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The International Subarachnoid Aneurysm Trial: full one year results and cumulative 7-year mortality data

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Objectives: The International Subarachnoid Aneurysm Trial (ISAT) is a multicentre randomized controlled trial (RCT) comparing the policies of endovascular versus neurosurgical treatments of aneurysmal subarachnoid haemorrhage (SAH) in an eligible population.

Design: Patients were considered suitable for randomization if there was uncertainty as to which was the best method of treatment.

Subjects: There were 2143 patients entered into the trial from 43 centres. ISAT ceased recruitment in May 2002.

Outcome measures: Neurological outcome was measured at 2 months and 1 year postrandomization using the modified Rankin Scale. The first results from ISAT were published in the Lancet in October 2002.

Results: One-year data have now been analysed in all patients. Results demonstrate a significant reduction in both relative and absolute risk in patients who were randomized to an endovascular treatment policy. These results have had a profound effect on the treatment of patients with SAH in certain areas of the world.

Conclusion: This paper will describe the full 1-year results along with new data on epilepsy, health economic data and the results of long-term follow up. It will also discuss the impact that the results have already had on the management of patients with aneurysmal subarachnoid haemorrhage and the treatments offered to them.

First analysis of EORTC trial 26951, a randomized phase III study of adjuvant PCV chemotherapy in patients with highly anaplastic oligodendroglioma

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Background: Anaplastic oligodendroglioma are sensitive to chemotherapy. The present trial was initiated

to investigate whether the addition of six cycles of PCV chemotherapy after radiotherapy (RT) improves overall survival (OS) and progression free survival (PFS).

Methods: The eligibility criteria were histologically confirmed, newly diagnosed anaplastic oligodendroglioma (AOD) or anaplastic oligoastrocytoma (AOA) with $\geq 25\%$ oligodendral elements; age between 18 and 70 years; ECOG Performance Status (PS) 0–2; adequate haematological, hepatic and renal function; written informed consent. After stratification for age, institution, extent of resection, ECOG PS, and prior surgery for a low grade oligodendroglioma patients were randomized to either 33×1.8 Gy radiotherapy (control arm) or to the same radiotherapy followed by six cycles of standard PCV chemotherapy (PCV arm). Patients were followed every 3 months for ECOG PS, MMSE, QOL and MRI until progression, thereafter for ECOG PS and survival.

Results: Three-hundred-and-sixty-eight patients were randomized, 185 to the PCV arm and 183 patients to the control arm. Median follow-up is 4.1 years and 204 patients (55.4%) have died. Treatment groups were well balanced with respect to known prognostic factors. The median number of administered PCV cycles was 3; 28% of patients completed six cycles. In 19% of patients PCV was discontinued for PD, in 33% for toxicity (mainly haematological), in 7% because of patient refusal, in 13% for other reasons. At recurrence, PCV chemotherapy was given to 64% of patients in the control arm *v.* to 11% in the PCV arm. In addition, 51% of the patients in the PCV arm and 48% of patients in the control arm received other

TABLE I. Overall survival and progression free survival, between brackets (95% CI)

Treatment arm	Overall survival		Progression-free survival	
	Median (months)	5 years (%)	Median	2 years
RT + PCV	36.8 [25.1;56.2]	41.9 [33.6;50.2]	24.3 [17.4;43.8]	50.9 [43.6;58.3]
RT	30.0 [21.9;42.2]	35.0 [26.8;43.3]	13.3 [9.5;21.5]	40.2 [33.0;47.3]

chemotherapy (mostly temozolomide) at the time of recurrence. PFS was significantly increased after adjuvant PCV chemotherapy [see Table I; hazard ratio (HR) 0.69; 95% confidence interval (CI) (0.53;0.88), $p=0.0035$]. However, no difference in OS was observed [HR 0.88; 95% CI (0.67;1.16)].

Conclusion: Adjuvant PCV chemotherapy prolongs PFS from 13 months to 24 months in AOD/AOA, without a statistically significant improvement of OS. Analysis of 1p/19q status is in progress.

Peripheral nerve regeneration through synthetic nerve grafts does not result in type grouping

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Objective: To elucidate the mechanism that causes type grouping (i.e. clustering of muscle fibres of the same metabolic type) in reinnervated muscles.

Design: Grafting of the sciatic nerve with either an autograft or a hollow synthetic nerve graft; 12 weeks survival.

Subjects: Adult female Wistar rats.

Outcome measures: The number and fibre area of the types I and II muscle fibres in the gastrocnemius and anterior tibial muscles were determined after ATP-ase staining. The number and diameter of peroneal nerve fibres distal to the grafts were measured, and the number of A α -nerve fibres (comprising the α -motoneuronal axons) was derived.

Results: The number of A α -nerve fibres remained equal or increased in both experimental groups, the diameter of the nerve fibres decreased similarly, and the number and fibre area of the types I and II muscle fibres also changed equally. However, type grouping occurred more frequently after autografting than after synthetic nerve grafting.

Conclusions: The observation that nerve and muscle morphometrical parameters changed equally in both experimental groups suggests that nerve regeneration in both groups is comparable. The type grouping results, however, are in contrast with this suggestion. Regenerating axons branch along their course through the peripheral nerve. We propose that in hollow synthetic nerve grafts emerging branches become dispersed throughout the graft. Subsequently, different muscle territories are innervated, not resulting in type grouping. In autografts emerging branches are kept together by Schwann cell basal lamina scaffolds. The sibling branches will arrive in the same muscle territory and we propose that this subsequently causes type grouping.

The introduction of an evidence-based protocol for the insertion of external ventricular drains (EVDs) is associated with a reduction in the infection rate

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Objective: To assess the impact on EVD infection rate of an evidence-based protocol for their placement.

Design: There were two phases over a 2-year period:

- a retrospective audit of the EVD infection rate at our institution over 12 months;
- a prospective re-audit of the infection rate after the implementation of an evidence-based protocol for EVD insertion.

The protocol included the use of specific prophylactic antibiotics, tunnelling of the EVD at least 10 cm, the avoidance of daily sampling and the avoidance of routine EVD change at day 5.

Subjects: Consecutive patients who had EVDs placed for intracranial pressure monitoring or cerebrospinal fluid drainage.

Outcome measures: EVD infection was defined as a positive microbiological culture from the CSF.

Results: In phase 1, the infection rate was 14 out of 51 EVDs (27%). In phase 2, the infection rate was 7 out of 59 EVDs (12%). This was a statistically significant reduction ($p \leq 0.05$; Chi-squared test).

Conclusions: EVD infection is a common clinical problem. This study demonstrates that adherence to a strict evidence-based protocol for their insertion is associated with a significant reduction in the infection rate.

Intracranial dural arterio-venous fistula: clinical features and results in 51 cases

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Objective: To assess the results of treatment for intracranial dural arterio-venous fistulae.

Design: Retrospective analysis of case notes and radiological investigations.

Subjects: Fifty-one consecutive patients with intracranial dural arterio-venous fistulae treated from 1991 to 2004 (excluding CCF).

Outcome measures: Neurological status and radiological evidence of obliteration of fistula.

Results: Peak age 51–70 years (range 19–83 years). Thirty (59%) patients were male. The commonest location was at lateral sinus (49%). Presenting symptoms were headache (50%), pulsatile tinnitus (23%) and seizures (13%), including haemorrhages in 49%. Cognard (1995) classification was used in evaluating angiogram findings. Commonest were Cognard Type IV in 19 (37.2%) and Type I in 13

(25%) patients. Out of 25 cases treated endovascularly, 11 (44%) were obliterated and 12 undergoing subsequent surgical disconnection. Fifteen patients were treated by surgical disconnection only, 13 (86%) successfully. Of 27 surgical cases 20 (75%) were cured (four with tiny residue and three not known). Nine patients with low risk fistula were treated conservatively (two further cases refused treatment). **Conclusions:** Intracranial dural arterio-venous fistula are distinct entities with pathophysiology dissimilar to cerebral A–V malformations. Venous hypertension and intracranial haemorrhage are two important causes for neurological deficits. Surgical disconnection and endovascular procedures are both effective in achieving obliteration.

Selective disconnection of cortical venous reflux as treatment for cranial dural arteriovenous fistulas

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Object: A consecutive single-institution series of 119 patients with a dural AV-fistula (DAVF) with cortical venous reflux (CVR) was reviewed to assess the overall clinical outcome of multidisciplinary management after long-term follow-up and to evaluate the selective disconnection of CVR versus the obliteration of the whole DAVF.

Methods: Cases were diagnosed between 1984 and 2001. Treatment was instituted in 102 patients. The outcome of adequately treated patients was compared to a control-group with persistent CVR and to literature data. In case of combined dural sinus drainage and CVR a novel treatment, concept of selective disconnection of the CVR was evaluated, leaving the sinus drainage intact and thus converting the aggressive into a benign DAVF.

Results: Endovascular treatment, primarily instituted in 78 patients, resulted in an obliteration or selective disconnection in 26/102 cases (25.5%). Seventy cases (68.6%) were surgically obliterated or disconnected. Six cases (5.9%) were left with persistent CVR. No lasting complications were noted. Follow-up angiography confirmed a durable result in 94 of 96 adequately treated cases (97.9%), with a mean follow-up of 27.6 months (range 1.4–138.3 months). Selective disconnection was done in 23 DAVFs with combined sinus drainage and CVR. Their long-term outcome was equal to obliterated DAVFs, at a lower complication rate.

Conclusions: Considering the ominous disease course of DAVFs with patent CVR, multidisciplinary treatment of is highly effective at a low complication rate. Selective CVR disconnection proves a valid treatment option in DAVFs with combined dural sinus drainage and CVR, as was already shown in cranial DAVFs with direct CVR.

Surgical treatment of partially coiled aneurysms

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Introduction: Aneurysm neck residuals or remnants after endovascular treatment are associated with a significant risk of recurrent subarachnoid haemorrhage (SAH). It was noted that clipping of partially coiled aneurysms can be difficult.

Methods: To elucidate what makes partially treated aneurysms more difficult to treat surgically we retrospectively analysed the data on 19 patients (21 aneurysms) that underwent clipping after (partial) coiling from 3/1995 to 3/2005. Seven aneurysms (33%) were in the posterior circulation and 14 (67%) in the anterior circulation.

Results: Arachnoid scarring with adherence of large perforators to the aneurysm was observed in 7/19 cases (37%). Intraoperative rupture of the aneurysm occurred in five (26%) patients. The coil mass caused the clip to slide down and occlude a PCA in two of five patients with basilar tip aneurysms necessitating clip repositioning. Follow-up angiograms, available in 18/19 cases, confirmed total occlusion in all. The Glasgow Outcome Score was Good in 53%, Moderately disabled in 16%, Severely disabled in 21% and Dead in 11%. Patients with posterior circulation aneurysms did significantly worse ($p < 0.05$). Temporary occlusion, intra-operative rupture and age did not predict poor outcome.

Conclusion: With the number of endovascular treatments for aneurysms rising more residuals will be expected. The poor results for surgically treated posterior circulation aneurysm residuals may indicate that when complete endovascular occlusion is not to be expected, surgical clipping should be considered as primary treatment.

Angiography postclipping and coiling of cerebral aneurysms

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Objective: To compare residual aneurysm rates and re-intervention rates in patients who had aneurysms coiled, compared to those who were clipped.

Subjects: Eighty-six patients who underwent clipping and 82 who underwent coiling between 1998 and 2003. The surgical group have previously been presented to the SBNS.

Methods: Six-month check angiography was performed on either group. We noted the rate of aneurysm exclusion from cerebral circulation and the rate of re-intervention with either technique.

Results: There were four 'dog-ear' remnants in the surgical population (of 86 patients), one of whom

required reoperation. Thirty-one of 82 coiled aneurysms was incompletely excluded from the cerebral circulation, four of these have undergone retreatment to date.

Conclusions: Although ISAT informs us that the immediate complications of clipping are less than those of coiling, the degree and permanence of exclusion of an aneurysm from the cerebral circulation may be more secure with surgery.

The use of OPS imaging to detect microvascular disturbances in cerebral ischemia

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Introduction: Microcirculatory function of the brain is essential for providing adequate oxygen to the tissue cells. In neurovascular diseases disturbances of the cerebral microcirculation possibly plays a role in the development of cerebral ischemia. Until recently, the *in vivo* observation and quantitative functional assessment of the human cerebral microcirculation were limited by the absence of appropriate investigational techniques. This limitation has been overcome with the introduction of orthogonal polarization spectral (OPS) imaging. We used OPS imaging on the brain cortex during aneurysm surgery and resection of an arteriovenous malformation (AVM) to directly observe the small cortical blood vessels and quantify the contractile properties and changes in microvascular flow (MFI) and functional capillary density (FCD).

Methods: In 24 patients undergoing aneurysm surgery the diameter changes of small cortical vessels (15–180 μm) were observed using OPS imaging. Seventeen patients were operated early (within 48 h after bleeding) and seven underwent late surgery. Immediately after dura opening, the response to hyperventilation ($n=16$) and papaverin ($n=8$) of arterioles and venules was observed with OPS imaging under sevoflurane anaesthesia. Six patients served as control. Furthermore, images of the cerebral microcirculation were obtained in two patients undergoing microsurgical removal of an AVM and in two patients undergoing craniotomy for a disease not affecting the cortical microcirculation.

Results: In the presence of subarachnoid blood a severe disturbed reaction of the microvessels was observed. More specifically, hyperventilation resulted in a $39 \pm 15\%$ ($p < 0.05$) decrease in arteriolar diameter with a 'bead string' constriction pattern occurring in 60% of patients. This reaction normalized in the absence of subarachnoid blood (late surgical patients and controls). The topical application of papaverine resulted in a $64 \pm 53\%$ (range 0–127%) for a period of 6 ± 2 min. Before

resection of an AVM, microvascular flow and FCD were decreased. After AVM excision a tremendous increase in microvascular flow was seen accompanied by an increase in FCD without a significant change in microvessel diameter.

Conclusions: OPS imaging allows direct *in vivo* observation and quantitative functional assessment of the cerebral microcirculation, enabling us, for the first time, to visually observe and quantify microvascular reactivity and haemodynamic changes in the human brain. These observations may provide a better understanding of the pathophysiology of cerebral ischemia.

Biological mechanisms of acute Pravastatin therapy on cerebral vasospasm, delayed ischaemic deficits and outcome on patients following aneurysmal subarachnoid haemorrhage: a randomized controlled trial

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Objective: Acute treatment with Pravastatin after aneurysmal subarachnoid haemorrhage (aSAH) can ameliorate vasospasm, improve autoregulation and reduce delayed ischaemic deficits (DID). We hypothesized that these effects were mediated through anti-inflammatory and anti-thrombogenic mechanisms.

Design: A phase II randomized controlled trial.

Subjects: Eighty aSAH patients (age 18–84 years) within 72 h from the ictus were randomized equally to receive either oral Pravastatin (40 mg) or placebo daily for up to 14 days.

Outcome measures: Laboratory data, including C-reactive protein (CRP), fibrinogen, d-dimer and lipid profiles, were measured every 3 days. Data were compared between the two groups, and between patients with/without vasospasm, DID or unfavourable outcome.

Results: Baseline laboratory data were similar in both groups. After the trial started, the total cholesterol levels were significantly reduced in the Pravastatin group (t -test $p < 0.001$), which correlated with the anti-vasospastic property (t -test $p = 0.082$). The increments in fibrinogen (t -test $p = 0.172$) and CRP levels (t -test $p = 0.116$) on Day 3 and decrements in d-dimer level on Day 6 (t -test $p = 0.23$) tended to be less pronounced in the Pravastatin group. These laboratory changes also correlated with the duration of vasospasm (t -test $p < 0.001$) and severe vasospasm (t -test $p < 0.001$), the incidence of DID (t -test $p = 0.034$), and unfavourable outcome (t -test $p = 0.024$).

Conclusions: These data support the anti-inflammatory and anti-thrombogenic mechanisms of Pravastatin therapy on aSAH patients.

Cerebral metabolic improvement following hypertonic saline administration in patients with severe subarachnoid haemorrhage

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Objective: To explore whether cerebral blood flow (CBF) enhancement with hypertonic saline (HS) in patients with severe subarachnoid haemorrhage (SAH) is associated with an improved oxygenation and metabolic profile.

Design: Continuous bedside multimodal monitoring of ABP, ICP, CPP, brain tissue oxygen (PtiO₂), middle cerebral artery flow velocity (FV) and microdialysis were recorded. Quantified xenon computerized tomography (XeCT) was performed before and after infusion of 23.5% HS in 12 patients, and CBF in a region of interest around the brain tissue oxygen and microdialysis probes was calculated (ROI CBF). Data is given as mean ± SE.

Subjects: Twenty-eight patients (age range 37–74) presenting with poor grade aneurysmal SAH.

