting resting state images from those during motor activity. Cortical stimulation using an Ojemann stimulator at the time of surgery verified the preoperative localisation. This preoperative cortical mapping allows more accurate surgical planning, reduced surgical morbidity and improved preoperative patient counselling.


A SIMPLE EX VIVO TECHNIQUE FOR TEACHING IMAGE GUIDED STEREOTACTIC NEUROSURGICAL METHODOLOGY

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Most surgeons learn the practical aspects of image guided stereotactic neurosurgery using the classical apprenticeship approach to surgical teaching. Unfortunately such an approach might lack the opportunity to be performed in a safe environment, or to have the feedback and take the time out of their day and hence be constrained in learning. As a result, trainee surgeons may be slow to familiarise themselves with the various practical and executive aspects of image guided stereotactic surgery. A simple teaching model that allows an ex vivo "hands on" type approach to the learning of the technical, computerised, and executive aspects of image guided stereotactic neurosurgery is described. This simple model uses a cadaver skull, a specially prepared cadaver brain, and a modified stereotactic probe that enables deposition of 1-8 mm diameter ball bearings at target points. Under image guidance training stereotactic surgery preparation surgeons can familiarise themselves with application of a stereotactic frame, fiducial and target point acquisition, and computation of both arc and probe depth settings.

The technique was initially developed for an experimental study evaluating the accuracy of thalamic and pallidal target localisation using the Brown-Roberts-Wells and axial GE8800 CT imaging.1 It was found, however, to be particularly useful for teaching trainee neurosurgeons "hands on" stereotactic methodology. The model could be applied to any stereotactic system and exercises such as stereotactic ventricular cannulation, estimation of the anterior and posterior commissural points, and the location of functionally important thalamic and pallidal nuclei can be performed. The last exercise, in combination with study of a human brain stereotactic atlas, provides excellent teaching and topographical familiarisation of the functionally important thalamic nuclei. Other additional practical teaching exercises were described.


VALIDATION OF CT TARGETING FOR FUNCTIONAL STEROETACTIC WITH POSTOPERATIVE MRI

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CT imaging has been common neurosurgical practice since the early 1970s, but its acceptance for use as functional stereotactic surgery has been surprisingly slow, with few units actively practising the technique. The stereotactic facility in our unit was specifically designed for use with CT, including its use for functional work. It would appear necessary to justify this choice and the accuracy of CT. Many of the MRIs have enabled us to assess the accuracy of lesion placement postoperatively.

In this study 13 patients underwent thalamotomy for movement disorders using the Dervin Miles Dervin (MDM) frame. The accuracy of the thalamotomies was determined by measuring the centre of the lesions on MRI scans. For the anterior-posterior co-ordinate, the centre of the lesion of the axis was within 1 mm, two within 3 mm and three outside 3 mm. For the lateral co-ordinate six were within 1 mm, five within 3 mm and two outside 3 mm. For the height co-ordinate six were within 1 mm, four within 3 mm and three outside 3 mm. It should be noted, however, that it is still of paramount importance to test for the appropriate site with functional testing and the electrode moved away from the standard target if necessary.

The results confirm that CT guidance is accurate enough for functional work and it is hoped to conclude that there is little justification for continuing the use of ventriculography with its acknowledged disturbing effect on patients when CT offers a satisfactory and less upsetting alternative.

EFFECTS OF CORPUS CALLOSUM DIVISION ON MEDICALLY INTRACTABLE EPILEPSY

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A series of 20 patients who underwent corpus callosotomy for medically intractable epilepsy was reported. The mean age of patients at the time of onset of seizures was nine years and at the time of callosotomy it was 26 years. The most common seizure types were generalised tonic-clonic (90%), myoclonic or tonic-atonic associated with falls (drop attacks) (65%), absences (60%), and complex partial seizures (40%). The most common EEG abnormality was multiple spike and wave activity in seven patients (35%), generalised or multifocal spike and slow wave activity in six patients (30%), one EEG normal (5%), and other abnormalities occurred in four patients (20%). The follow up was 5-6 (SD 0-6) years. Fourteen patients (70%) experienced significant sustained reduction in the severity and frequency of their two-thirds have remained free of generalised and partial seizures. The types of seizures associated with improved outcome were drop attacks 85%, generalised tonic-clonic seizures 78%, complex partial seizures 63%, and absences 60%. No definite relationship was established between preoperative EEG abnormalities and callosotomy-induced seizure control in this series, and CT and MRI data did not carry prognostic value. There was no mortality and the most frequent complication was a transient mild left hemiparesis in 35%. This study confirms the efficacy of corpus callosum division as a surgical option for selected patients with medically intractable epilepsy. Furthermore, our results suggest that the history and clinical classification of the seizures have prognostic value and are valid selection criteria for patients referred for this operation.
STEREOTACTIC GUIDED CRANIOTOMY FOR CAVERNOUS ANGIOMAS PRESENTING WITH EPILEPSY

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With the wider availability of MRI, angiographically occult vascular malformations are being recognised with increasing frequency in those patients with medically refractory epilepsy. Surgical resection is the best treatment, but because these lesions are usually small and can be located in eloquent areas, stereotactic resection should be considered. Stereotactically guided resection of pathologically verified cavernous angiomas was performed in nine patients presenting with epilepsy (seven men, two women, mean age 34 years). Eight patients presented with medically refractory epilepsy (five complex partial seizures, three grand mal seizures) and the other patient presented with repeated intracranial haemorrhages and epilepsy. All patients had normal neurological examinations, and were assessed by CT, MRI angiography, Wada, and neuropsychological testing. Operative resection was guided by stereotactic localisation using the Leksell or CRW stereotactic systems. Peroperative electrocortigraphy, cortical stimulation with speech mapping, and ultrasonography were employed in selected cases.

MRI findings typically consisted of mixed T1 and T2 signals with a rim of low density suggestive of haemosiderin deposition. Pathological findings were also indicative of previous haemorrhagic episodes. Following resection of these lesions all patients experienced improved epilepsy control (mean follow up 19±6 months). It was concluded that stereotactically guided resection offers significant advantages in the management of angiographically occult vascular malformations. Surgical indications would include medically refractory epilepsy, repeated haemorrhage and those cases where there is diagnostic uncertainty.

IMAGE-GUIDED INTRACRANIAL ANEURYSM SURGERY

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Most intracranial aneurysms have a well-defined anatomical position and may be approached via standard surgical exposures. Rarer aneurysms of the distal anterior and posterior circulations may be difficult to locate using conventional angiography alone, often necessitating extensive dissection in the subarachnoid space and cerebral fissures. These problems may be partly overcome by the use of stereotactic angiography. We describe an alternative method of aneurysm localisation using an image-guided mechanical arm registered intraoperatively to three-dimensional reconstructions of conventional CT or MRI scans (ISG Technologies). Using this system, intracranial localisation can be achieved with an accuracy of ±2 mm.

We report the management of five patients with distal aneurysms of the middle cerebral, pericallosal, superior cerebellar, and anterior inferior cerebellar arteries. Intraoperative image guidance allowed for accurate planning of the surgical approach, minimal brain exposure and retraction, identification and control of proximal vessels before exposure of the fundus, and a shorter operating time. All five patients made an uncomplicated recovery with no increased postoperative neurological deficit.