Better Prognosis for HER2-Positive Breast Cancer Brain Metastases

Risk Factors and Survival Outcome in Cerebral Metastatic Breast Cancer.

Bachmann C, Schmidt S, et al:

Med Oncol 2014; 31 (March): 862

Patients with HER2-positive breast cancer brain metastases have better survival than HER2-negative patients.

**Background:** Brain metastases (BM) occur in about 30% of breast cancer patients, particularly those who are young, have poorly differentiated tumors, are estrogen receptor (ER)-negative, have triple-negative status, or are HER2 positive.

**Objective:** To determine the prognostic significance of breast cancer risk factors for time to BM occurrence and survival after BM diagnosis.

**Design:** Retrospective, single-institution case series.

**Participants/Methods:** Consecutive patients from 2001 to 2010 with primary breast cancer that was operable and had not metastasized were reviewed. Initial treatment consisted of mastectomy or breast-conserving resection with axillary lymph node dissection. HER2-positive patients could receive trastuzumab. Positive hormone status patients were treated with hormone therapy. BM was diagnosed by MRI or CT when clinical symptoms occurred or during routine staging. After BM diagnosis, all patients had whole-brain radiation therapy (WBRT) with or without surgical resection. Immunohistochemistry was performed on resected specimens, with ER or progesterone receptor (PR) staining positivity when present in >10% of cells. HER2 was defined by American Society of Clinical Oncology/College of American Pathologists guidelines (0 – no reaction; 1 – weak reaction in <10% of cells; 2 – moderate reaction in >10% or strong reaction in >10% and <30% of cells, or 3 – strong reaction in >30% of cells.) HER2 scores were negative if 0 or 1, equivocal if 2, and positive if 3. Triple-negative status was defined as ER negative, PR negative, and HER2 negative.

**Results:** 80 patients (median age, 49.5 years) had mean follow-up of 30.5 months after BM diagnosis. BM was more likely in patients with small tumor size (T1/T2), ductal histology, grade 3, lymph node involvement, HER2-positive, and triple-negative status. BM occurred 35 months (median) after initial cancer diagnosis. ER, PR, and HER2 immunohistochemistry status had no statistical impact on time to BM development. Higher tumor grade was associated with short BM development interval. HER2-positive patients had longer survival after BM development (12 months) versus HER2-negative patients (5 months), but ER, PR, and triple-negative status were not significantly associated with survival.

**Conclusions:** Routine screening for BM may be warranted in patients with HER2-positive, hormone receptor-negative, triple-negative status, or grade 3 tumor patients. HER2-positive patients who develop brain metastases have a better prognosis than do HER2-negative patients.

**Reviewer's Comments:** Brain metastases are the most common tumors for which neurosurgeons provide care; breast cancer with brain metastases is particularly common among women. This study illustrates the prognostic significance of HER2 positivity in BM from breast cancer. Immunohistochemistry is becoming increasingly powerful as a prognostic tool across the field of neuro-oncology. As neurosurgeons involved in the care of these patients, we need to be more attentive to the immunohistochemical status of the primary tumor. (Reviewer-N. Scott Litofsky, MD, FACS).

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Keywords: HER2, Breast Cancer, Brain Metastases, Prognosis, Immunohistochemical Status, Risk Factors, Therapy

Print Tag: Refer to original journal article
Cell Phones -- Should We Hang Up?

Mobile Phone Use and Risk of Brain Neoplasms and Other Cancers: Prospective Study.

Benson VS, Pirie K, et al:

Int J Epidemiol 2013; 42 (June): 792-802

Cell phones are possibly associated with brain neoplasia, but this study did not find an association with an increase in gliomas, meningiomas, or extracranial cancers.

**Background:** In 2011, the International Agency for Research on Cancer (IARC) declared that cell phones were possibly carcinogenic to humans (group 2B of the IARC). This was based on retrospective data, mainly from 2 studies. There are, however, many issues with these studies. For instance, in a good number of patients the information on cell phone usage was obtained from the recollections of a relative. Also problematic is that, in 2011, a prospective study concluded that cell phones are not associated with an increase in intracranial tumors *(BMJ* 343:d6387, 2011).