Outcome measures: Change in regional CBF, PtiO₂, cerebral glucose, lactate, pyruvate and glutamate during HS administration.

Results: Average baseline ROI CBF was 31.6 ± 3.6 ml/100 g/min. In four patients, ROI CBF decreased after HS. In the remainder, a significant increase in ROI CBF was observed ($p < 0.05$). Pooling the data for all patients, at 30 min postHS infusion a significant increase in ABP, CPP, FV and PtiO₂ was seen, together with a significant decrease in ICP ($p < 0.05$). At 60 min, ICP, CPP, FV and PtiO₂ still showed significant changes ($p < 0.05$), blood pressure returned to baseline levels and a significant increase in glucose was seen. In 18 patients, a decrease in lactate-pyruvate ratio was seen at 60 minutes following HS. No side effects have been observed.

Conclusion: HS safely and effectively augments CBF in patients with poor grade SAH and significantly improves cerebral oxygen and glucose. An improvement in cerebral metabolic status in terms of lactate-pyruvate ratio is also associated with HS infusion.

Spreading depolarization occurs in patients with aneurysmal subarachnoid haemorrhage: the definitive explanation for delayed deterioration?

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Objective: One concept of delayed ischaemic neurological deterioration (DIND) after SAH proposes that K⁺ and free oxyhaemoglobin from haemolysis cause local ischaemia that spreads, linked with cortical spreading depression (CSD). We sought evidence for CSD in patients with SAH.

Design: Analysis of electrocorticographic (ECoG) data obtained from continuous recording for up to 10 days from a Wyler 6-electrode subdural strip placed at the conclusion of surgery.

Subjects: Seventeen patients with proven aneurysmal SAH in four European centres, requiring craniotomy and consenting to enrolment in the Co-Operative Study of Brain Injury Depolarizations (www.cosbid.org).

Outcome measures: Incidence of CSD-like events.

Results: Seven patients had no spreading events, while 10 had total 165 spreading events (8; 2–41 (median; range). In five patients, ECoG activity recovered in under 10 minutes following CSD events, while in another five patients some recovery times were longer; one such patient also had peri-infarct depolarizations (PIDs: large SPC's on a background of persistently depressed ECoG). Other variables monitored (TCD, CSD recovery time, microdialysis) provided examples of metabolic stress associated with CSD events.

Conclusions:

- There is clear evidence for the occurrence of CSD events after surgery in ~60% of patients with SAH.
- Taken together with newly detected mechanisms in cerebral cortical ischaemia, the results support a concept of separate proximal (major vessels) and distal (microcirculation) ischaemic insults to explain DIND and its clinical features.
- We suggest that susceptibility to CSD might contribute to risk of postoperative DIND.

Outcome after subarachnoid haemorrhage in neurosurgical units in the UK and Ireland

Steering Group of the National Observational Study of SAH (Society British Neurological Surgeons, Society British Neuroradiologists, Clinical Effectiveness Unit, Royal College of Surgeons of England, London, UK)

Objectives: To identify risk factors (case-mix, treatment and neurosurgical unit characteristics) associated with outcome in patients with subarachnoid haemorrhage (SAH).

Design: A prospective observational cohort study of unselected patients admitted to all neurosurgical units in the UK and Ireland between September 2001 and September 2002. Data quality and case ascertainment were validated by visits to every unit.

Subjects: Patients over 15 years of age with a confirmed SAH were eligible. Analysis focused on those with a confirmed aneurysm.

Outcome measures: Functional status at 6 months was measured by the extended 8-point Glasgow Outcome Scale derived from a postal questionnaire.

Results: Of 3174 patients entered, 2397 (75.5%) had a confirmed aneurysm; 1269 underwent clipping and 905 underwent coil embolization. Multivariate logistic regression identified age, admission WFNS

grade, blood on CT scan and the presence of comorbidity as significantly relating to an unfavourable outcome. Site and size of the aneurysm, method of repair and unit level characteristics (participation in ISAT, availability of coiling and volume) were not associated with outcome in the multivariate model. Using a multilevel model, no significant difference existed in outcome between individual neurosurgical units after adjustment for risk factors.

Conclusions: This study identifies the main risk factors associated with an unfavourable outcome after subarachnoid haemorrhage. Results can help develop a minimal dataset to assess outcome in SAH patients.

Organotypic spheroids of malignant glioma: an ex vivo, quantitative, multiplex, high-throughput screening model in 3D

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The plethora of newly-developed potential therapeutics for glioblastoma requires a test model that adequately quantifies response and is biologically valid. Historically, monolayer cultures and commercially available cell lines are used for this purpose. However, there is marked discrepancy in responses of these widely used test systems and human tumour responses, which illustrates the biological invalidity of these cell suspension test models. This is partially explained by clonal selection and loss of intercellular cross-talk. To circumvent these problems surgical specimens are cultured in medium as explants in the short term and grown as organotypic spheroids as previously described by Bjerkvig *et al.* (*J Neurosurg* 1990;72(3):463). Limitations for use in drug experiments were based on:

- lack of quantitation of response using only qualitative morphological assessment;
- heterogeneity of spheroids with undetermined implications for design of experiments;
- only hypothesized superior biological validity as compared with widely-used and easily-quantitated cell-suspension models.

Therefore, first, a semi-automated method has been developed that facilitates quantification of viability, proliferation and apoptosis, and this appears to be a valid quantitative approach to determine response. Images of enzyme histochemically and immunohistochemically stained cryostat sections of spheroids are digitally captured and analysed using automated image cytometry. Secondly, the natural variance of measurements dictates the number of spheroids to be used in experiments. This is shown to be within ranges that allow for high throughput screening.

Thirdly, to demonstrate the biological validity of the spheroid test model, DNA microarrays experiments are performed to compare the genetic profile of the original tumour with both monolayer culture and organotypic spheroids from the same material. It is hypothesized that the organotypic spheroids show good correlation with the original tumour, in contrast to the monolayer culture. In conclusion, an organotypic spheroid test system for in vitro drug screening in malignant glioma has been developed that rapidly quantifies response, allows for high throughput screening and appears to be superior to cell suspension models in genetic profile as compared with the original tumour.

Systemic immune modulation in Glioblastoma Multiforme

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Introduction: The Central Nervous System (CNS) has been thought of as an immune privileged site until recently, but as our understanding of the immune system has improved this idea is under review. Recent studies have shown that tumours in the CNS have a major effect on the systemic cytokine profile and immune modulation may occur due to CNS pathology.

Aim: To determine the change in the serum cytokine levels in Glioblastoma Multiforme (GBM) patients as compared with normal controls, looking at pro-inflammatory cytokines and T-helper cells type 1 and 2 (Th1 and Th2) cytokine balance.

Methods: A prospective analysis of the serum samples from 40 GBM patients were compared with age and sex matched controls ($n = 20$). The cytokines analysed were pro-inflammatory IL-1 α , IL-1 β , IL-6 and TNF α ; Th1 cytokines IL-2, IL-12p70 and IFN γ ; Th2 cytokines analysed were IL-4 and IL-10.

Analysis: The samples were analysed using a Proteoplex 16 well human cytokine array kit (Merck biosciences), and the results were analysed. For statistical significance using the Mann-Whitney *U*-test.

Results: There was a statistically significant rise in the pro-inflammatory cytokines IL-1 α and IL-1 β (IL-1 α $p = 0.010$; IL-1 β $p = 0.030$). The Th2 cytokines also showed an increase (IL-4 $p = 0.039$ and IL-10 $p = 0.004$), while there were no changes in the Th1 cytokines.

Conclusion: We have shown an increase in the pro-inflammatory cytokines, as well as an increase in the Th2 cytokine profile. Previous studies in malignant melanoma reported an imbalance in the Th1/Th2 profile showing a decrease in Th1 cytokines and an increase in the Th2 cytokines. The reason for the difference between the studies is unknown but could be due to the unique environment of the CNS.

Patients with brain tumours have significantly elevated levels of serum Vegf-A and Vegf-C

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Objective: Vascular endothelial growth factor (VEGF)-A is known to be one of the most important angiogenic factor under physiological and pathological conditions, whilst VEGF-C is implicated in the development and sprouting of blood vessels and lymphatic vessels. Here we aim to investigate the concentration of serum VEGF-A and VEGF-C in patients with brain tumours compared with controls.

Design: A prospective analysis to compare the concentration of serum VEGF-A and VEGF-C in patients with newly diagnosed brain tumours against age- and sex-matched controls.

Subjects: The cohort of 65 tumours comprised: 13 meningioma, four anaplastic astrocytoma and 48 GBM patients. Controls were 50 patients with degenerative spinal disease.

Outcome measures: Serum samples were analysed in duplicate via quantitative ELISA (BioSource and Bender MedSystems).

Results: Serum VEGF-A and VEGF-C was detected in all patients and controls. There was a significant increase in serum VEGF-A levels in meningioma ($p=0.039$) and GBM ($p < 0.001$) patients compared with the controls. Significant increases were also seen in VEGF-C levels in all grades of tumour compared with controls: meningioma ($p < 0.001$), anaplastic astrocytoma ($p=0.023$) and GBM ($p < 0.001$) patients.

Conclusions: Both VEGF-A and VEGF-C are elevated in patients with brain tumours with the highest levels being observed in the most advanced tumour grade. These findings are in keeping with results from systemic tumours and suggest that generalized immune imbalances occur in brain tumour patients. Furthermore, these data may have potential usefulness as biological markers of disease progression and out-come in patients with brain tumours.

Cerebral structure-function correlation with 3D FLAIR and functional MR imaging in patients with intracranial lesions

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Objective: Structural magnetic resonance (MR) imaging is essential in the presurgical evaluation of patients with intracranial lesions. Successful presurgical planning requires knowledge of the spatial relation between the lesion and eloquent cortex. Large interindividual differences between structural

and functional neuroanatomy make it difficult to accurately assess this relation, especially in the presence of intracranial lesions with oedema or brain shift. Recently, we optimized a new isotropic single-slab three-dimensional (3D) fluid-attenuated inversion recovery (FLAIR) sequence for the detection of brain lesions in patients with multiple sclerosis. Using this MR sequence with surface rendering of the cortex it is possible, due to local cortical signal intensity differences, to visualize the central sulcus (CS) region and visual cortex. To test the hypothesis whether the functional MRI (fMRI) motor activation corresponds to the visible CS region, we subsequently used this 3D FLAIR technique for patients with intracranial lesions.

Methods: Twelve consecutive patients with intracranial lesions (eight male, four female), age 30–69 years (mean 46 years) who underwent functional MR imaging in the preoperative evaluation for surgery were studied. Functional MRI was performed with a 1.5 Tesla MR scanner (Siemens Sonata, Erlangen, Germany) using the echo-planar imaging (EPI) T2* technique. The motor paradigm consisted of self-paced clenching and spreading of the hand during 15 s alternated with rest periods of 15 s, during a total of 10 epochs. Five patients had bilateral fMRI motor evaluation, 6 only unilateral at the affected hemisphere, and one patient had no fMRI. A single-slab 3D FLAIR sequence was used, with an acquisition time just below 10 min. Postprocessing and visualization software (Neuro 3D, Siemens, Erlangen, Germany) was used to make surface renderings. Because the voxels are nearly isotropic ($1.2 \times 1.2 \times 1.3 \text{ mm}^3$), reconstruction could be done in all orientations without blurring or image degradation.

Results and Discussion: In 17/24 (71%) of the hemispheres the CS region could be visualized on 3D FLAIR, due to lower signal intensities in this area and in 14/16 (88%) of the hemispheres fMRI activation was successful. In those cases fMRI activation was found in the CS region as observed with 3D FLAIR. Failures to visualize the CS region with 3D FLAIR are due to peritumoural oedema or infiltration of tumour. We used an isotropic 3D FLAIR imaging technique of the brain, which is suitable for 3D surface rendering. The images have no signal from CSF and low signal from skull and skin, which allows a reconstruction of the cortical surface without preprocessing steps like skull-stripping. We have shown that cortical rendering of these 3D FLAIR images can be used to visualize different cortical areas, especially the CS region and visual cortex. It can be used as an additional tool to determine the spatial relationship between a lesion and the central sulcus.

Conclusion: The data from the functional MRI confirmed the visible area of the central sulcus in most cases, which offers new possibilities to use structural MR imaging with functional characteristics.

Intra-operative ultrasound elasticity imaging techniques: a method for identifying brain/tumour boundaries

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London, UK)

Objective: Ultrasound elasticity imaging techniques can be used to detect mechanical properties within a scan plane. The objective of this study was to determine whether these techniques could be used to detect the brain/tumour interface and adherence of tumour to brain.

Design: This was a prospective single blinded study. Spatial positions were recorded using StealthStation neuro-navigation co-registered with ultrasound. Ultrasound elastography was performed intra-operatively in real time and following off line data processing. Relative stiffness of brain *v.* tumour and adherence of tumour to brain was measured using ultrasound elasticity imaging techniques. The results were compared to surgical findings on relative stiffness and brain tumour adherence, and Young's modulus estimates following *ex vivo* mechanical testing of tumour specimen.

Subjects: Ten patients undergoing craniotomy and tumour removal.

Outcome measures: Graphical elastograms representing stiffness and slip boundaries were produced and correlated to surgical findings. Relative strain ratios on elastograms were compared to ratios of young's modulus of brain to tumour measured *ex vivo*.

Results: Elastogram findings on stiffness correlated well with surgical findings and Young's modulus findings. Elastogram findings on the brain tumour adherence correlated exactly with the surgical findings.

Conclusion: Ultrasound elastography can detect differences in stiffness of tumour compared to brain and can accurately delineate the brain/tumour interface. Tumour pedicles can be detected assisting surgical planning. Ultrasound elasticity imaging techniques can accurately provide absolute values on the force required to produce slip between tumour and brain. This may have prognostic implications and assist surgical resection.

Use of Gliadel[®] (BCNU) Wafers in high grade glioma

C. E. G. Uff & R. Bradford (Royal Free Hospital,
London, UK)

Objective: Gliadel[®] wafers have been shown to improve predeterioration survival in patients with high grade glioma with no significant increase in peri-operative side effects. We have used them on selected patients at since January 2004. The aim of this study is to review our experience with Gliadel[®], and to illustrate the complications encountered with its use.

Design: Retrospective review.

Subjects: Thirteen patients with supratentorial high grade glioma, 12 WHO grade IV glioblastomas and one WHO grade III anaplastic oligodendroglioma.

Outcome measures: Survival time, frequency, type and severity of complications.

Results: Survivors (eight cases): mean survival of 30.75 months from high grade diagnosis, 6.88 months from Gliadel[®] implantation. Patients who have died (five cases): mean survival of 7.0 months from high grade diagnosis and 2.4 months from Gliadel[®] implantation.

Complications: Four wound infections requiring bone flap removal, three patients with neurological deterioration, one fatal stroke.

Conclusions: The high rate of wound infection is thought to be related to inadequate dural closure and subsequent leakage of BCNU into the wound. All four patients had onlay synthetic dural grafts and we suggest that autologous grafts should be used wherever possible. Timing of adjuvant therapy and reopening of wounds did not appear to be related.

Free flaps in skull base neurosurgery: a management plan

M. Taha, J. McMahon, A. Fitzgerald & T. Carroll
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Sheffield, UK)

Objective: The use of free flaps in skull base surgery is not universally practiced in the UK. Recently published NICE Guidelines on head & neck cancers promoting closer association with a regional skull base service will likely lead to more aggressive management of malignancies involving the skull base necessitating a standardized approach to skull base reconstruction. We present a modified algorithm for the use of free flaps in skull base surgery on the basis of our experience, i.e., of a regional skull base multidisciplinary service.

Design/subjects: Thirteen patients (seven male, six female, age 39–72 years) underwent skull base procedures involving free flaps over a 2-year period. The indications for surgery included malignancy (nine) and benign neoplasia with previous radiotherapy (two). Eight procedures involved resection of anterior cranial fossa floor/orbit and four involved the lateral skull base.

Results: Free flaps used included rectus abdominis (eight), latissimus dorsi (three), and radial forearm (two). There were no deaths. One patient underwent flap revision due to anastomotic failure. A further patient had flap modification due to excessive tension of skin paddle. One patient had a CSF leak, but at a site separate from his free flap.

Conclusions: We recommend free flap reconstruction for any significant skull base defect, which involves both skull and dura, that can't be closed by mobilization of a regional rotation flap or where a potential regional rotation flap has been in an irradiated field.

Important factors determining outcome include appropriate pedicle length, flap thickness, adequate flap assessment, and controlled lumbar CSF drainage.

Initial experience with transnasal endoscopic pituitary surgery

H. C. Patel, A. Likith, S. Parkington, et al.
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Objective: The technique of transnasal endoscopic pituitary surgery (TNES) is still in its infancy, although slowly gaining widespread acceptance. Results following this surgery have been reported previously, but few reports have documented their initial experience. The aim of this study was to document our initial experience of TNES.

Design: Retrospective analysis of patient records.

Subjects: All patients undergoing TNES ($n = 48$) at the Royal Preston Hospital.

Outcome measures: Patient presentation, and outcomes particularly complications of septal perforation, epistaxis, sinusitis, carotid artery injury, CNS injury, haemorrhage of tumour, visual deterioration, CSF leak, meningitis, pituitary sufficiency and mortality were recorded.

Results: Forty-eight patients with a median age of 61 (range 21–84) years at initial presentation were identified. Visual disturbance was the most common presentation (31/48) and non-functioning pituitary adenomas were the most commonly encountered pathology (30/48). The overall mortality in this study was 2/48 (4%). The most common complication was anterior pituitary insufficiency 11/27 (40%) followed by posterior pituitary insufficiency was observed in 4/40 (10%). Postoperative CSF leak seen in 9/48 (18%) was further complicated by meningitis in 5/9 patients. Epistaxis was seen in three patients (6%), whilst sinusitis, carotid artery injury or CNS injury was observed in one patient each (2.2%). No patients reported visual deterioration, septal perforation or had evidence of postoperative tumour swelling.

Conclusion: Serious complications may occur following TNES. Pituitary surgery has been shown to be safer in experienced hands, and improvements can be expected with greater experience.

Neuronavigation-guided endoscopic trans-sphenoidal surgery: the first 74 cases

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(The Royal London and St Bartholomew's Hospitals, Barts and the London NHS Trust, London, UK)

Objective: Neuronavigation assisted endoscopic trans-sphenoidal surgery is a relatively new procedure in our unit. Evidence for a 'learning curve' was sought.

Design: Retrospective review of the cases divided into three cohorts (A/B/C) of sequential fourteen months each.

Subjects: All patients who underwent neuro-navigation-guided endoscopic pituitary fossa surgery from October 2001 to March 2005.

Outcome measures: Group characteristics including further treatment for residual/recurrent lesions and complications were analysed.

Results: Seventy-four patients (34 males, 40 females) with a mean of 50.4 years (range 16–85), were operated by one neurosurgeon with an endoscopic nasal surgeon. Twenty-seven presented with visual deficit, 42 with endocrine manifestations, four with both visual and endocrine features, and one was asymptomatic. Histology confirmed non-functioning pituitary adenoma 37, Cushing's disease 14, acromegaly seven, prolactinomas five, Rathke's cleft cysts two, hypophysitis two, craniopharyngioma two, mixed adenoma one, other diagnoses four. Six had concurrent apoplexy. There were 39, 16 and 19 patients in the groups A, B and C, respectively. Seventeen (nine transient) cases had CSF leaks (3, 8 and 6 in groups A, B and C, respectively). Ten patients (5, 3 and 2 in groups A, B and C, respectively) required further surgery for tumour removal/CSF leak repair. Three patients had clinically significant intraoperative bleeding in A-group. There was one peri-operative death in A-group (Chi-square test for statistical significance).

Conclusions: Neurosurgeons skilled in pituitary surgery can safely move from open approaches to neuronavigation-guided endoscopic surgery. The transition is aided by collaboration with a skilled nasal endoscopist. There will undoubtedly be a surgeon-varying learning curve, but certain complications can be reduced by attention to technique/modifications of the approach.

Use of computerized tomography with 3-D reconstruction in the evaluation of the lumbar spine for preoperative planning for fusion

S. R. M. Qadri, T. Muthu, K. Abbasi, et al. (Coventry and Warwickshire NHS Trust, Coventry, UK)

Objective: Pedicle screw fixation has become the main stay of posterior lumbar fusion. Optimal placement of the pedicle screw is essential for prevention of complications. The consequences of straying in any direction can be disastrous. Surveys of screw placement in most series suggest a mal-position rate of 3–7%. We present our series of patients operated for posterior lumbar fusion.

Design: Patients planned for posterior lumbar fusion prospectively, were evaluated with a pre-operative CT scanning protocol of the lumbar spine, devised by the senior author and the radiologist. CT was used to measure the inter-pedicular distance, the thickness and depth of the pedicle, and the length of

the screw that could be safely placed in the vertebral body.

Subjects: One-hundred-and-six patients consisting of 52 males and 54 females were operated for degenerative disc disease, spondylolysis/lithesis or spinal tumour. Total of 524 screws were placed.

Outcome measures: Pedicle screw position was assessed by conventional postoperative AP and lateral radiographs.

Results: One patient had a cracked pedicle perioperatively and one had infection. No cases of screw mal-position, CSF leak, nerve root damage or neuropraxia were noted.

Conclusion: Neurosurgeons appreciate the value of precise operative localization during surgery. We feel that this approach, using preoperative CT scanning, would appeal to those becoming familiar with pedicle screw placement. It has been especially useful for trainees in neurosurgery as it teaches them to understand the three-dimensional anatomy of the vertebra. This is particularly beneficial when the anatomy is distorted or difficult to visualize due to previous surgery or congenital abnormality.

C1–C2 transarticular screw fixation for atlantoaxial instability due to rheumatoid arthritis: analysis of outcome

J. Nagaria, L. McEvoy & C. Bolger (Department of Neurosurgery, Beaumont Hospital, Dublin, Irish Republic)

Objective: To review the clinical outcome of 37 consecutive patients undergoing C1–C2 transarticular fixation for patients with Rheumatoid Arthritis.

Design: Prospective observational study.

Methods: There were 37 patients at two centres. The age range was 37–82 years. The time since diagnosis to treatment was 2–23 years. Clinical presentation included suboccipital pain in 26/37 patients and neck pain in 29/37 patients. Twenty-two patients had presented with myelopathy (Ranawat grade II or III A). The preoperative imaging included Plain X-rays, CT scans and MRI scans. All patients underwent C1–C2 transarticular screws (Stealth guided), except four patients in which an aberrant course of the vertebral artery was identified.

Outcome measures: Functional outcome, complications, Postoperative Neurological Status, Neck Disability index, Myelopathy Disability Index and Health Status Profile SF-36.

Results: One patient had died at 12 months follow-up. Neck pain improved in 22 (75%) of patients by >5 points on the VAS. Suboccipital pain had improved in all patients. Seventeen patients (80%) improved following operation on the Ranawat Grading, two patient were worse and three patients remained the same. More than 70% patients reported improvement in neck disability index and >50% patients reported improvement in myelopathy disability index.

Conclusions: C1–C2 Transarticular fixation with spinal navigation is a safe technique for treating atlantoaxial instability in patients with Rheumatoid Arthritis. This study demonstrates improvement in all domains including neck disability, myelopathy scores and functional outcome.

Delphi E(RCT)². Surgery for rheumatoid craniocervical instability? Rationale and design of an European randomized controlled trial

W. C. Peul, A. T. H. Casey, J. F. C. Wolfs, et al. (Leiden University Medical Centre, the Netherlands)

Introduction: Pannus formation and laxity of the transverse and apical ligaments are known rheumatoid changes in the craniocervical area. Rheumatoid atlantodental instability and secondary basilar impression will lead to serious myelopathic disability and sudden death. Population based epidemiological studies report a lifetime incidence in rheumatoid patients of 10–15%. Which proportion of radiological craniocervical pathology will develop neurological problems and in which time window? The latest results led to the establishment of another treatment philosophy, advocated by well-known surgical experts. This strategy is centred around early timing of surgery based on radiological abnormalities and prevention of neurological sequelae. Although attempting to follow this treatment strategy, evidence is still lacking. Critical analysis of the results in the Netherlands and comparison with the existing literature is the basis for developing a randomized trial.

Methods: In the LUMC(1999–2000), 82 consecutive patients with rheumatoid arthritis underwent craniocervical stabilization. Only C1C2 instability was seen in 18 patients obviating the need for extensive craniocervical fixation. The other 64 patients were prospectively followed over a minimum of 2 years. The primary outcome measure was the Ranawat scale. Secondary outcome measurements include CT en MRI and neurological deficit. Major events such as death, progression of neurological deficit and reoperation were registered. Second a Delphi Questionnaire was sent throughout Europe to all members of the Cervical Spine Research Society and Rheumatologists to evaluate the international differences concerning the timing of surgery.

Results: A majority of 71% Ranawat Class 3A patients did improve to Class 2, whereas only 16% of 3B patients did improve to Class 2. The great majority of Class 3B patients (84%) did not improve and had more complications. Two 3B patients died and a few hardware complications are reported. The Delphi Questionnaire did show huge variations in the treatment strategies between countries and between medical specialties resulting in a doubtful range of surgical indication between 5 and 12 mm C1–C2 slip.

Discussion: Although this is not a scientific investigation, it may be concluded that current craniocervical techniques are safe to apply and result in immediate rigid fixation. Most patients were classified as Ranawat 3B. These patients do have according to Crockard an unacceptable high mortality rate of 40% in the first six postoperative months, in contrast with Ranawat 2 and 3A (2%). Although the surgical risk seems high the complication rate is low in experienced hands and when performed early in the natural course of disease. The guideline should be altered and early surgery advocated in case of a C1–C2 slip without neurological deficit. However evidence is lacking prohibiting implementation of this invasive treatment strategy. The Delphi Trial is an international multi-centre Cost-Effectiveness Clinical Trial, comparing early timing of surgery with a longer wait and see policy in patients without any neurological deficit. The Myelopathy Disability Index will be the primary outcome measure of neurological deficit. This epidemiological study will be carried out following the current methods of research, and will lead to a proper treatment strategy and multidisciplinary consensus in the future. The intake will start during autumn 2005 in the Netherlands, spring 2006 in the United Kingdom, Sweden, France and Switzerland. Other countries with their own randomization strategy will start during the following months. Total follow-up will be 10 years, whereas the main research question will be answered after 5 years.

Should surgery be the primary treatment for metastatic spinal disease?

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(Department of Academic Neurosurgery,
Addenbrooke's Hospital, Cambridge, UK)

Objective: A prospective analysis of survival and functional outcome in patients with metastatic spinal disease treated primarily by acute surgical decompression, with stabilization when indicated.

Design: A prospective cohort study of patients managed by one consultant neurosurgeon from 1995 until 2004.

Subjects: Sixty-two patients with radiologically suspected metastatic spinal disease.

Outcome measures: Survival, continence, walking, analogue pain scores and short form 36 (SF-36) scores.

Results: Sixty-two patients (median 62 years, range 22–79 years, 35 female, 27 male) with metastatic breast (26%), lymphoma (13%), prostate (10%), myeloma (8%), melanoma (5%), thyroid (3%), kidney (3%) unknown primary (16%) or other (16%). Survival rates were 56% at 1 year, 39% at 2 years and 28% at 3 years. Functional outcome data will be presented in detail.

Conclusions: A recent phase III randomized trial has strongly suggested that early surgery plus radio-

therapy is significantly better than radiotherapy alone for patients with MSCC 1. Our data indicate that with careful patient selection, long-term survival and favourable functional outcomes can be achieved. We strongly advocate that patients presenting with metastatic spinal disease be considered for primary surgical treatment.

Balloon kyphoplasty in neurosurgery

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Objective: Balloon kyphoplasty is a relatively new procedure for the treatment of vertebral compression fracture. We describe our experience.

Design: Analysis of the first 31 consecutive patients with 36 painful vertebral body compression fractures treated at our unit.

Subjects: Thirty-six procedures were performed (20-thoracic, 16-lumbar) in 31 patients (19 males) aged 24–83 years (mean: 60) from August 2003 to April 2005. Presentations were backache without neurological deficit. Symptom duration ranged from 1 to 104 weeks (mean: 14). Thirteen patients had osteoporosis, 10 tumours, six trauma and two renal osteodystrophy. Mean follow-up was 22 weeks (range: 4–78).

Outcome measures: Visual Analogue Pain Scale (VAPS), Oswestry Disability Index (ODI), vertebral body height, kyphosis and wedge angles.

Results: Mean kyphosis, and wedge angle restorations were 26.3 and 36.1%, respectively. Anterior, middle and posterior vertebral body mean height gains were 15.2, 20.4 and 13.1%, respectively. Pain improved in 97% of patients. Mean VAPS improved by 3.4 (95% CI 1.9–4.9) and 5.5 (95% CI 4.1–6.9) points at 24 h and 1 month postprocedure, respectively, and was maintained throughout follow-up. One trauma patient required thoracolumbar bracing postprocedure. Mean ODI reduced from 60.6 to 41.9%, and 29.8% at 24 h and 1 month postprocedure, respectively. There were no neurological complications. One patient had further vertebral collapse necessitating surgery. Two died of unrelated illness.

Conclusions: Sustained improvement in function and pain was observed in 97% of patients. Balloon kyphoplasty appears to be a safe and effective minimally invasive treatment for vertebral compression fractures.

Neurosurgery in the elderly: futile endeavour or lost opportunity?

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Plymouth)

Objective: To establish preoperative factors affecting outcome in patients aged 75 and over undergoing neurosurgical operations.

Design: Retrospective study of patients operated on between 2001 and 2003. Preoperative health status, diagnosis, ITU admission, operation and outcome data were collected and analysed.

Subjects: Two-hundred-and-twenty-six patients aged 75 years and over.

Outcome measures: Duration of neurosurgical unit stay, ITU admission details, discharge GCS, Glasgow Outcome Scale.

Results: One-hundred-and-eighty-six (82.3%) cases were known to be independent prior to the current illness. Sixty-five per cent of patients were ASA grade 3 and 4. Only two cases were ASA grade 5. One-hundred-and-six (46.9%) cases were emergency admissions. Seventy-nine (35%) cases underwent surgery for spinal degenerative disease. Of the 66 cases with chronic subdural haematoma 16% underwent repeat surgery. Five out of six (83%) patients with acute SDH died. Thirty-one (13.7%) cases had CNS tumours. Thirty (13.3%) cases were admitted to ITU with a mean stay of 4.2 days (range 1–16). Seven (5.8%) elective and 21 (19.8%) emergency admissions died. Ninety-seven (80.8%) elective and 58 (54.7%) emergency cases had favourable outcomes. Multivariate regression analysis demonstrated that premorbid level of independence ($p=0.001$), admission GCS ($p=0.006$) and ASA grade ($p<0.0001$) were all significant predictors of outcome.

Conclusions: Premorbid level of independence, admission GCS and ASA grade are easily obtainable data, which the authors consider to be useful at predicting outcomes in elderly patients referred to neurosurgical centres. Such information may be utilized in a fuzzy logic approach to decision making in this challenging group of patients.

Fourteen years of critically ill neurosurgical transfers: where are we now?

M. Crocker, P. Hardy, S. Fairley, et al. (The National Hospital for Neurology and Neurosurgery, Queen Square, London, UK)

Objective: Analysis of transfer quality of critically ill neurosurgical patients over a 14-year period, by comparison against nationally recognized, contemporaneous guidelines.

Design: Review of five periods of audit data collected prospectively between 1991 and 2004. A proforma was completed for each patient admitted to a level 3 neurosurgical bed during the relevant period.

Subjects: Consecutive adult patients admitted to a neurosurgical critical care unit from the A&E department of referring hospitals during each period.

Outcome measures: Percentage of patients in whom management of airway, arterial blood gases

or blood pressure did not meet published standards, or who received inadequate physiological monitoring or drug therapy during transfer.

Results: Data from 1991 to 1996 show improvements in all areas, especially airway and blood pressure management. Studies in 2000 and 2004 demonstrate deviation from the more stringent 1996 guidelines, particularly regarding control of arterial blood gases and drug therapy. These deficiencies remained when audited against pre-1996 guidelines.

Conclusions: There was improvement in management of airway and hypotension during transfer in this period. There is worsening adherence to published standards of ventilation and drug therapy, persisting when earlier guidelines are used as the audit standard. Strategies addressing this problem are discussed.

Categorization of delay in transfer of patients with acute traumatic brain injuries

N. H. Taylor, E. Corteen, J. E. Davis, et al. (Addensbrooke's Hospital, Cambridge, UK)

Objective: Following traumatic brain injury, patients who require emergency decompressive surgery should undergo such surgery within 4 h from time of injury. In current UK practice this target is rarely met. The objective of this study was to categorize the nature of delays.

Design: This was a prospective observational study.

Subjects: Patients transferred to a regional neurosciences unit with acute traumatic brain injury from September 2003 to March 2005.

Outcome measures: Epochs of critical time points: injury to ambulance call, ambulance call to ambulance arrival, time ambulance spent on scene, ambulance journey time, time from arrival in accident and emergency (A&E) to secondary ambulance call, secondary ambulance call to ambulance arrival, ambulance arrival to departure, secondary ambulance journey time to regional neurosciences unit.