**Objective:** To determine if cell phone usage increases the risk of neoplasia.

**Design:** Prospective cohort study.

**Methods:** In the U.K., 1.3 million middle age-women were recruited from 1996 to 2001 and surveyed every 3 to 4 years until 2009.

**Results:** The final data are based on 791,710 women who were followed for an average of 7 years. During that period, 1261 intracranial neoplasms were diagnosed in addition to 51,680 extracranial cancers. The long-term use of cell phones was associated with an increased incidence of vestibular schwannomas, but no increase in other intracranial tumors, such as gliomas, meningiomas, or pituitary adenomas. There was no increase in extracranial cancers, including eye and neck cancers. In fact, the risk of all extracranial cancers, including lung cancer, was reduced in the cell phone users. Unexpectedly, short-term (<5 years) use of cell phones was associated with an increase in pituitary adenomas; however, this trend did not persist long term. Finally, individuals using a cell phone were at greater risk of stroke but not of cardiac disease.

**Conclusions:** Cell phone use is not associated with an increase in gliomas, meningiomas, or extracranial cancers.

**Reviewer's Comments:** Even prospective studies have flaws. Here, the long-term user group is different from the non-user group. The former had high stress jobs and a different lifestyle related to their higher income. Complicating matters, over time many non-users became users, which means they are not a homogenous control group. So, we have not heard the end of this. This month, an ENT group reported that cell phone usage leads to larger-size vestibular schwannomas, rather than to an increase in their incidence *(Tumor Biol* 35:581-587, 2014). When it comes to preclinical data, recent animal studies cannot establish carcinogenic effects from cell phone-related emissions *(Crit Rev Environ Sci Technol* 41:1-32, 2011; AGNIR, UK 2012). Everyone agrees that longer observation periods are needed, as well as prospective data and consistent findings across studies. A number of ongoing studies, such as the COSMOS, CEFALO, and MOBI-KIDS, will bring new data. Note that the recent data in children and adolescents, the most vulnerable group, does not show any association between cell phone usage and intracranial tumors. (Reviewer-Luc Jasmin, MD, PhD, FRCS (C), FACS, FAANS).

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Keywords: Radiofrequency Electromagnetic Fields, Cell Phones, Cordless Phones, Brain Tumor, Intracranial Tumors, Carcinogenicity, Epidemiology

Print Tag: Refer to original journal article
Retinal nerve fiber thinning measured by optical coherence tomography is a prognostic indicator for poor visual recovery following surgery for meningiomas of the anterior visual pathway.

**Objective:** To evaluate the value of peripapillary retinal nerve fiber layer (RNFL) thickness measurements by optical coherence tomography (OCT) in predicting the visual outcome after surgery for compressive optic neuropathy in patients with anterior visual pathway meningiomas.

**Design:** Retrospective, clinical case series.

**Participants/Methods:** This study included 14 eyes of 12 patients in which pre- and postoperative OCT images of the peripapillary RNFL were available. All patients were imaged with the time-domain Stratus OCT, using a circumpapillary circle scan. Patients also underwent comprehensive ophthalmic evaluation including visual field testing before and after surgical excision or radiation therapy of the meningioma causing a compressive optic neuropathy.

**Results:** Significant improvement in visual acuity, color vision, and mean deviation and foveal sensitivity on visual field testing was seen after surgery in patients with normal preoperative RNFL thickness. Improvement was not seen in patients with thin baseline RNFL thickness. Multivariate statistical analysis identified longer duration of symptoms, in addition to RNFL thickness, as predictors of improved visual function.

**Conclusions:** Baseline RNFL thickness and duration of symptoms are the most important predictors of visual improvement after treatment of patients with compressive optic neuropathy due to meningiomas of the anterior visual pathway.

**Reviewer's Comments:** Abnormal RNFL thickness measurements should not be used to determine whether intervention should take place. Some patients with abnormal RNFL thinning experienced improved visual function after treatment. However, this imaging modality can be of value when counseling patients and helping them to have appropriate expectations with respect to the probability of visual recovery after surgery or radiation therapy. (Reviewer-Scott D. Smith, MD, MPH).

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Keywords: Imaging, Optic Nerve

Print Tag: Refer to original journal article
Juvenile Parkinsonism May Be Initial Sign of Gliomatosis Cerebri

Juvenile Parkinsonism as an Initial Manifestation of Gliomatosis Cerebri.