Results: One-hundred-and-fifteen patients were transferred and of these, 18 were appropriate for transfer for emergency craniotomy for space occupying lesions (haemodynamically stable, without multiple life-threatening other injuries). Of these 18 patients, the mean age was 43; the age range was 17–73 years. The gender distribution was 33% female and 67% male. The mean time from injury to arrival at the regional neurosciences unit was 420 min (7 h). The mean time spent in the prehospital arena was 43 min, the mean time spent in the primary A&E and was 311 min, and the mean time spent transferring the patient by ambulance was 52 min. There was considerable variation in the time spent in A&E departments (range 42–651 min).

Conclusions: These results confirm that the four hour target is still not being achieved. The majority of time is spent in primary A&E departments. Whether

the 4-h target is realistic under the current referral system remains to be seen.

Acute neurosurgical bed occupancy and rapid access rehabilitation

L. J. Bradley, S. G. B. Kirker, E. Corteen, et al. (Addenbrooke's Hospital, Cambridge, UK)

Objective: To establish the need for rapid access, acute and slow stream rehabilitation facilities for inpatients occupying acute neurosurgical beds.

Design: Over a 3-month period, patients occupying acute neurosurgical beds for over 2 weeks were followed through their admission, and their need for appropriate inpatient care facilities for each day was identified and coded in accordance with established categories. The total number of bed occupancy days (BODS) required for each service was then identified.

Subjects: All patients between the ages of 16 and 65 who had been admitted to the regional neurosurgical unit for more than 2 weeks were included in the study. Patients from outside this age range were not included as other rehabilitation/discharge pathways were appropriate.

Outcome measures: The number of BODs taken up by each clinical sub group as a proportion of the total bed occupancy.

Results: A total of 1778 BODs were taken by patients staying for longer than 2 weeks. This represents 35% of the total neurosurgical BODs available. Of these, 44% were inappropriate for acute neurosurgical care facilities. Of patients presenting with subarachnoid haemorrhage, only 25% were in an appropriate bed for ongoing care. For trauma, this figure was 30%.

Conclusions: The application of definitions for each step of the care pathway has allowed the need for rehabilitation facilities following acute neurosurgical intervention to be quantified. Further studies are required to demonstrate the long-term value of rapid access rehabilitation in patient recovery. The provision of greater resources for inpatient rehabilitation would allow acute neurosurgical services to be used more appropriately.

Effect of age and initial Glasgow Coma Score on outcome following decompressive craniectomy for traumatic brain injury

P. J. Hutchinson, I. Timofeev, E. Corteen, et al. (Addenbrooke's Hospital, Cambridge, UK)

Objective: To determine the relationship of age and initial Glasgow Coma Score (GCS) with outcome in patients undergoing decompressive craniectomy for refractory intra-cranial hypertension following traumatic brain injury.

Design: Observational study combining case record analysis and follow up.

Subjects: Forty-nine patients requiring ventilation and ICP monitoring, managed using protocol-driven therapy with decompressive craniectomy performed following failure of medical treatment to control ICP.

Outcome measures: Glasgow Outcome Score (minimum 6 months).

Results: The mean age was 30 years (range was 9–67 years). Of patients with initial GCS 3–8 favourable outcome (good recovery, moderate disability) was achieved in 23/40 (58%), with severe disability in 9/40 (22%) and 8/40 (20%) died. Of patients with initial GCS 9–12 and subsequent deterioration, favourable outcome was achieved in 6/8 (75%) with no severe disability and death in 2/8 (25%). Favourable outcome in relation to age was achieved in 10/15 (67%) in the 9–20-year cohort, 8/13 (62%) in the 21–30-year cohort, 6/10 (60%) in the 31–40-year cohort, and 6/10 (60%) in those greater than 40 years.

Conclusion: Although outcome was related to initial GCS, the majority of patients presenting in coma (GCS 3–8) had a favourable outcome. In this group of patients there was no significant difference in favourable outcome between age cohorts. A prospective randomized trial of decompressive craniectomy (www.RESCUEicp.com) has now commenced.

Recurrent trigeminal neuralgia following microvascular decompression procedures

E. Shenouda, M. Foster & H. Coakham (Department of Neurosurgery, Frenchay Hospital, Bristol, UK)

Objectives: To outline the management, surgical findings and outcome in patients with persistent or recurrent Trigeminal Neuralgia (TGN) following microvascular decompression (MVD).

Design: Retrospective analysis of prospectively collected data.

Subjects: Four-hundred-twenty-two patients underwent posterior fossa exploration for TGN in the period between 1980 and 2004 by the senior author. Twenty-four patients had recurrent TGN at variable intervals following surgery. Records were analysed retrospectively for age, sex, distribution of pain, intraoperative findings and intervention, outcome of surgery, time lapse before recurrence of symptoms, management of recurrent TGN with emphasis on the surgical findings at re-exploration, and outcomes. All patients had preoperative Magnetic Resonance Imaging (MRI) and MR Angiography before first exploration. All patients underwent standard retro-mastoid craniotomy.

Results: Four patients had persistent TGN following MVD and 20 had recurrent symptoms at a mean interval of 13.8 months (range 1–54 months). Sixteen patients underwent posterior fossa re-exploration. At surgery, nine had partial sensory rhizotomy (PSR), three had a trigeminal vein at the juxta-petrous portion of the nerve and three had recurrent arterial compression. One patient died of a

pontine haemorrhage, one developed anaesthesia dolorosa and two developed CSF. Although the glycerol injections needed to be repeated all patient remain pain free at the time of follow-up.

Conclusion: Recurrent vascular compression was rarely identified during posterior fossa re-exploration for failed MVD in patients with persistent or recurrent TGN. PSR is often an effective alternative in cases when neurovascular conflict is not identified. However, because of the relatively high incidence of complication associated with re-exploration, we recommend medical treatment or percutaneous procedures for most of the patient following failed MVD.

Microvascular decompression for hemifacial spasm: long-term review and patient satisfaction score

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Bristol, UK)*

Introduction: Over 22 years, 126 patients were treated by MVD for HFS.

Aim: To review operative findings, complications, results and patient satisfaction in a FU of 6 months to 22 years (mean 7.6 years).

Methods: Retrospective case review, postal questionnaire and telephone interview.

Outcome measures: Cure, partial cure, failure. Visual satisfaction score 0–100; high satisfaction 76–100, average satisfaction 51–75, low satisfaction 0–50.

Results: Operative findings—compressive vessel: PICA 59%, AICA 30%, VA 31% (combined vessels in 32 cases). Initial cure at 6 months = 77%, partial 14%, failure 11%. Long-term FU efficiency (80%), some cases relapsed, some cured at second operation—7/8, others improved giving final cure 81%, partial 12%, failure 7%. Satisfaction scores: high 84%, average 11%, low 5%.

Complications: Delayed 7th nerve paralysis with recovery 5%, CSF leak 3%, total unilateral deafness 6%, partial 4%.

Conclusions: MVD for HFS is highly effective and safe, giving high satisfaction to patients. Late improvement occurs after 6 months and, therefore, long FU is necessary. Re-operation is usually successful.

Technical and clinical assessment of neuronavigation. Thesis

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Abstract: Since its first introduction in 1986 by Roberts *et al.*, neuronavigation has become increasingly popular to transpose preoperative imaging informa-

tion to the surgical field. Although it is now widely used in routine neurosurgery and its technical accuracy has been well established, there are surprisingly few studies detailing its clinical impact. The thesis discussed in this paper revolves around the assessment, and subsequent enhancement, of the clinical impact of neuronavigation and is subdivided into three parts. Their combined results will be discussed.

Part I—accuracy: Using a newly developed multimodality neuronavigation phantom, the application accuracy of the MKM-system (Carl Zeiss, Germany) was assessed. Further assessments included a clinical comparison between different patient-to-image registration techniques and a feasibility experiment regarding the prediction of application accuracy with a Monte Carlo simulation technique.

Part II—clinical application: Using an MKM-mounted instrument holder, the MKM was adapted to (minimally invasive) point-stereotactic procedures. The application accuracy was compared to that of the BRW-frame in a phantom set-up, followed by clinical introduction and evaluation. The evaluation of the impact of neuronavigation in open neurosurgical procedures was a greater challenge. We chose to perform a randomized controlled trial in a very specific patient population: patients harbouring a solitary intracerebral contrast enhancing lesion, eligible for complete resection, in which the surgeon did not feel navigation was necessary due to lesion size or location.

Part III—system enhancement: Since the impact of neuronavigation most likely not only depends on the usefulness of the navigation information, but also on the effectiveness with which this information is communicated to the surgeon, we developed auditory feedback software and tested its effect in a phantom set-up. Finally, a feasibility study was performed, involving the use of 3D rotational angiography for neuronavigation.

Temporal lobe epilepsy surgery. Experience at a single centre over 14 years

A. W. McEvoy, S. Sinha, M. Thom, et al. (National Hospital for Neurology and Neurosurgery, Queen Square, London, UK)

Aim: To analyse the outcome following temporal lobe epilepsy surgery with respect to pathology and type of surgical procedure performed over a 14-year period. Secondly to ascertain if a surgical learning curve was observed.

Methods: A total of 480 patients (33.3 ± 10.4 years; M:F 29:31) with refractory seizures were treated surgically from 1990 to 2003. Engel's classification was used to record seizure outcome 1-year following surgery. Seizure outcome was assessed in relation to pathology and surgical procedure. The results were analysed for two time frames 1990–1996 ($n = 209$) and 1997–2003 ($n = 271$) to assess the effect of the surgical learning curve.

Results: There were 371 anterior temporal lobe resections (ATLR), 75 lesionectomies, 15 extratemporal resections, seven hemispherectomies, seven multiple subpial transections and five corpus callosotomies performed during the study period. Overall, surgical outcome at 1 year following surgery was (Engel): I = 81%; \geq II = 19%. Subgroup analysis for seizure freedom (Engel 1) at 1 year revealed: ATLR for hippocampal sclerosis (HS)—85.1%, temporal lesionectomy—82.3%, ATLR with dual pathology—80%, ATLR without HS—78.7%. There was no significant difference in outcome for ATLR cases of pure HS and those with dual pathology ($p = 0.2$). In the first 7 years of the study (1990–1996) more lesionectomies were performed (21.1% *v.* 11.4%). However, in the last 7 years (1997–2003) more ATLRs were performed (222 *v.* 147). In patients who underwent ATLR for HS the Engel 1 rate increased from 79 to 86.6% between the two time periods.

Conclusion: Temporal lobe surgery for epilepsy can produce seizure freedom in excess of 80% in carefully selected patients. The extent of temporal lobe resection did not affect seizure freedom in purely lesional cases. Experience improves seizure freedom in surgery for HS.

Thalamic deep brain stimulation versus thalamotomy for tremor

J. A. Hyam, X. Liu, P. G. Bain, et al. (Department of Neurosurgery, Charing Cross Hospital, London, UK)

Objective: To establish the optimum mode of thalamic surgery for tremor.

Design: Retrospective analysis.

Subjects: Twenty-six patients underwent thalamotomy and 20 patients underwent thalamic stimulation for intractable tremor under the same functional neurosurgeon between 1996 and 2002. The disease processes included were Parkinsonism, dystonic tremor, multiple sclerosis, essential tremor, progressive supranuclear palsy and Holmes' tremor.

Outcome measures: Severity of rest, postural and intention components of tremor were assessed before surgery and on follow-up using an established ten-point scale, allowing tremor improvement to be calculated.

Results: Mean time until follow-up assessment was 23 months after thalamotomy and 15 months after thalamic stimulation. Mean improvement after thalamotomy compared with thalamic stimulation for rest tremor was 79% compared with 89%, for postural tremor was 63% compared with 66% and for intention tremor was 64% compared with 39%, respectively. These differences were not statistically significant ($p > 0.1$ using Student *t*-tests). 30% of patients suffered permanent adverse effects after thalamotomy and 8% required further thalamic surgery. After thalamic stimulation, only 5% had permanent adverse effects and 25% needed battery replacement surgery.

Conclusions: Both interventions produced improvement of all components of tremor. However, thalamotomy caused more permanent adverse effects.

Subthalamic nucleus stimulation inhibits dorsal raphe 5-HT neurons

Y. Temel, V. Visser-Vandewalle, L. J. Boothman, et al. (Maastricht University, Maastricht, Netherlands, University Department of Pharmacology, University of Oxford, Oxford, UK)

Despite long-lasting beneficial effects on motor disability, deep brain stimulation (DBS) of the subthalamic nucleus (STN) in Parkinson's disease (PD) often produces unwanted emotional disturbances. To investigate the mechanisms underlying these effects, we studied the effect of DBS of the STN on 5-HT neuronal activity in the dorsal raphe nucleus (DRN). Extracellular single-unit recordings of putative DRN 5-HT neurones were made in the anaesthetized rat. Bilateral DBS of the STN inhibited the firing rate of 5-HT neurones by 35–40% during the period of stimulation. This inhibition was apparent in the vast majority of 5-HT neurones tested, and was both current- and frequency-dependent (effect commencing at 30 A and 100 Hz, respectively). STN DBS inhibited 5-HT neurones in both normal and dopamine-depleted rats (reserpine plus alpha-methyl-tyrosine). Bilateral injection into the STN of the GABA-A receptor agonist muscimol also inhibited 5-HT neuronal activity, suggesting that STN DBS may act through inhibition of STN neurones. These data show that bilateral DBS of the STN has a striking inhibitory effect on the firing of DRN 5-HT neurones. We suggest that this effect may contribute to the emotional disturbances observed in PD patients subject to DBS of the STN.

Complications of deep brain stimulation

A. Paluzzi, A. Belli, P. Bain, et al. (Charing Cross Hospital, London, UK)

Objective: To analyse the incidence of complications among patients who underwent deep brain stimulator insertion in a single centre.

Design: Retrospective study of patients operated on at Charing Cross Hospital between 1999 and 2005.

Subjects: Fifty-nine patients were included and divided into four diagnostic categories: dystonia (19 patients), Parkinson's disease (21), multiple sclerosis (10) and tremor (nine). Outcome measures: Incidence of early (intra-cerebral haematoma, wound haematoma, infection and lead erosion through the skin) and late complications (electrode migration, electrode breakage, battery failure and malfunction). Logistic regression analysis was applied to determine the influence of individual risk factors on outcome.

Results: Thirty-two per cent of the patients operated developed one or more complications. Patients with Parkinson's disease had a significantly higher proportion of early complications ($p=0.042$), while late complications were significantly more common in dystonic patients ($p=0.009$).

Conclusions: DBS is associated with a high complication rate. Delay in diagnosing electrode malpositioning in dystonia may be related to a lack of reliable methods for assessing electrode position peri-operatively. There is a significant difference in the type of complications occurring in dystonic and Parkinsonian patients suggesting that these two categories of patients need a different follow-up plan.

Proof of principle investigation: working memory system a promising candidate for a brain-computer interface

G. J. M. Rutten, M. P. Van Den Heuvel, K. H. Kho, et al. (Rudolf Magnus Institute, Utrecht, Netherlands)

Brain-computer interface (BCI) research has mainly focused on the primary motor regions for the translation of brain signals for controlling computer programs and machines. However, the use of cognitive processes in BCI has recently gained interest, as such may be highly versatile in terms of multidimensionality control. We report on a proof of principle study for the use of the higher cognitive working memory (WM) system for BCI. A positive result would be accomplished if signals in the primary region of this system (dorsolateral prefrontal cortex, DLPFC) evidenced clear on- and offset, and show controllable duration. A mental calculation task was used, in which subjects had to decide whether a given equation was correct or incorrect. Equations came in one of three degrees of difficulty. Increasing difficulty was correlated with increasing reaction times, and should result in increased and/or sustained WM activation. Ten healthy subjects were tested with fMRI, and two epileptic patients with subdural electrodes for extra-operative seizure source localization were tested with both fMRI and electrocorticography (ECoG). Event-related BOLD signals increased in amplitude and duration with increasing degree of difficulty within DLPFC in every individual. In the same region, ECoG recordings revealed that power in the gamma frequency band (30–90 Hz) increased dramatically during calculation and the duration corresponded to reaction time. Amplitude remained constant. These results indicate that the neural response to WM load can be readily detected, and is tightly coupled to duration of mental calculation. In conclusion, we show here proof of principle that the spatial and temporal features of ECoG signal in DLPFC makes the WM system a promising candidate for BCI control. This system is strongly influenced by conscious control and exhibits promis-

ing features in terms of activity detection and a subjects ability to self-regulate duration of activity.

Five-year audit of inpatient deaths in a neurosurgical unit: analysis of avoidable adverse events

R. J. Nelson & S. Smithson (Frenchay Hospital, Bristol, UK)

Objective: To determine the nature and frequency of adverse events (AEs) contributing to in-patient mortality in a neurosurgical unit.

Design: Peer-reviewed analysis of all in-patient deaths in a neurosurgical unit April 1999–March 2004 using a structured case report and audit form.

Subjects: Four-hundred-and-twenty-two patient (231 men), mean age 54 (range 1–93) years, of whom 358 (85%) were admitted as emergencies.