Jang W, Ha SH, et al:

J Neurol 2013; 260 (December): 3161-3163

Gliomatosis cerebri is a rare primary brain tumor that can be difficult to diagnose early in the course of its development. Negative brain MRI does not exclude tumor-induced parkinsonism.

Background: Gliomatosis cerebri (GC) is a rare primary brain tumor that can be difficult to diagnose because it may not be evident on brain MRI early in the course of its development. Headache and/or neurological deficits, such as gait difficulty, cognitive changes, seizure, and, rarely, parkinsonism, have been described previously as first clinical manifestations of GC. Tumor-induced parkinsonism usually presents with key signs such as cognitive decline, seizure, and pyramidal tract involvement, which can be helpful in the diagnosis of GC. Case Report: A 17-year-old female presented with a 1-month history of left-hand tremor (resting and postural), mild hypomimia, unremarkable brain MRI with and without contrast, negative serological screening (thyroid, autoimmune, ceruloplasmin, pyruvate/lactate ratio, and toxicology, including manganese), and no improvement after an L-DOPA (1200 mg) challenge. Her symptoms progressed to involve her right upper extremity, bilateral bradykinesia, and cogwheel rigidity. A pull test was positive, demonstrating postural instability. Discussion: At 3 months, brain MRI, PET imaging, electromyography, electroencephalography, and genetic testing (PARK2; PANK2; FXTAS; ATP7B; SCA 1, 2, 3, 6; DYT 1; DYT 5; and Huntington disease) were negative. By 7 months, she had cognitive decline and recurrent syncope. Brain MRI revealed T2 high-signal intensity lesions in the right parietal lobe. By 8 months, these lesions had spread to involve the bilateral temporo-occipito-parietal lobes. There were epileptiform abnormalities in the left frontal region on EEG, decreased overall cognitive performance on neuropsychometric testing, reduced glucose metabolism diffusely throughout the brain on FDG-PET imaging, and a high choline peak in the right parietal lobe on magnetic resonance spectroscopy (MRS). Brain biopsy revealed tumor cells with elongated, spindle-shaped nuclei on hematoxylin-eosin staining, which is characteristic of GC.

Reviewer's Comments: This was a very interesting case of tumor-induced parkinsonism demonstrating that a structural brain lesion cannot be entirely excluded based on negative imaging, especially if the patient continues to deteriorate clinically. The authors were meticulous in getting repeat brain imaging with conventional MRI. Retrospectively, it may have been helpful to perform MRS earlier, but she did not have the "key signs" of tumor-induced parkinsonism until she presented with cognitive decline at >6 months into the course of her disease progression. Also, the basal ganglia were not structurally compromised as in previous reports of tumor-induced parkinsonism. To explain the patient's parkinsonism, the authors postulate that the connection between striatal output and supplementary motor area was compromised. The authors suggest that GC be added to the list of causes for juvenile parkinsonism. I think perhaps, in a broader sense, in a case with any type of neurological deterioration, especially with a young age of onset, a structural brain abnormality should be seriously considered even with initially negative brain imaging. (Reviewer-Amy Katherine Sullivan, MD, PhD).

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Keywords: Tumor-Induced Parkinsonism, Juvenile Parkinsonism, Gliomatosis Cerebri

Print Tag: Refer to original journal article
Fat-Water Interface More Prominent on Standard TE Setting Used for Clinical SWI

Fat-Water Interface on Susceptibility-Weighted Imaging and Gradient-Echo Imaging: Comparison of Phantoms to Intracranial Lipomas.

Mehemed TM, Yamamoto A, et al:
AJR Am J Roentgenol 2013; 201 (October): 902-907

Susceptibility-weighted imaging shows a characteristic surrounding peripheral low signal intensity rim in intracranial lipoma.

**Objective:** To evaluate the differences in fat-water interface chemical shift on susceptibility-weighted imaging (SWI) and gradient-echo imaging in phantom and intracranial lipoma cases.

**Design:** Prospective evaluation of a lard-water phantom and retrospective study of 5 central nervous system lipoma patients.