Outcome measures: Diagnostic, logistic, clinical management and resource related AEs.

Results: No avoidable AEs were identified in 71% of patients. One-hundred-and-ninety-three possible and probable avoidable AEs contributing to death were identified in the remaining patients. Neurosurgical and neuro-interventional procedures accounted for 8.1% of these AEs. Availability of ICU/HDU beds was the next commonest adverse event (6.4%).

Conclusions: This audit indicates that a majority of in-patient deaths are unavoidable and that major reductions in in-patient mortality will not be achieved by focusing solely on surgical and interventional procedures.

The neurosurgical Spice Girl. An account of the life and achievements of Miss Diana Beck (1902–1956)

C. E. Gilkes (Derriford Hospital, Plymouth, UK)

Objective: 'Girl power' may have been a term created by/for the Spice Girls, but this account demonstrates it is a phenomenon that far precedes them.

Design: Diana Beck (1902–1956) played a large part in establishing neurosurgery in the South West region. She was the consultant advisor in neurosurgery for the emergency medical service in the South West during the Second World War and subsequently set up the neurosurgical unit at Frenchay Hospital. The only female neurosurgeon in Western Europe and the USA during her career and the first female to be 'given charge of men in a consultant capacity in a major London teaching hospital' when made a consultant at the Middlesex (1947); she provides an excellent role model. Miss Beck came to the attention of the general public when she operated on A. A. Milne in 1952; however, she was better known in neurosurgical circles for her interest in intracranial haemorrhage. I present some of her original research, case reports

and her seminal paper on the surgical treatment of intracerebral haemorrhage, which was presented to the SBNS in Zurich, 1952. They are a stark reminder of the limited investigations available at that time. In addition to her neurosurgical achievements, Miss Beck was quite a remarkable character and teacher. 'Her Saturday ward rounds proved so popular that they competed successfully with the students week-end plans'. I have rarely read such warm obituaries.

Conclusions: The first neurosurgical spice girl, may there be many more!

Use of the axillary vein as an alternative point of venous access for insertion of ventriculo-atrial shunts

M. Murphy, D. Choi, E. Chemla, et al. (St Georges Hospital, London, UK)

Objective: To describe a technique using the axillary vein as the point of venous access for insertion of a ventriculo-atrial shunt.

Design: This technique was applied to complex shunt patients who required insertion of a ventriculo-atrial shunt, but for whom access via the external jugular and subclavian veins was impossible.

Subjects: Two very complex shunt patients, both of whom had failed ventriculo-atrial shunting using the subclavian and external jugular veins.

Outcome measures: One-year follow-up for both patients.

Results: Both patients were well and neither required a shunt revision during the follow-up period.

Conclusions: The axillary vein is a good alternative venous entry point for ventriculo-atrial shunting in cases where the external jugular and subclavian veins cannot be used. The vessel has good calibre and flow and the angle of shunt insertion is not too acute.

Emergency inter-hospital patient transfers: can they be improved?

J. R. Goodden, J. J. D. Bosma & T. A. Carroll (Royal Hallamshire Hospital, Sheffield, UK)

Objective: To assess the amount and quality of patient information received with inter-hospital patient transfers for emergency neurosurgery.

Design: Tick-box survey evaluating presence or absence of key information.

Subjects: Sixty-six patient transfers over 1 year randomly selected and analysed.

Outcome measures: Factors assessed: transfer letter and medical records, demographics (name, date-of-birth, hospital number), hospital details (referring hospital, Consultant name), clinical information (history, examination, medication, scans), prescription chart, hard copy imaging.

Results: Twenty-one (31.8%) had a transfer letter. Sixteen (76.2%) had full demographic details, 13 (61.9%) had full hospital details and seven (33.3%) had full clinical information. Letters were written by preregistration house officers (four), SHO's (eight), Specialist Registrar's (three) and one Consultant. Four authors did not identify themselves or their grade. Thirty-eight (57.6%) had photocopy notes and 26 (39.4%) had original notes. Sixty-two (93.9%) had full demographic details, 28 (42.4%) full hospital details and 42 (63.6%) full clinical information. Where transfer letters were received, 12 (57.1%) also had photocopy notes, eight (38.1%) had original notes and one had no notes in accompaniment. Original notes are photocopied for local records. Forty-four (66.7%) had prescription charts, though only 26 (39.4%) were photocopies. Forty-nine (74.2%) had hard-copy imaging.

Conclusions: Significant gaps in inter-hospital transfer information are identified. These affect patient care and increase clinical risk. They also add to local workload and delay transfer back through uncertainty over the responsible consultant team. Improvements in standards are clearly required possibly through inter-hospital transfer protocols distributed to referring hospitals.

Are we achieving standards? A prospective evaluation of the patients' perception of the neurosurgical ward round

N. Haden, S. Mathew, O. Judd, et al. (Derriford Hospital, Plymouth, UK)

Objective: To assess and compare patient and staff perceptions of the extent to which the morning neurosurgical ward round meets the standards in the General Medical Council's document 'Good Medical Practice'. To investigate at a team level the type of assessment achieved by the validated Doctors' Interpersonal Skills Questionnaire for individuals.

Design: Prospective, anonymous cohort study using patient and staff completed surveys undertaken over two periods of seven days each. Staff were blinded except during completion debriefing at the end of the first period.

Subjects:

- Neurosurgical patients with a Glasgow Coma Score of 15.
- The ward round multidisciplinary team (medical, nursing, physiotherapy, pharmacy).

Outcome measures: Degree to which 10 standards were met, graded for each on a five-point scale. Correlation of patient and staff perceptions.

Results: Ninety-six per cent of patient completed outcomes ($n = 1130$) were perceived as acceptable or better, with 77% recorded as 'could not be better'. During the first survey 8% of the time patients did

not understand their clinical plan, this had improved to only 1% after debriefing and repetition. There was no significant correlation between patient and staff perceptions (Mann–Whitney *U*-test). Nursing staff were the group least likely to feel the standards had been achieved.

Conclusions: The majority of patients were at least 'content' during both periods, although staff had difficulty in estimating patient perceptions. The clinical plan was more effectively communicated during the period after staff debriefing.

Posterior fossa operations and the role of intraoperative burr hole placement

A. Harries & H. Brydon (North Staffordshire Infirmary, Stoke-on-Trent, UK)

Objective: To determine whether prophylactic occipital burr hole during posterior fossa procedures is necessary.

Design: A retrospective audit of posterior fossa operations undertaken between 1998 and June 2004.
Subjects: Eighty-six cases (42 female, 44 male); age range: 3–78 years; 17 emergency cases, 69 elective. Forty-five patients had hydrocephalus diagnosed preoperatively.

Results: Twenty-nine patients had an occipital burr hole placed at the time of operation (33%). Only 27 of these were used for intraoperative CSF drainage and 22 for postoperative CSF drainage. Two prophylactic occipital burr holes were placed. One patient had a lumbar drain *in situ* 11 patients (13%) deteriorated on the ward postoperatively. The occipital burr hole placed at the time of the original operation was never used for CSF diversion. All patients had a new burr hole and EVD sited, or underwent a lumbar puncture.

Conclusion: Seventy-seven per cent of patients didn't have a prophylactic burr hole and didn't run into any complications, while 13% of patients deteriorated postoperatively; the intraoperative burr hole was never reused. Those patients whom deteriorated, a new burr hole was placed to drain CSF. We therefore conclude that placing a prophylactic burr hole is an unnecessary procedure when performing operations in the posterior fossa and should only be performed if intraoperative CSF drainage is required.

In vivo measurement of brain relaxation after lobectomies

N. Mukerji, P. Mitchell & C. Soh (Newcastle General Hospital, Newcastle, UK)

Objective: To measure the rate of relaxation of brain that has been compressed by tumour after surgical decompression. Very little data exists on the visco-elastic properties of the living human brain tissue and collection of such data is vital for mechanical modelling.

Design: Prospective observational study.

Subjects: Seven consecutive patients who had a lobectomy for brain tumour.

Outcome measures: Rate of postoperative brain shift to occupy the void left after lobectomy seen on serial CT scans.

Results: Rapid expansion of the normal brain occurs in the first 24 h after a lobectomy. Complete filling up of the void may take between 18 and 96 h.

Conclusions: It is possible by our method to calculate an *in vivo* coefficient of brain relaxation and, hence, go a step further towards *in vivo* study of human brain biomechanics.

Innovative stereoscopic 3D visualization of CT angiograms using a low cost PC system

M. Foroughi, N. Rodwell, S. Corner, et al. (Morriston Hospital, Swansea, Wales, UK)

Objective: To develop a new low-cost computer based stereoscopic-3D system for analysing volume data from CT angiograms, and ascertain any advantages for a neurosurgeon over standard 3D systems.

Design: The system has been designed around a standard PC workstation with a dedicated low cost Volume Pro rendering card, with total cost of £3500. The Volume Pro architecture employs the Ray Casting algorithm, with access to the data based on the Shear-Warp factorization. The system uses this technique to visualize standard Dicom files and allows creation of complex selection sets for the data, dependent on the original greyscale values. The system then generates two perspective stereoscopic-3D views allowing images to be projected out of the screen. The stereoscopic-3D imagery can be produced in active or passive form. Active Stereoscopy allows the user to observe the image on a standard CRT computer monitor using specialized shuttered glasses (around £30 a pair). Passive stereoscopy uses two projectors to produce the left and right field polarized images, and uses polarized glasses (around £2 a pair) to view the 3D images at any projection size.

Subjects: Volume CT angiogram datasets were recorded from 10 Neurosurgical cases using the CD writer in the scanner system, and transferred into the PC system within 20 min.

Outcome measures: A subjective comparison was made by one neurosurgeon using the standard 3D techniques and our PC-based active stereo system.

Results: The stereoscopic 3D system enhanced orientation and depth perception of the neurovascular anatomy.

Conclusions: Our PC-based stereoscopic system is a low cost and user-friendly method of enhancing orientation and depth perception of three-dimensional CT angiogram images.

Clinical and prognostic features in adult spinal epidural abscesses (SEA): a 4-year review

A. K. Demetriades, S. Naik, A. Liebenberg, et al.
(Hurstwood Park Neurological Centre, Haywards Heath, Sussex, UK)

Objective: To identify the features relating to an increased incidence of SEA in the catchment area of our unit.

Design: Retrospective and prospective case note review over a period of 40 months.

Subjects: those identified microbiologically to have had an epidural abscess. Outcome measures: resolution of infection; resolution of symptoms, especially paresis, plegia, cauda equina or other presenting neurological syndrome.

Results: Twenty-one adult patients with SEA were identified. The mean age was 47 years (21–81) and the male:female ratio was 16:5. The level of involvement was three (14%) cervical, nine (43%) thoracic and nine (43%) in the lumbar spine. One case had multi-level involvement. Commonest presenting features were spinal back pain (71%), pyrexia (57%), radicular pain (52%) and bladder disturbance (33%). Signs on examination included paraparesis (14%), paraplegia (5%), cauda equina (5%) and central cord syndrome (5%). Two patients were in septic shock (10%) and myelopathic features present in 14%. ESR and CRP were elevated uniformly in all cases, but the white cell count only in 24%. MRI was the imaging investigation of choice. Growth of an organism was obtained in 33% with blood cultures, but in 86% with tissue sample. The commonest pathogen was *Staphylococcus aureus* in 11 cases, one MRSA, two Streptococci, one mixed Staph/Strep, two *Mycobacterium tuberculosis*, one *Pseudomonas aeruginosa* and three sterile. Commonest risk factors: diabetes mellitus five patients (24%) and previous epidural treatment 19%. Others included previous spine surgery 5%, intravenous drug abuse 5%, psoas abscess 5%, cellulitis 5%, chest trauma (5%) and chest infection 10%. Two of the epidural treatments were for Inflammatory Bowel Disease-related pain in patients with an ileostomy, and the average time between epidural treatment and presentation was 5 weeks. Two of the patients who had received epidural treatment were also diabetics. Treatment was surgical in all but one case with 8–10-week intravenous antibiotic treatment followed by another 4–6 weeks of oral antibiotics. Symptom improvement was achieved in 100% with back/neckpain with no neurology and 86% with bladder/bowel dysfunction. All patients with paraparesis improved. In plegia there was marginal return of movement and full return of sensation. Myelopathic patients improved in motor and sensory control with only 1 remaining incontinent of urine. In septic shock one patient recovered with a footdrop, whereas the other died on ITU.

Conclusion: Preoperative plegia was identified as a poor prognostic factor. Prompt diagnosis and treat-

ment are necessary before the deterioration of neurological symptoms.

Intracranial infections with inconsistent inflammatory indices

J. R. Goodden, J. J. D. Bosma & T. A. Carroll
(Royal Hallamshire Hospital, Sheffield, UK)

Objective: To highlight inconsistency in inflammatory indices in patients with intracranial infection.

Subjects: Three patients with postoperative bone-flap infection with positive microbiology cultures had c-reactive protein (CRP), white cell count (WCC) and erythrocyte sedimentation rate (ESR) levels checked at time of diagnosis.

Results: Case 1, a 23-year-old man who had craniectomy and evacuation of extradural haematoma. Cranioplasty subsequently performed. Presented 2 months later with discharge from the head wound. Clinically, patient afebrile, CRP 5.7, WCC 9.0. Pus swab grew *Staphylococcus aureus*. At operation, pus was found surrounding bone flap with obvious osteomyelitis. Case 2, 50-year-old woman presenting with wound discharge 3 months after skull base meningioma excision. Clinically, patient afebrile, CRP 5.5, WCC 4.6, ESR 7. Pus swab and tissue culture grew *Staphylococcus aureus*. At operation, pus was present around bone flap. Case 3, 25-year-old man who had craniectomy for acute subdural and extradural haematomas. Cranioplasty subsequently performed. Two-and-a-half months later he presented with discharge from the head wound. Clinically, patient afebrile, CRP 8.5, WCC 8.5, ESR 3. Pus swab grew mixed skin flora. At operation, pus was found surrounding bone flap.

Conclusions: Three cases are highlighted where postoperative bone-flap infection was suspected and subsequently proven. However, inflammatory indices provided false reassurance that infection was unlikely. These markers are tools to aid diagnosis and must not replace the neurosurgeon's clinical judgement and decision-making.

Pregnancy in dystonic women with *in situ* deep brain stimulators

A. Paluzzi, P. G. Bain, X. Liu, et al. (Charing Cross Hospital Campus, London, UK, South Tees Hospitals NHS Trust, Northallerton, Yorkshire, UK)

Introduction: It is the nature of severe dystonia that the muscle spasms and resulting markedly abnormal postures make a woman socially and sexually less attractive, and intercourse difficult. Consequently, we envisage that dystonic women would struggle to initiate or maintain lasting sexual relationships with a partner.

Case histories: We report on the first three women with dystonia who, after insertion of bilateral globus pallidus internus (GPi) stimulators, succeeded in

conceiving and completing pregnancies. These histories illustrate the significant positive impact that DBS can have on women's social relationships.

Objectives: To provide, based on this experience, an overview of some of the issues that might arise in pregnancy and during delivery in dystonic women with an in situ deep brain stimulator.

Recommendations: Women with implanted DBS systems should give birth in hospital, rather than at home until more data is available to guide advice. In the eventuality that a caesarean section is required, electrocautery should be performed in the bi-polar mode. There is no DBS-related contraindication to the administration of general or regional anaesthesia or in the use of the Valsalva manoeuvre in labour. DBS system is a foreign body and our patients received intravenous cefuroxime (1.5 g), one dose before and two doses postpartum. Short wave (around 27 MHz) and microwave (about 2.45 GHz) diathermy are contraindicated in patients implanted with the Medtronic[®] DBS systems.

Conclusions: We hope our work will be of some assistance to neurologists and neurosurgical staff advising obstetricians about these complex patients.

Role of tumour necrosis factor and Toll-like receptor 4 in induction of monocyte chemoattractant protein 1 in injured nerves

K. S. Karanth & P. M. Richardson (Royal London Hospital, London, UK)

Objective: Wallerian degeneration in peripheral nerve injury involves a selective infiltration of monocytes, which contributes to nerve regeneration and is much less evident in the central nervous system. This selective innate immunity response in peripheral nerves is mediated in part by MCP-1 (monocyte chemoattractant protein). We have been investigating the molecular signals from degenerating nerves that trigger the induction of MCP-1 and in particular the possible function of tumour necrosis factor α (TNF- α).

Design: *In vivo*, TNF- α & MCP-1 mRNAs were measured in the distal segments of rat sciatic nerve 0–4 days previously. *In vitro* MCP-1 mRNA was measured in Schwann cells from neonatal rats exposed to putative signals.

Results: Changes in TNF- α mRNA during Wallerian degeneration were not significantly different from changes in contralateral and sham-operated nerves, and did not correlate with changes in MCP-1 mRNA. *In vitro*, freeze-killed nerve segments, nerve homogenates, TNF- α and LPS (lipopolysaccharide) can all stimulate MCP-1 mRNA in Schwann cells. Antibodies that block TLR 4, the LPS receptor, but not TNF- α receptor, blocked the action of nerve tissue on Schwann cells.