**Methods:** SWI and T2-weighted imaging were performed using a 3T MRI scanner and use of a 32-channel head coil with a central frequency of 123.15 MHz; in-phase and out-of-phase timing were 19.7 and 20.9 ms, respectively. The following acquisition parameters for T2-weighted imaging in axial acquisition were used: TR/TE, 500/20.0, 19.7, and 20.9; receiver bandwidth, 199 Hz/pixel; acquisition matrix, 256.0 x 224.0; 0.39 x 0.39 x 3.0 mm; 1.0-mm gap; frequency-encoding direction in left-to-right direction; number of averages, 1; and acquisition time, 1 minute, 58 seconds. The following parameters for SWI in axial acquisition were used: TR/TE, 28/20.0, 19.7, and 20.9; receiver bandwidth, 120 Hz/pixel; acquisition matrix, 320.0 x 230.0; 0.625 x 0.625 x 2.0 mm; no gap; frequency-encoding direction in left-to-right direction; number of averages, 1; and acquisition time, 4 minutes, 46 seconds. SWI, its underlying magnitude, and high-pass filtered phase images were evaluated in the 3 different TE settings to identify which setting best visualized the fat-water interface as a low signal. All were compared with T2-weighted imaging in-phase and out-of-phase fat-water interface appearances. SWI parameters for evaluation of intracranial lipomas were the same as for the phantom experiment, with a TE of 20.0 ms and acquired with phase encoding in a left-to-right direction.

**Results:** TE at 19.7 ms (in-phase) showed the minimum fat-water interface low signal in the phase-encoding direction on magnitude, high-pass filtered phase, and SWI. TE at 20.9 ms (out-of-phase) showed the maximum fat-water interface in the phase-encoding direction on magnitude, high-pass filtered phase, and SWI. TE at 20.0 ms (partially out-of-phase) showed more fat-water interface low signal on SWI than on T2-weighted imaging, especially in the phase-encoding direction. Five lipoma cases showed high signal intensity with surrounding peripheral dark rim on SWI. Presence of fat was confirmed by CT in all cases.

**Conclusions:** The fat-water interface is more prominent on the standard TE setting used for clinical SWI (20.0 ms) than that of T2-weighted imaging, and shows a characteristic surrounding peripheral low signal intensity rim in lipoma.

**Reviewer's Comments:** I agree with the authors in that fat-water interface is more prominent on the standard TE setting used for clinical SWI. More studies should be conducted to confirm that peripheral low signal intensity rim seen on SWI is a phenomenon associated with lipoma rather than hemorrhage. (Reviewer-Sebastian Sadowski, MD).

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Keywords: Susceptibility-Weighted Imaging, Gradient-Echo Imaging, Intracranial Lipoma

Print Tag: Refer to original journal article
Levetiracetam is comparable to phenytoin in efficacy of post-traumatic seizure prophylaxis at a lower cost.

**Background:** Phenytoin is recommended to prevent early post-traumatic seizures (within 7 days), which occur in 2% to 30% of patients after traumatic brain injury (TBI). Because of side effects, bioavailability, and drug level monitoring issues, levetiracetam is being used by many with conflicting outcomes.

**Objective:** To determine the prevalence of post-traumatic seizures in TBI patients, comparing those treated with levetiracetam to those treated with phenytoin.

**Design:** Retrospective, single-institution case series.

**Participants/Methods:** Patients aged >18 years admitted to the intensive care unit after TBI, treated with either phenytoin or levetiracetam >48 hours, and monitored with electroencephalogram (EEG) on at least 1 day for at least 30 minutes were included for analysis. EEG was obtained for suspicion of seizures in the presence of coma, decreased mental status, or seizure activity. Total antiepileptic drug therapy (AED) and costs were determined. Time of therapeutic AED was defined as the number of days with a phenytoin level in the therapeutic range (10 to 20 mg/L).