Conclusions: Signals other than TNF- α must be involved in MCP-1 induction during Wallerian degeneration. One of these endogenous signals

conveying information from Schwann cells is a ligand for TLR4.

Expression of VEGF-A and VEGF-receptors in patients with brain tumours

R. Kumar, D. Kamdar, L. Madden, et al. (Hull Royal Infirmary, Hull, UK)

Objective: Vascular endothelial growth factor (VEGF) signalling via its receptors significantly contributes to tumour growth by promoting blood vessel growth. Both VEGF and its receptors (VEGFR-1, 2 and 3) have shown increased expression in many tumour types and this correlates with poor prognosis. Here, we aim to investigate the tissue distribution of VEGF-A and its receptors in patients with intracranial tumours and compare these findings with serum expression of VEGF-A.

Design: A prospective analysis to compare the distribution of serum VEGF-A and expression of tissue VEGF-A and VEGFR-1, 2 and 3 in patients with newly diagnosed brain tumours.

Subjects: The patient cohort ($n = 33$) comprised: seven meningiomas, two low grade ganglioglioma, two anaplastic astrocytoma and 22 GBM.

Outcome measures: Serum samples were analysed in duplicate via quantitative ELISA (BioSource). Tumour tissues were analysed via immunohistochemistry.

Results: VEGF-A and its receptors were expressed on all tumour samples. There was a significant association between serum VEGF-A and tissue VEGF-A ($p = 0.011$); however, there was no association between serum VEGF-A and any of the tumour tissue-expressed VEGF receptors. There was no correlation in VEGF-A staining with any of the VEGF receptors, nor was there any correlation between the staining patterns of individual receptors.

Conclusions: The prevalence of VEGF-A and its receptors support the hypothesized role of VEGF-A exerting an autocrine effect on the growth of brain tumours. The association between serum and tissue VEGF-A also supports the concept that the level of some circulating angiogenic factors reflects the overall angiogenic activity of the tumour.

Microglial infiltrate in diffuse low grade and anaplastic astrocytomas

A. Paluzzi, F. Mann, J. Lafuente, et al. (Department of Neurosurgery, Charing Cross Hospital, London, UK)

Objective: To assess whether activation of microglia correlated with tumour grade in diffuse low grade and anaplastic astrocytomas.

Design: Retrospective study of patients operated on at our neurosurgical department between 1992 and 2004.

Subjects: We have investigated 27 low grade and anaplastic diffuse astrocytomas operated between 1992 and 2004 at our centre. Seven patients were

female, age ranged between 28 and 63 (mean 42 years). All tumours were supratentorial. Fourteen patients underwent excisional and 13 stereotactic biopsy. The biopsies were immunostained with MHC Class II antigen for microglial cells.

Outcome measures: The microglia/tumour cell ratio was measured with a quantitative method. This ratio and the pattern of microglia distribution were then correlated to the WHO grade and clinical history using Student's test.

Results: The mean microglia/tumour cell ratio in low-grade tumours was 0.5, while in anaplastic tumours it was 1.5. Activation of microglial cells was diffuse in anaplastic tumours and scattered in low-grade tumours. Microglia was observed in areas of the biopsy where tumour proliferation was absent. There was a statistically significant correlation between microglia/tumour cell ratio and WHO grade ($p < 0.006$).

Conclusions: We suggest that microglia/tumour cell ratio can be used to increase accuracy of grading in tissue diagnosis of diffuse astrocytomas.

Factors influencing survival of malignant glioma and the role of radical resection

V. Petrik, B. A. Bell, A. Loosemore, et al. (St George's Hospital University, London, UK)

Objective: To assess the management of histologically confirmed malignant glioma and to establish factors which significantly contribute to survival.

Design: Prospective study.

Subjects: Seventy patients with histologically confirmed malignant glioma were recruited between June 2002 and November 2004. There were 44 males and 36 females aged (mean \pm standard deviation) 57.6 ± 11.5 and 57.5 ± 10.1 years, respectively.

Outcome measures: Kaplan–Meier survival analysis and the log-rank test for assessment of individual factors: gender, age, side, tumour volume, associated oedema, demarcation and surgical accessibility of the lesion, type of surgery (biopsy, partial and radical resection), radio and chemotherapy and initial Karnofsky score.

Results: The overall mean survival was 49 weeks (median 30 weeks) with 73% patients dying at the end of the first year. At the end of the second year there were still 19% of patients alive. The influence of following factors on survival was statistically significant (p -value): age (0.045), type of surgery (0.011), radiotherapy (0.004), chemotherapy (<0.001) and Karnofsky score (<0.001). The mean survival of patients after biopsy, partial and radical resection was 26, 46 and 88 weeks, respectively. For the glioblastoma group alone, mean survival was 21 weeks for biopsy, 40 for subtotal and 75 for radical resection.

Conclusions: Our results suggest important roles of age and initial clinical score on overall survival, but also support the growing opinion on the beneficial role of radical surgical treatment of malignant gliomas.

Imaging cellular proliferation in brain tumours with 18FLT positron emission tomography

S. J. Price, D. D. Wang, T. Fryer, et al. (Addenbrooke's Hospital, Cambridge, UK)

Objective: To evaluate 18FLT PET as a marker of glioma cellular proliferation and to examine the heterogeneity of cellular proliferation in high and low grade gliomas.

Design: Patients were imaged preoperatively with MRI and a dynamic 18FLT PET study. The PET data was reconstructed using an irreversible two compartment kinetic model. Maps of KI (FLT uptake rates) were coregistered to an SPGR image using SPM. The maps were compared to histology and MRI findings. Immunohistochemistry for MIB-1 and MCM expression was performed on all biopsy samples.

Subjects: Fifteen patients with brain tumours (mean age 50.5) who required image-guided brain biopsy.

Outcome measures: Appearance of FLT uptake images; comparison of FLT uptake areas with MRI; Correlation of FLT uptake rates and histological markers of proliferation.

Results: In all patients there was minimal uptake in the normal brain. There was little obvious uptake in low grade gliomas, but marked uptake in high grade gliomas and a lymphoma. A threshold of 1.5–10.3 mLplasmamin-1 mLbrain-1 could differentiate tumour from normal brain. In the high grade gliomas the highest FLT uptake was found largely in areas of contrast enhancement and increased perfusion as detected by perfusion MRI. Uptake was found, however, outside these regions. Maximal FLT uptake correlated with the highest MIB-1 labelling index ($r = 0.7$; $p = 0.01$).

Conclusions: FLT PET is a good marker for tumour cellular proliferation and would be a useful technique to aid biopsy targeting and as a marker of response to cytostatic treatments, where changes in tumour size occur late.

The quantitative evaluation of a micro multileaf collimator's positional and dosimetric accuracy for shaped beam stereotactic radiosurgery

A. Richmond, J. Pearn, P. Kelly, et al. (Derriford Hospital, Plymouth, UK)

Objective: Quantitative evaluation of positional accuracy and target dose delivery in LINAC-based shaped beam stereotactic radiosurgery.

Design: The various stages of the imaging, planning and treatment process were evaluated for positional and dosimetric uncertainties. Materials used for this purpose include a multi purpose SandStrum Inc. LUCYTM SRS phantom and GAFCHROMICTM radiochromic dosimetry film. Independent methods of absolute dose determination were performed using a Pin point ionization chamber and thermoluminescent dosimetry using

TLD100TM. Subjects: SandStrum Inc. LUCYTM SRS phantom.

Outcome measures: Outcome measures are the positional accuracy of the treatment dose distribution. Determination of the absolute dose delivered to the target volume.

Results: The positional accuracy of the isocentre and isodoses was found to be 1 mm. The dose delivered to the target volume was within 3%.

Conclusions: SRS can be delivered with comparable accuracy to Gamma KnifeTM provided appropriate methods and standards of quality assurance are implemented.

Management of glioblastoma multiforme in elderly patients. Should we be ageist?

*D. Rodrigues, G. Hendry, P. Kane, et al.
(James Cook University Hospital,
Middlesbrough, UK)*

Objectives: To audit the outcome of elderly patients with GBM.

Design: Retrospective audit of outcome in all elderly patients (>60 years) with GBM in our institution (2001–2003).

Subjects: The records of 50 cases identified were audited with respect to the treatment offered and the groups were compared for outcome measures.

Outcome measures: For purpose of analysis patients receiving biopsy or resective surgery alone and biopsy with radiotherapy were grouped as a single group (Group I), and compared with those having resective surgery plus radiotherapy \pm chemotherapy (Group II). Outcome was analysed based on Karnofsky Performance Scale (KPS) and on survival. Statistical analysis performed using Student's *t*-test and Chi-square test, where $p < 0.05$ was considered significant.

Results: There was no statistically significant difference in the pre- and posttreatment KPS in the two groups. The mean survival in months in Group I was 3.6 ± 2.9 versus 9.7 ± 5.5 in Group II ($p < 0.001$).

Conclusion: Outcome in elderly patients with GBM in general remains poor. However, elderly patients should not be treated as a homogenous group, as appropriately selected patients can have a good functional and survival outcome.

Does stereotactic radiosurgery (SRS) alter the natural history of vestibular schwannomas (VS)?

D. Rodrigues, F. Aziz & F. P. Nath (James Cook University Hospital, Middlesbrough, UK)

Objectives: To determine whether SRS affected the natural history of VS.

Design: Retrospective study (1997–2001). All patients who were either observed with serial Magnetic Resonance Scans (MR) or offered SRS were analysed.

Subject: Thirty-one patients were identified (16 males, 15 females) at a mean age of 63.48 ± 14.26 years.

Outcome measures: The patients were divided into two groups depending on the treatment: Group I Serial MR and observe, 17 patients; Group II SRS with serial MR, 14 patients. Outcome was analysed based upon progression of symptoms and change in size over time. Statistical analysis done using ANOVA analysis and Fisher exact test where $p < 0.05$ was considered significant.

Results: Increase in size tumour size was seen in three and five patients over a mean follow up 34.74 ± 12.53 months with a mean increase in size of 2.00 ± 5.29 and 1.57 ± 2.62 ($p = 0.79$) in group I and II, respectively. Three patients in each group had progression of symptoms.

Conclusion: Our early observations indicate no significant difference between the two groups and might suggest that the treatment is not effective. However, this requires further multicentre study.

Assessment of smell in patients undergoing pituitary surgery

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Neurosurgery, London, UK)*

Objective: Olfactory function in patients undergoing trans-sphenoidal surgery using a new smell test. There are few studies assessing olfactory function following trans-sphenoidal surgery, but most are based on questionnaires, rather than tests. Some suggest severe impairment in a significant number of patients (12%).

Design: First, a new smell test using six common and easily available smells was evaluated in a group of healthy volunteers. We then assessed patients post-operatively who underwent trans-sphenoidal surgery.

Subjects: Validation group: 30 volunteers with no previous olfactory complaints or surgery aged 22–61 (mean age 34.6) from diverse ethnic origin. Study group: 17 patients who underwent trans-sphenoidal surgery in the past (2 months–8 years). Outcome measures: correct identification of six different smells repeated five times. Normal olfactory function: >95% correct identification after initial round.

Results: Validation: normal smell 93.3%, 6.7% mild impairment. Test group: normal smell 65%, 24% mild reduction (all asymptomatic), 11% moderate reduction (only 5.5% symptomatic) No patients had severe impairment/anosmia.

Conclusions: Our new smell study seems a reliable, simple and inexpensive test to assess clinically relevant olfactory function. Early results from this pilot study group show that the risk of clinically relevant impairment of smell is very small (5.5%). No patient had severe impairment. A prospective

study of pre- and postoperative olfactory function is required to assess changes of smell more accurately. This has been started at our institution.

Reference

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Can the SF-36 satisfy a Neurosurgeon? Or does it leave them wanting for more?

R. Baron, R. Elashaal, T. Germon, *et al.*
(Derriford Hospital, Plymouth, UK)

Background: The study aimed to evaluate the ability of a quality of life scale (the SF-36) to satisfy the clinical and research needs of cervical spine surgeons.

Method: SF-36 data from 147 patients undergoing cervical spine surgery were examined. We tested the assumptions underpinning the two standard ways of reporting SF-36 data: as scores for eight scales, or as scores for two summary measures. We also examined how well the SF-36 was targeted to the sample, and its ability to detect change.

Results: Evidence supports the reporting of SF-36 scale scores. However, three of the eight scales had notable floor/ceiling effects indicating poor targeting. Evidence does not support the reporting of summary measures. Responsiveness was good for all scales except those with high floor/ceiling effects.

Conclusions: The SF-36 fails to satisfy the measurement needs of cervical spine surgeons. Although SF-36 scale scores appear reliable and valid, the associated floor and ceiling effects mean that changes in quality of life associated with surgery are under represented. It is not valid to report SF-36 summary scores. These results highlight that generic outcome measures may not be as generic as they claim, and neurosurgeons need scales with a greater range of measurement.

The Oswestry: a measure for pain or a pain of a measure?

R. Baron, R. Elashaal, T. Germon, *et al.*
(Derriford Hospital, Plymouth, UK)

Background: The Oswestry Questionnaire is one of the most widely used, self-report measures of the functional effect of low back pain. Despite this important role its scientific properties as a rating scale have received only limited attention.

Objective: To assess the extent to which the Oswestry Questionnaire provides reliable and valid measurements in lumbar spine surgery.

Method: Data from 135 people undergoing lumbar surgery were Rasch analysed. Reliability and validity were assessed in terms of standard criteria (targeting, fit statistics, item locations and ordering of response thresholds).

Results: The scale was generally satisfactory in terms of fit statistics, targeting and item locations. However, item thresholds were disordered for several items, indicating that patients are not able to distinguish reliably between the response options. Empirically, and clinically, fewer options per item (two, three or four, rather than the current six) would improve reliability.

Conclusion: The Oswestry is a measure for pain. This study indicates it is also a pain of a measure for patients to complete reliably. However, with empirically driven appropriate adjustments this problem can be corrected.

Pitfalls and problems with outcome scores

A. M. Hussain, R. Kett-White, R. M. Redfern, *et al.*
(Morriston Hospital, Swansea, Wales, UK)

Objective: Accurate outcome data is demanded not only within the NHS, but also by outside agencies, e.g. patient groups and health commissioners. A system that could produce accurate and appropriate prospective valid audit data would be valuable, not only in fulfilling clinical governance and surgeon revalidation, but also in lobbying commissioners for more resources. We report some pitfalls with the development of such a system.

Design: Patients with degenerative spinal conditions completed a questionnaire before and after treatment. Details recorded included employment and litigation status, Visual Analogue Scales, Oswestry Disability Index and SF36. An audit clerk entered data onto the database.

Subjects and outcome: Seven-hundred patients completed the questionnaire, of which 30% underwent spinal surgery. We assessed capture rate, patient compliance, missing data, as well as teething problems.

Results: Capture rate was 90% with 88% patient compliance and missing data was 10%. The most dramatic adverse event was deletion of the database.

Conclusion: Initial enquires around UK neurosurgical centres suggested that prospective data collection was still in early stages. Establishment of a database for a specific condition is relatively straightforward. The maintenance of such a system and the ability to exchange data with national database are critical areas. The employment of a dedicated audit clerk for such a purpose is essential. Always keep an updated back-up copy!

Pulsed radiofrequency rhizotomy in the treatment of trigeminal neuralgia

C. R. Jones & C. Hardwidge (Hurstwood Park Neurological Centre, Haywards Heath, UK)

Objective: Radiofrequency rhizotomy is an established treatment for trigeminal neuralgia, but may induce sensory disturbance, including anaesthesia

dolorosa, in up to 15% of patients. Pulsed radiofrequency lesioning has been used extensively in several pain syndromes and its use in trigeminal neuralgia has been reported recently. Because the lesion is pulsed and results in a lower tip temperature than traditional radiofrequency lesioning, it may cause less sensory disturbance, and be better tolerated by patients.

Design: Prospective observational study of patients undergoing pulsed radiofrequency rhizotomy.

Subjects: Eleven patients undergoing pulsed radiofrequency rhizotomy (age 45–87, mean 70 years, eight females).

Outcome measures: Improvement in, or resolution of, trigeminal neuralgia pain. Incidence of complications, particularly sensory disturbance.

Results: Mean follow-up was 8 months (range 4–16 months). Seven patients' pain had completely resolved. A further three had noticed significant improvement in their symptoms. One patient experienced no improvement. Two patients required repeat treatment, with improvement in their symptoms after the second treatment. Two patients experienced some increase in numbness following treatment. There were no other complications relating to the treatment.

Conclusions: Pulsed radiofrequency rhizotomy is safe and may be an effective treatment for trigeminal neuralgia. To fully assess its potential, a prospective comparative study of pulsed versus standard radiofrequency lesioning is necessary.