**Results:** Of 420 patients receiving phenytoin or levetiracetam, 125 had EEG monitoring and 90 were included for analysis. In total, 75.6% were male, and median age was 50 years. Most injuries resulted from motor vehicle accidents (41%) and falls (31%). Overall, 63.3% had severe brain injury and median Glasgow Coma Scale score was 5; 55.6% had subdural hematoma; 53.3% had frontal lobe injury; and 5.5% had seizure activity within 24 hours. Eighteen of 90 received levetiracetam and 72 received phenytoin; temporal lobe injury was less likely in those treated with levetiracetam (22.2% vs 61.1% in those treated with phenytoin). Median duration of AED therapy was 9 days for levetiracetam and 14 days for phenytoin. No patients treated with levetiracetam had drug levels drawn, but 98.8% of phenytoin patients did. Initial phenytoin levels were therapeutic in 52%. Median number of phenytoin levels drawn was 5, at a cost of $141 per level. The prevalence of EEG-proven seizures was similar at 28% for levetiracetam and 29% for phenytoin. Additional AED administration was not statistically different (22% for levetiracetam and 49% for phenytoin). Study AED and monitoring costs were not significantly different ($43/day for levetiracetam and $55/day for phenytoin), but total AED costs were significantly less for levetiracetam ($45/day) versus phenytoin ($83/day).

**Conclusions:** Post-traumatic seizure incidence was similar between levetiracetam- and phenytoin-treated patients, with lower costs associated with levetiracetam treatment.

**Reviewer's Comments:** This study demonstrates similar seizure prophylactic efficacy of levetiracetam and phenytoin at a lower cost for levetiracetam; monitoring drug levels appears to increase phenytoin costs. The value of monitoring drug levels for a short AED course is questionable. One study weakness is including only patients with EEG monitoring; thereby, excluding patients with seizure activity without EEG monitoring; how that patient selection impacts results is unknown. We will continue to use levetiracetam as our first-line treatment. (Reviewer-N. Scott Litofsky, MD, FACS).

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Keywords: Brain Injuries, Head Injuries, Intensive Care Unit, Levetiracetam, Phenytoin, Seizures

Print Tag: Refer to original journal article
The Rapid Arterial Occlusion Evaluation scale is highly effective in predicting patients with large vessel occlusion.

**Background:** Treatment for acute ischemic stroke is limited to intravenous thrombolytics up to 4.5 hours and endovascular therapy, which can provide a longer time window and increased revascularization, especially in large vessel occlusions (LVOs).

**Objective:** To develop a simple and accurate scale used by paramedics to predict the presence of LVOs in patients with acute stroke.

**Methods:** Items with the highest predictive value of an LVO in the National Institutes of Health Stroke Scale (NIHSS) were identified, and the predictive value of different combinations was determined. Five items were used to build the Rapid Arterial Occlusion Evaluation (RACE) scale: facial palsy, arm motor function, leg motor function, gaze, and aphasia/agnosia. From February 2011 to March 2013, the RACE scale, along with baseline characteristics, stroke subtype, presence of LVO, and revascularization treatment were prospectively recorded.

**Results:** 357 patients were included for analysis, 54% of whom were men. In total, 29% of the patients had unknown time of onset. Mean time from symptoms onset to emergency medical services (EMS) was 40 minutes, and 95 minutes to neurological evaluation. RACE scale was highly effective in identifying patients with LVO (c-statistic, 0.82; 95% CI, 0.77 to 0.87). The higher the RACE score, the higher the likelihood of ischemic stroke caused by LVO. Overall, 19% of patients with RACE ≥5 received endovascular therapy compared with 2% of those with score <5 (P <0.001). RACE scale and NIHSS were comparable in predicting LVO (c-statistic, 0.85; 95% CI, 0.81 to 0.89).

**Conclusions:** The RACE scale is a simple tool for prehospital use by EMS that can detect acute stroke from LVO, which can help these patients be transferred and treated quicker.

**Reviewer's Comments:** In my opinion, one of the biggest reasons endovascular treatment of stroke has not been shown to be of benefit in recent trials is because the mantra "time is brain" has not been applied to thrombectomy like it has to intravenous therapy. It has been shown in multiple studies that earlier recanalization time results in better outcomes. This article introduces a new scale that may be able to get patients evaluated, transferred, and treated quicker, and that's the kind of help and data we need to show efficacy of a treatment we have all seen work with our own eyes, but have yet to be able to prove its value in our literature. (Reviewer-Sharon Webb, MD).