The relationship between distribution of pain and vascular compression in trigeminal neuralgia: the findings following 378 microvascular decompression operations

E. Shenouda, R. Cove, M. Foster, et al. (Department of Neurosurgery, Frenchay Hospital, Bristol, UK)

Objectives: To find out the relationship between distribution of pain and vascular compression in trigeminal neuralgia (TGN).

Design: Retrospective analysis of prospectively collected data.

Subjects: Three-hundred-and-seventy-eight patients underwent posterior fossa exploration for TGN in the period between 1980 and 2002 in one institution. Patient's age, sex, distribution of pain and operative findings were recorded, and in many cases photographed. All patients presented with typical TGN and the distribution of pain was recorded. Preoperative imaging was mostly Magnetic Resonance Imaging (MRI) however; a few early series patients had computed tomography (CT). All patients underwent standard retromastoid craniotomy and the details of the vascular compression nerve were recorded.

Results: Cases were categorized according to distribution of pain within the three trigeminal divisions and all combinations were noted. Seventeen patients had pure ophthalmic (V1) division TGN and 73

had V1 plus maxillary (V2) and/or mandibular (V3) division TGN. Significant neurovascular conflict (NVC) was recorded in 100% of patients with pure V1, 90.47% with V1 to V3, and 94.23% with V1 to V2 TGN compared to an average of 79.78% in 288 patients with V2, V2 to V3, and V3 neuralgia.

Conclusions: Microvascular decompression is the treatment modality of choice in otherwise healthy patients with TGN and the NVC can be seen on MRI. Patients with pure V1 neuralgia or when V1 is involved have a higher incidence of NVC. The reason for this remains to be determined. On careful inspection there was no obvious correlation between the site of nerve root compression and the distribution of pain.

Retropharyngeal pseudomeningocele: report of a rare case and review of literature

S. Achawal, A. Casey & G. Etherington (National Hospital for Neurology and Neurosurgery London, UK)

A 38-year-old male was found to have a retropharyngeal pseudomeningocele at craniovertebral junction along with C1–C2 dislocation. To our knowledge, only four cases with this condition have been reported in the literature. Absence of any possible history, misleading circumstantial evidence and rarity of the entity made it impossible to diagnose the condition preoperatively. Once it was diagnosed intraoperatively, it was treated. However, concurrent medical problems dominated and the patient died. As a result, the outcome of pseudomeningocele treatment could not be evaluated. Review of literature of the previous reported cases is presented and possible pathogenesis discussed. As the case gives an opportunity of a rare MRI image multiple photographs of the scans are presented.

Anterior cervical discectomy and fusion with an interbody cage implant packed with locally harvested bone graft. An effective alternative to iliac crest bone harvesting

S. Akmal, C. E. Gilkes & N. R. Patel (Frenchay Hospital, Bristol, UK)

Objective: A retrospective audit of fusion rate and functional outcome after anterior cervical discectomy and fusion (ACDF) using interbody carbon fibre cages (CFC) packed with locally harvested bone shavings and osteophyte fragments. Controversy and variation continues with regard to the technique used for interbody fusion following anterior cervical discectomy. The traditional technique of using tricorticate iliac crest graft is associated with various donor site complications. In recent years, alternative materials have been used including allografts, hydroxyapatite, titanium and other synthetic cages. CFC implants are usually packed with cancellous iliac bone graft to promote interbody fusion. We present an retrospective audit of our practice using CFC

implants filled with locally harvested drill shavings and osteophyte fragments thus avoiding the morbidity associated with an iliac crest donor site.

Design: Retrospective study of consecutive patients undergoing anterior cervical discectomy using CFC cages packed with locally harvested bone graft. Clinical and radiological follow-up.

Subjects: Eleven patients, eight single level ACD, three multiple level ACD; seven male, four female.

Outcome measures: Inpatient stay, operative time, radiological and clinical follow-up.

Results: Mean: postoperative stay 2.4 days, operative time 1.5 h (single-level). Radiological follow up: No graft complications and CT evidence of fusion in 100%. Good clinical outcome in all patients.

Conclusions: A CFC interbody implant packed with locally harvested bone graft offers excellent fusion rates with good functional outcomes. This technique is associated with acceptable operative times and post operative stay, whilst avoiding the morbidity associated with iliac crest bone harvesting.

Anterior cervical microforaminotomy for cervical nerve root compression

C. Balasubramanian, A. Harries, L. Ball, et al. (Royal Infirmary, North Staffordshire University Hospital, Stoke-on-Trent, UK)

Objective: Surgical results of anterior cervical microforaminotomy are reported.

Methods: A retrospective study was performed for 26 patients (20 males, six females) with cervical disc disease who had been surgically treated with anterior cervical microforaminotomy at Royal Infirmary between 2000 and 2005. Age ranged from 37 to 75. MRI findings were, disc prolapse in 20 and additional osteophytes in six. Microforaminotomy was performed according to the published technique. Long term telephone follow up is by questionnaire.

Results: Twenty-three patients had radiculopathy, with or without impaired neurology, and the other three had impaired neurology alone. Fourteen patients underwent single level unilateral operations, one had a single level bilateral operation and the remainder had multi-level operations. Sixty-one per cent had excellent results (improvement in all symptoms), 31% good (radiculopathy relieved, but mild non-radicular discomfort persisting), 8% fair (persistent mild radiculopathy \pm non-radicular discomfort) and none had poor (persistent severe radiculopathy) results. The duration of hospital stay ranged from 2 to 12 days, with 50% being discharged 2 days postoperatively. Postoperative complications include one patient with partial C6 root damage, which was identified intraoperatively, but had excellent results at 2 months postoperation. Re-operation: One patient, who had 2 level bilateral surgery, needed discectomies with fusion for new-onset myelopathy 18 months later.

Conclusion: Anterior microforaminotomy provided good to excellent surgical results in 92% of patients with minimal morbidities.

Polyunsaturated fatty acids: a new agent in the treatment of acute traumatic spinal cord injury

K. J. George, W. Huang, V. King, et al. (London School of Medicine and Dentistry, London, UK)

Objective: To assess whether polyunsaturated fatty acids (PUFAs) are neuroprotective in acute traumatic spinal cord injury.

Design: Rats were subjected to laminectomy and T12 spinal cord compression using a 50-g weight for 5 min. Thirty minutes later they were injected with saline, DHA (docosahexaenoic acid) or EPA (eicosapentaenoic acid). Two groups were also fed DHA or EPA enriched diet. Animals were followed for up to 6 weeks after surgery and were then perfused for histological examination.

Subjects: Adult female Sprague–Dawley rats. Fourteen animals that had laminectomy and thoracic compression alone were controls. Six animals had DHA injected (250 nmol/kg bodyweight). A further six had DHA injection plus 400 nmol/kg DHA daily in their diet. Two further groups had EPA at the same doses. Six animals had a 2500 nmol/kg DHA injection.

Outcome measures: The BBB1 score was used to assess hind limb locomotor recovery. NeuN, GFAP and ED1 were used as histochemical markers for neurons, astrocytes and macrophages, respectively.

Results: Animals that received 250 nmol/kg injection DHA or EPA regained weight-bearing locomotion 35 and 30% quicker than controls. The lesion size was also significantly smaller compared to controls. However, animals that received high dose DHA (2500 nmol/kg) took 100% more time than controls to regain weight-bearing locomotion.

Conclusions: This is the first study of neuroprotection with PUFAs in (compressive) traumatic spinal cord injury. The improvement in motor function was substantial as was the reduction in lesion size—better than the nearest comparable study with methylprednisolone. Whilst further work is needed to elucidate dosing and the underlying mechanisms PUFAs are already in clinical use and have a low side effect profile. Rapid progress to clinical trials in this setting, as well as chronic compressive pathologies such as myelopathy, may be possible.

Spinal decompression for degenerative disc disease: Cross-match or Group & Save

M. Gupta, J. Hyslop, T. Muthu, et al. (Walsgrave University Hospital, Coventry, UK)

Background: The Neurosurgery Department, in this trust sees 1000 patients a year with degenerative

disc Disease, of which more than 350/year undergo decompressive surgery. The procedure, like all other surgical procedures, carries a risk of excessive bleeding. There are currently no standard guidelines regarding preoperative blood bank preparation for such patients, with every NHS Trust employing their own protocols. Our Trust recommends a cross match of 2 units of blood for all such operations. An audit was conducted to ascertain the amount of blood transfused following the procedure, thereby formulating a rational guideline.

Design: Fifty-six consecutive patients undergoing spinal decompression for degenerative disc disease were audited retrospectively. Operating theatre log-books and online Clinical Results Reporting System was used to identify and determine patient demographics and perioperative blood counts. Blood Bank records were utilized in establishing the cross-match status and to confirm the amount of blood transfused to these patients. Case records were checked to identify reasons for transfusion. Findings were analysed using simple statistical tools.

Results: The mean age of patients was 49 years with a range of 27–79. There were 29 men and 27 women. Thirty-nine procedures were done on the lumbar region and 17 on the cervical region of the spine. The mean haemoglobin was 13.4 g/dl preoperatively and 12.2 g/dl postoperatively. A total of 38 units of blood were cross-matched for 18 patients. The remaining 38 patients had a Group & Save. Only one patient received a unit of blood transfusion.

Conclusion: Patients undergoing spinal decompression for degenerative disc diseases rarely, if ever, require blood transfusion. In such circumstances, a Group & Save would conserve precious resources and man-hours. It is, therefore, recommended to not cross-match such patients on a routine basis.

Modern non-fusion stabilization techniques for multilevel degenerative disc disease: indications, outcome and complications using disc replacement

J. C. Sutcliffe & D. V. Plev (London, UK)

Objective: Indication, outcome and complications following dynamic stabilization using Dynesys, Cosmic and total disc replacement (TDR) with the Link Charité and ProDisc prosthesis.

Methods: Retrospective review of 127 patients who underwent dynamic stabilization (79 cases) or TDR (51 cases) following multilevel lumbar provocative discography. All patients were assessed with the Oswestry Disability Index Questionnaire, MRI and flexion/extension X-Rays 1.5, 3, 6 and 12 months postoperatively.

Results: Twenty-one patients displayed concordant pain reproduction due to posterior tears and underwent dynamic stabilization with the Dynesys or the Cosmic system. If an anterior disc tear was

identified in a patient with posterior tears, an anterior fusion was added at that level (eight cases) using the Topaz anterior cage. 51 patients with anterior or anterolateral tears (\pm posterior tears) underwent TDR at one level (27 patients), two levels (16 patients) and three levels (7 patients), using the Charité (23 cases) or ProDisc (28 cases) prosthesis. Two patients underwent single level fusion and single level TDR. Complications were device related in 17 cases, non-device related in 10 and medical in seven cases. Surgical revision was required in 10 Dynesys cases and one disc replacement case. There were no discography-associated complications.

Conclusions: Non-fusion stabilization modalities maintain or restore the intersegmental motion and should not affect the adjacent segment. Assessment of anterior versus posterior disc pathology is important in planning surgical treatment. Anterior disc tears can be managed by disc replacement; posterior disc tears by dynamic stabilization, which may subsequently be removed once the disc has healed.

Modern non-fusion stabilization techniques for degenerative disc disease: indications, outcome and complications using dynamic stabilization and total disc replacement

D. V. Plev & J. C. Sutcliffe (London, UK)

Objective: Outcome and complications following multilevel anterior total disc replacement (TDR) using Link Charité and ProDisc prosthesis.

Methods: Fifty-one patients underwent TDR over a 4-year period, 16 patients have been treated with a two-level and 7 patients with a three-level TDR using the Charité (5 two-level cases, one three-level case) and the ProDisc prosthesis (6 three-level cases, 11 two-level cases). All patients underwent pressure-controlled provocative discography. All patients have failed multidisciplinary conservative treatment and were assessed using the Oswestry Disability Index Questionnaire (ODI), MRI scanning and flexion/extension X-Rays 3, 6 and 12 months postoperatively.

Results: Clinical presentation included lower back pain associated with radicular involvement (13 and 4 patients, respectively), sensory deficits (4 and 3 patients, respectively), motor deficits (1 patient), anterior abdominal (7 and 1 patient, respectively) and posterior tenderness (6 and 2 patients, respectively) with initial or recurrent disc herniation (four and one patient, respectively), degenerative disease with signs of segmental instability (11 and four patients, respectively) and foraminal stenosis (one patient). There was overall significant long-term improvement assessed with the ODI in both groups (preoperative range 20–68 and 26–54, postoperative range 2–14 and 2–24, respectively). Complications were non-device related in 4 cases (subsidence, sympathectomy), medical in two cases

(oral infection) and device-related in two cases (facet mediated pain). Surgical revision was required in one case.

Conclusions: The acceptance of discogenic pain as a diagnosis confirmed with discography and the desire to avoid multi-level fusions will lead to an increase in indications for multilevel disc replacements.

The outcome of spinal instrumentation in patients 75 years and older

D. Rammarine, S. B. Mirza & T. J. Germon (Derriford Hospital, Plymouth, UK)

Objective: To determine the clinical and radiological outcomes and complications in patients 75 years and older undergoing spinal instrumentation.

Design: Retrospective review of patient records over a period of four years from January 2001 to December 2004.

Subjects: All patients 75 years and older who underwent spinal instrumentation by a single surgeon during the study period.

Outcome measures: Clinical assessment of symptoms and signs following surgery, and comparison with preoperative condition. Radiological assessment of spinal alignment and fusion at follow-up. Complications of surgery.

Results: Study of 24 patients with a mean age of 82.5 years. Eleven patients were male and 13 were female. Nineteen patients had cervical pathology, one had thoracic and four had lumbosacral pathology. Fourteen patients had degenerative spinal disease, six had sustained spinal injury, three had tumours and one had had recent discitis. At follow-up, symptoms and signs remained unchanged in four patients, 11 had significant improvement and five had a complete resolution of symptoms. There was no clinical or radiological evidence of implant failure in any patient at follow-up. Four patients died. Complications included one fatal myocardial infarction, death due to respiratory failure in three patients, pneumonia in one patient and non-fatal pulmonary embolus in another. Postoperative haematoma occurred in three patients and superficial wound infection in one patient.

Conclusion: Spinal instrumentation is successful in patients over 75 years and there does not appear to be an increased risk of implant failure in this age group. Mortality appears to be related to pre-existing co-morbidity.

Meralgia paraesthetica: an alternative cause for postdiscectomy leg pain

③ *G. M. Spink, Deniz, N. Farooq, et al. (Charing Cross Hospital, London, UK)*

Objective: To identify the role of Meralgia Paraesthetica (MP) in postdiscectomy leg pain.

Design: Retrospective study of all patients over a 5-year period who underwent surgery for MP.

Subjects: Patients identified from theatre logbook ($n = 15$).

Outcome measures: Incidence of previous spinal surgery in patients with MP.

Results: Fifteen patients underwent 21 operations. Sixty per cent of patients were male. The average age was 45.9 years (male 49.3; female 40.7). Thirty-three per cent of patients had undergone previous surgery to the groin/lower abdomen on the same side. Thirteen per cent of patients had a history of peripheral nerve entrapment syndromes elsewhere. The relapse rate was 23% (Consultant cases 25%; SpR cases 20%). Eighty per cent of the relapses were female. Twenty per cent of patients had previously undergone surgery for a prolapsed lower lumbar disc on the same side as the MP. The average time between spinal surgery and onset of MP symptoms was 3 years.

Conclusion: Lumbar disc disease is involved in the aetiology of MP. Traditionally, MP can develop either as a result of an L2/3 or L3/4 disc, or as a complication of positioning during surgery. In this study, the patients developed late onset symptoms and had no evidence of disc disease at the higher levels. It may be that lower lumbar disc surgery leads to altered biomechanics of the lumbar spine and pelvis. This may cause pelvic tilt, bowstringing the inguinal ligament causing MP. This should be considered in patients who present with leg pain following lumbar disc surgery with normal post-operative imaging.

Can we improve the trauma teams interpretation of emergency CT brain scans?

A. Durham-Hall, W. A. Liebenberg, D. Horney, et al. (Hurstwood Park Neurological Centre, Haywards Heath, UK)

Objective: Interpretation of emergency CT brain scans by junior doctors is a basic skill, which is underdeveloped and may be remedied by placing a reference poster of common pathology in A&E.

Design: We designed two prospective questionnaires with a total of 22 scans. The first assessed the ability of junior doctors to correctly interpret emergency scans. The second assessed improvement in interpretation following the introduction of reference images.

Subjects: Junior doctors were asked randomly to complete our questionnaires. We had 74 respondents in the first and 34 in the second questionnaire.

Outcome measures: We used Wilcoxon signed rank test to evaluate the improvement in interpretation.