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Keywords: Cerebrovascular Occlusion, Stroke, Emergency Medical Services

Print Tag: Refer to original journal article
Aggressive Surgery Indicated for Most Brainstem Cavernomas

Hemorrhage Risk, Surgical Management, and Functional Outcome of Brainstem Cavernous Malformations.

Li D, Yang Y, et al:

J Neurosurg 2013; 119 (October): 996-1008

Aggressive surgical treatment is indicated for most brainstem cavernous malformations that have bled.

**Background:** About 20% of cavernous malformations (CMs) are in the brainstem.

**Objective:** To identify factors contributing to the natural history, hemorrhage risk, and long-term outcome of brainstem CMs.

**Design:** Retrospective review.

**Participants:** 242 patients who were surgically treated for brainstem CMs.

**Methods:** Each patient's data were reviewed. Lesions were classified according to location. MRI was used to define a new hemorrhage (intralesional vs extralesional), and new neurological symptoms were recorded. Surgical indications were (1) ≥2 hemorrhages, lesion size ≥2 cm, and serious or progressive neurological deficit; (2) lesion in the medulla; (3) acute or subacute hemorrhage with significant mass effect; and (4) exophytic lesion or a lesion abutting the pial surface accessible via safe entry zones. Operations were preferentially done at 4 to 6 weeks after the most recent hemorrhage, and MRIs were performed before and after surgery. Gross total resection was attempted in all patients. Complete resection was determined by MRI within 72 hours of surgery. Follow-up was by telephone, clinic visit, or questionnaire. Those with recurrent hemorrhage were examined for follow-up treatment. Statistical analyses were performed.

**Results:** 255 brainstem CMs were found in the 242 patients. The most common symptoms/signs were related to cranial nerve involvement (n=200), which most commonly involved cranial nerves V, VI, VII, IX, and X. Other symptoms included weakness, paresthesia, vertigo, gait problems, headache, dysarthria, hydrocephalus, and respiratory difficulties. In the 242 patients, there were 391 hemorrhages. The annual hemorrhage and recurrent hemorrhage rates were 5.0% and 60.9%, respectively. Recurrent hemorrhages occurred within 6 months in 129 patients (58.9%) and within 24 months in 85.3%. Gross-total resection of the CM was achieved in 230 patients (95%). Failure of gross-total resection was due to firm lesion consistency, lobulated lesions, ill-defined boundary, or tight adhesion. Surgical morbidity occurred in 112 patients, and was most commonly a cranial nerve deficit. Others included intracranial infection, hematoma, pneumonia, hydrocephalus, stroke, pulmonary embolus, and cerebrospinal fluid leak. At discharge, the modified Rankin score improved in 7.9%, was unchanged in 57.0%, and worsened in 35.1%. The scores stabilized by 3 months postoperatively and improved by 6 months. In total, 70 patients (28.9%) could live independently, and 76 (31.4%) were functioning sufficiently for full- or part-time work. On long-term follow-up, patient condition had improved in 147 (60.7%), was unchanged in 70 (28.9%), and had worsened in 25 (10.3%). Adverse prognostic factors were increased age (≥50 years), multiple hemorrhages, ventrally located lesions, and poor preoperative status.

**Conclusions:** Surgery for brainstem CMs leads to good long-term outcomes and low postoperative hemorrhage rates.

**Reviewer's Comments:** The results of this study suggest that total resection of brainstem CMs that have bled favors a better long-term prognosis and a markedly decreased risk of rebleeding. (Reviewer-John Schwankhaus, MD).

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Keywords: Brainstem Cavernous Malformation, Cavernoma, Microsurgery, Vascular Disorders

Print Tag: Refer to original journal article
Polyarterial Dissections Not as Fearsome as One Might Think

Characteristics and Outcomes of Patients With Multiple Cervical Artery Dissection.
Béjot Y, Aboa-Eboulé C, et al:

Stroke 2014; 45 (January): 37-41

At 3 months after presenting with cervical artery dissections, 12% of patients have moderate-to-severe handicap, regardless of the number of arteries dissected.

Background: Why some patients develop simultaneous or near simultaneous nontraumatic cervical artery dissections (CeAD) in multiple arteries is poorly understood. It is often widely assumed that these polyarterial dissections have a worse prognosis than do single-vessel dissections. However, the minimal available literature does not suggest this to be true.