Results: In the first questionnaire, 85% doctors were in surgical specialities and 94% in second. Fifty-six

per cent in first and 82.3% in second series attended trauma calls, and 71.7% within 5 years of qualification in first, 23.5% in second series; 67.5% of first and 50% of second series were SHO's. In 39.7% correct interpretation CT scans first series and 49.1% correct interpretation second series. Introducing reference images similar to those of questionnaire improved correct interpretation to 82.6%. In 7/10 scans statistical significant improvement in interpretation. There was a 55.86% improvement in diagnosing ischaemic infarct ($p < 0.001$), 52.94% for brain abscess ($p < 0.004$), 41.16% for acute subdural haematoma ($p = 0.001$), 41.16% for chronic subdural haematoma ($p = 0.025$) and no statistical significant improvement in diagnosing brain tumour, hydrocephalus or extradural haematoma.

Conclusions: Introducing a simple poster to A&E departments will allow junior doctors to make the correct diagnosis of basic emergency CT scans in more than 80% of cases.

External ventricular drains and traumatic brain injury: an effective method of ICP control

N. Keong, L. Corteen, M. Czosnyka, et al. (Department of Neurosurgery, Addenbrooke's Hospital, Cambridge, UK)

Objective: To assess the effectiveness of External Ventricular Drains (EVDs) in the management of raised intracranial pressure (ICP) in patients with traumatic brain injury (TBI).

Design: Retrospective case-note review.

Subjects: Patients presenting with traumatic brain injury in 2004 who required EVD insertion to control ICP despite optimal medical management appropriate to established ICP protocols.

Outcome measures: Primary end point, ICP control 24 h postEVD insertion. Secondary end points, cerebrospinal fluid (CSF) infection, admission period and permanent CSF diversion.

Results: In the 12-month period, 27 patients with TBI required EVD insertion of ICP control. Mean EVD duration was 6.9 days, with 29.6% of the patient group required multiple EVDs. EVD insertion significantly reduced mean ICP from 26.4 to 13.8 ($p < 0.0001$). When the first postinsertion day was analysed in quarters, the benefit was greatest in the first 6 h, but remained significant throughout the entire 24 h. 11.1% needed a subsequent ventriculo-peritoneal shunt and 4/27 (14.8%) had culture-positive CSF.

Conclusions: EVDs are effective at reducing raised ICP in patients with TBI. EVDs do not significantly increase the shunt requirement rate. This intervention may reduce the necessary intensity of potentially harmful ICP control methods, such as hyperventilation and hypothermia.

Is acute rehabilitation of benefit following traumatic brain injury? A multi-centre trial proposal

C. Liu, R. Greenwood, P. J. Hutchinson, et al. (Regional Neurological Rehabilitation Unit, Homerton Hospital, London, UK & Addenbrooke's Hospital, Cambridge, UK)

Background: Traumatic brain injury (TBI) is one of the five most prevalent long-term neurological conditions, but service provision for its acute rehabilitation (AR) remains virtually non-existent. Have national guidelines published since the Galasko RCS working party report (1999) addressed this issue?

Review of National Guidelines: Galasko (1999) stated that patients with severe TBI who no longer required intensive care or neurosurgical interventions should be admitted to rehabilitation facilities, and not acute surgical beds. The RCP & BSRM guidelines (2003) proposed 'post-acute inpatient specialist rehabilitation' following 'acute care/neurosurgery ward-based therapy', but where there is poor insight and awareness, intervention should be deferred until the patient 'is ready to engage'. The NSF for long-term conditions (2005) recommended that patients are assessed in acute settings by a neurorehabilitation team, and should receive 'timely' rehabilitation.

Conclusion: AR following TBI, at a time when patients are medically 'stable', but often confused and in post-traumatic amnesia, is thus not addressed by guidelines postGalasko. How should one take this further?

Recommendations: There are three ways of introducing AR after TBI: 1. Peripatetic model: comprises a team visiting patients in acute beds and proposed in the RCP (2003) guidelines despite studies showing unit-based stroke rehabilitation is more effective than visiting teams. 2. District level 'mixed' acute unit: for patients after stroke, subarachnoid haemorrhage and TBI, thus facilitating the process and practice of AR without prolonging length of stay. 3. Supra-district AR unit: a tertiary unit providing 1.5–2 beds/100,000 for AR after TBI. Its efficacy versus 'standard care' has not been subjected to scrutiny. We are planning a multi-centre, randomized study using the MRC methodology to investigate complex interventions to trial this model.

SAH on the NICU: demographic features, treatment and outcome

S. Bojanic, S. Sheikh, A. Molyneux, C. Kearns & J. Millo (The Radcliffe Infirmary, Oxford, UK)

Objective: To assess the demographic features, treatment and outcome of patients with SAH on the NICU. This study particularly focuses on elderly and high grade patients.

Design: A retrospective study of patients admitted to NICU from January 2001 to June 2004. Data extracted from the clinical notes included age, sex, WFNS grade, Fisher Grade, treatment and outcome. Outcome at three months was coded as dead/alive and further subdivided according to the Modified Rankin Score.

Subjects: One-hundred-and-sixty-three subjects, 105 female. Mean age 54.9 (range 20–81 years).

Outcome measures: Alive versus Dead at 3 months. Subdivided according to Modified Rankin Score.

Results:

Fifty-four (33.3%) were in Fisher grade 3, 87 (53.7%) in Fisher grade 4. Twenty of 57 (35%) patients above the age of 60 years were in high grade. Twenty-two (38.6%) of elderly patients made a good recovery. Of 31 elderly high grade patients, seven (35%) made a good recovery.

Conclusions: High grade in this group was associated with a poor outcome. Overall, there was a good outcome in 44.4% of patients and 38.6% of elderly SAH patients made a good recovery.

The effect of craniotomy approach on postoperative mortality for anterior circulation, good grade, aneurismal subarachnoid haemorrhage

H. Brydon, L. Marshman & J. Dhir (North Staffordshire Royal Infirmary, Stoke-on-Trent, UK)

Objective: To determine whether the craniotomy approach/technique affected postoperative mortality for good grade, anterior circulation, aneurysmal subarachnoid haemorrhage.

Design: A retrospective review of case notes of patients identified from a computerized operative database.

Subjects: Two-hundred-and-sixty-two patients who were admitted between 1 January 1998 and 31 March

2005 with a good grade subarachnoid haemorrhage, and underwent clipping of an anterior circulation aneurysm.

Outcome measures: Death within 1 month of surgery.

Results: Six different craniotomy techniques were identified, with three of them being used for a wide range of proximal anterior circulation aneurysms, with the others were used a few times for specific aneurysms only (pericallosal or giant aneurysms). The commonest technique was the pterional approach (179 patients) followed by supraorbital microcraniotomy (60 cases). An orbital rim/ trans-orbital approach was used 16 times as a transitory technique to a minimally invasive procedure. The postoperative mortality of the 179 patients who underwent a pterional clipping was 7.8% (14 deaths), with the commonest cause of death being cerebral vasospasm/ infarction (10 cases). The mortality of the orbital rim approach was 12.5% (two deaths), both due to vasospasm. However, there were no deaths among the supraorbital microcraniotomy group. The difference between this and the pterional group was statistically significant ($0.02 > p > 0.01$).

Conclusions: The craniotomy approach used for aneurysm surgery significantly affects postoperative mortality. The supraorbital microcraniotomy offers significantly improved survival over other approaches.

Intracranial aneurysms in children under one year of age: a systematic review of the literature

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Objective: To assess the clinical and radiological signs, and the outcome of intracranial aneurysms (IA) in children under one.

	< 50 years	51 – 60 years	61 – 70 years	> 71 years	Total WFNS
Low grade	43 (26.5%)	27 (16.6)	23 (14.2)	12 (7.4)	105 (64.8)
High grade	18 (11.1)	15 (9.3)	13 (8.0)	9 (5.6)	55 (33.9)
Fisher grade					
I	3	1	3	0	7 (4.3)
II	7	1	3	1	12 (7.4)
III	26	13	8	7	54 (33.3)
IV	26	27	21	13	87 (53.7)
Treatment					
Clipping	10	4	2	1	17
Wrap	1	0	0	0	1
Coil	47	31 (1W + C)	26	14	118
Failed coil	2	1	1	1	5
None	3	7	7	5	22
Outcome					
Good	32	14	15	7	68
Poor	28	27	19	12	86

Design: Systematic review of the literature.

Subjects: Case reports and clinical studies in which an IA in a child < 1 year old was demonstrated.

Outcome measures: Clinical and radiological signs at presentation were registered. The outcome was categorized according to the Glasgow Outcome Scale (GOS).

Results: We found 129 cases of IA in children < 1 year old. The mean age at diagnosis of the IA was 4.9 ± 3.6 months with a male:female ratio of 1:1. Presentation was hemorrhagic in 73%. These patients were younger (mean 4.2 *v.* 6.8 months, $p < 0.001$) and had smaller sized IA's. Fourteen and 13 IA's were from traumatic or infectious aetiology, respectively. In 21% there was various co-morbidity. The prevalence of IA's on the MCA was higher than all other vessels. Mean aneurysm size was 1.8 ± 1.4 cm, with 29 giant aneurysms. Giant aneurysms were more often located in the posterior circulation (45 *v.* 16%, $p = 0.005$). The GOS was 5 in 50% after a mean period of follow-up was 12.3 ± 23.4 months.

Conclusions: The presentation of IA in children < 1 year old differs from adults with a higher prevalence of giant IA in the posterior circulation, as well as on the MCA. Patients presenting with a haemorrhage are younger and tend to have smaller-sized IA's. There was no male predominance. Outcome is comparable, or slightly better than in adults.

Utility of USPIO as a magnetic resonance dual contrast agent able to identify both fibrous cap and inflammation in-vivo in carotid atheroma: can we improve patient selection for endarterectomy?

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Background: It is well described that 'vulnerable' atheromatous plaque has a thin, fibrous cap and extensive lipid core with associated inflammation. This inflammation can be detected as areas of signal drop on high resolution MR imaging using a novel contrast medium, Sinerem, an ultrasmall superparamagnetic iron oxide (USPIO). Studies using USPIO have, thus far, not reported its additional T1 effect of enhancing fibrous cap.

Methods: Twenty patients with carotid stenosis (10 symptomatic, 10 asymptomatic) were imaged at 1.5T, pre- and 36 h postUSPIO infusion. Images were anonymised, plaque seen was manually segmented into quadrants (CMR tools, London) and focal regions of signal drop post contrast. Signal change was normalized to adjacent muscle.

Results: There were nine males and 11 females, and mean ages were 71 (symptomatics) and 73 (asymptomatics).

Mean stenoses were 82% (symptomatics) and 72% (asymptomatics). Symptomatics had significantly more quadrants with signal drop post USPIO than asymptomatics (75 *v.* 32%, $p < 0.01$) and more focal regions of signal drop (0.68 *v.* 0.26 regions/image, $p < 0.01$). Asymptomatics had more quadrants with signal enhancement than symptomatics (68 *v.* 25%, $p < 0.05$).

Conclusions: Symptomatic plaques had more focal areas of signal drop than asymptomatic plaques, suggesting that they harboured a greater inflammatory burden. Asymptomatic plaques showed more enhancement than symptomatic plaques, suggesting thicker fibrous caps and greater stability, although some focal areas of signal drop were noted suggesting vulnerability. If validated by larger studies, USPIO may be a useful dual contrast medium, able to enhance risk stratification of patients with carotid stenosis, improving selection for intervention.

The association of uncoupling protein-2, Interleukin-6 572 G > C and ENOS polymorphisms in 660 Japanese patients with subarachnoid haemorrhage, intracerebral haemorrhage and cerebral infarcts

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Objective: To determine whether there is an association with UCP-2, IL-6 572 G > C and ENOS 298 G > T polymorphisms in Japanese patients with subarachnoid haemorrhage, intracerebral haemorrhage or infarct.

Design: Genotypes were determined by DNA extraction, polymerase chain reaction amplification and endonuclease digestion.

Subjects: Six-hundred-and-sixty Japanese patients presenting to two different centres in Japan with subarachnoid haemorrhage, intracerebral haemorrhage, cerebral infarcts and controls.

Outcome measures: Allele frequencies were determined via gene counting and differences between the genotype distributions and allele frequencies for the four different groups of patients were considered via chi-squared tests or Fisher's exact tests as appropriate.

Results: For the UCP 2 polymorphism the results were not significant for patients with SAH, haemorrhage or infarcts *v.* controls. There was an association for the genotype frequency in the SAH group *v.* the other groups ($p = 0.08$). For the IL-6 572 G > C polymorphism there was an association between the infarct patients *v.* the controls ($p = 0.09$) with an increase in the CC genotype. For the ENOS polymorphism there was an association for the allele

frequency between the infarct patients *v.* controls ($p = 0.06$).

Conclusions: This is the first study to look at these candidate polymorphisms in this group of patients. An association was seen in the infarct group *v.* the controls for the UCP 2 and ENOS polymorphisms. There was also an association between the SAH group and other groups for the IL-6 572 polymorphism.

The genetics of subarachnoid haemorrhage using candidate gene approaches

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Objective: To determine whether there is an indication of the likely candidate genes involved in the pathogenesis of subarachnoid haemorrhage.

Design: A review of all published data to date in which there has been a significant contribution to the understanding of the genetics of SAH.

Subjects: Patients with subarachnoid haemorrhage.

Outcome Measures: Possible candidate genes involved in SAH are those that are associated with matrix deposition (Stromelysin-1 MMP3, MMP-9, elastin), inflammation (Interleukin-6), lipid metabolism (Hepatic Lipase, APOE, PON1) and thrombosis (factor V Leiden, fibrinogen).

Results: Studies to date have shown that for the ACE gene there does appear to be a consistent trend with overrepresentation of the I allele. For the stromelysin, MMP-9, Elastin, IL-6, and APOE genes inconsistent associations have been reported.

Conclusions: Further larger studies are required. To date, the majority of studies have been too small to explore the possibility of interaction between environmental factors (e.g. smoking, hypertension and diabetes) and genotype in the risk of aneurysmal subarachnoid haemorrhage.

Spreading depolarization is a critical component in the evolution of ischaemia in the cerebral cortex

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Objective: Ischaemic infarct size is a function of number of peri-infarct depolarizations (PIDs) and is usually attributed to cytotoxic effects of PIDs. We examined the effects of PIDs on cortical perfusion.

Design: Quantitative mapping of cortical perfusion (laser speckle imaging) in an animal model of stroke.

Subjects: Eleven cats (non-recovery anaesthesia, α -chloralose) undergoing middle cerebral artery occlusion (MCAO) for 4 h.

Outcome measures: Severity and duration of changes in perfusion linked to PIDs.

Results: Ten minutes after MCAO, there was good collateral perfusion in most experiments; this was extensive in four experiments and resulted in minimal infarct size. In two, there was no collateral perfusion, and infarcts were large from the outset. In five experiments with intermediate collateralization there was substantial secondary deterioration in perfusion between 10 and 240 min: one or more spontaneous, marked reductions in perfusion occurred in the penumbra in all five experiments. In video sequences, these propagated in 1, 2 or 3 gyri, with a rate characteristic of spreading depression or of PIDs. In four of the five studies, these were associated with sustained reductions in perfusion and enlargement of the area of ischaemia.

Conclusions: As well as being an effect of ischaemia, PIDs themselves initiate further, critical reductions in perfusion. Initial occlusion often serves only to sensitize grey matter to the effects of later PIDs, suggesting that a combination of proximal and distal mechanisms determines infarction. Since depolarizations are now known to occur in patients with subarachnoid haemorrhage (SAH), this concept may apply to ischaemic deterioration after SAH.

Cerebral haemodynamic deficits in patients with moderate ICA stenosis

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Objective: To determine whether moderate internal carotid artery (ICA) stenosis results in a delay in blood flow to the ipsilateral cerebral hemisphere.

Design: A single-centre prospective MR perfusion imaging study of symptomatic individuals with moderate ICA stenosis.

Subjects: Twenty consecutive patients with moderate ICA stenosis, confirmed by catheter angiography, underwent dynamic MR perfusion imaging.

Outcome measures: Differences in mean time to peak (mTTP) and relative cerebral blood volume (rCBV) between cerebral hemispheres were calculated for middle cerebral artery territory regions by a reader blinded to the angiographic and clinical details.

Results: There were significant differences in mTTP between cerebral hemispheres in 16 patients (80%) with an inter-hemispheric delay in mTTP of 0.51 s (95% CI, 0.25–0.72; $p < 0.001$). In three patients

with unilateral disease and a mean ICA stenosis of 57% and one patient with bilateral moderate stenosis there was no inter-hemispheric delay in mTTP. There were no significant inter-hemispheric differences in rCBV.

Conclusions: Dynamic MR perfusion imaging can identify cerebral perfusion deficits attributable to ICA stenosis of less than 70%, which could complement selection criteria for cerebral revascularization in these patients.