Objective: To evaluate factors associated with multiple CeADs, and to compare outcomes for multiple versus single-vessel dissections.

Participants: 983 patients (mean age, 43 years) with CeAD enrolled (partly prospectively, partly retrospectively) in the Cervical Artery Dissection and Ischemic Stroke Patients (CADISP) study.

Methods: CeAD was defined by standard imaging criteria developed for the study. Intracranial dissections were excluded. Data recorded included the usual stroke risk factors, body mass index, history of migraine, fibromuscular dysplasia (FMD), head or neck surgery, recent infection, and trauma to the head or neck. Clinical data recorded included presence/absence of neck pain, headache, cranial nerve palsy, Horner syndrome, tinnitus, and brain or ocular ischemia. Stroke was evaluated by the National Institutes of Health Stroke Scale scores. Imaging studies were analyzed for degree of arterial occlusion/stenosis, aneurysmal dilatation, and hemorrhage. Outcome was assessed with the modified Rankin Scale (mRS). Baseline characteristics and outcomes of patients with a single CeAD were compared to those with polyarterial CeAD. Follow-up was out to 3 months.

Results: About 15% of the cohort presented with multiple CeAD. Approximately 75% of each group presented with brain or retinal ischemia, and the remainder presented with only local signs (pain, Horner syndrome, pulsatile tinnitus, or lower cranial nerve palsies). The following were statistically more likely in polyarterial dissections: cervical pain, recent infection, cervical manipulation, and a remote history of head/neck surgery. Imaging findings more likely with polyarterial CeAD were FMD of the cervical arteries and pseudoaneurysm. The number of arteries with CeAD had no effect on mRS score at 3 months (moderate-to-severe handicap defined as mRS ≥3). Only about 12% of either group had an mRS >2. Rates of recurrent stroke and recurrent dissection were low in both groups and were not statistically different. Intracranial hemorrhage during follow-up was uncommon, but was significantly more likely with multiple CeAD (2.1%) than with single CeAD (0.4%). This difference could not be attributed to antithrombotic drug therapy.

Conclusions: This is the largest published series of patients with CeAD. A pre-existing underlying vasculopathy (FMD) and provocative events, such as a recent infection, cervical manipulation, and perhaps prior head and neck surgery, were statistically associated with polyarterial CeAD.

Reviewer’s Comments: This study should produce additional data on the risk factors for and outcomes from CeAD. No data were presented on antithrombotic use before or after the diagnosis of dissection. Perhaps this will be the subject of a forthcoming paper. (Reviewer-James Warne Schmidley, MD).

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Keywords: Cervical Artery Dissection. Multiple vs Single Artery Dissections, Outcomes

Print Tag: Refer to original journal article
Lumbar Spine Attenuates Lower-Extremity Motions During Gait

Assessment of Three-Dimensional Lumbar Spine Vertebral Motion During Gait With Use of Indwelling Bone Pins.
MacWilliams BA, Rozumalski A, et al:


The lumbar spine contributes more coronal motion than transverse plane motion during gait.

Background: The movement of the spine in real life is very difficult to study. Imaging in 3D is not possible in space, especially during gait. Surface markers do not reflect the underlying vertebral movements.

Objective: To capture the movement of the spine during gait using internally anchored markers.

Participants: 8 human volunteers (mean age, 25 years).

Methods: Patients were examined and verified to be free of spinal pathology. They were then given local anesthesia over each of the spinous processes from L1 to S1. A pair of 1.6-mm K wires were drilled into each spinous process and linked to 3D markers. The markers were then registered to the underlying spine using CT scans. Additional markers were placed on the trunk and pelvis. Subjects then walked at self-selected velocities, and spinal movement was measured using gait lab equipment. The intersegmental movements in all 3 planes were then measured.

Results: The lumbar spine contributed most notably to coronal plane movement (abduction and adduction). It moved into abduction soon after foot contact, then back to the midline. The greatest amount of coronal motion was contributed in the midlumbar spine, with lesser amounts in the upper and lower lumbar spines. It contributed the least to transverse plane rotation, which was the chief function of the thoracic spine. The amount of motion in flexion-extension was in between these 2 values. It was greatest in the lower lumbar spine, L4 through S1. Mean intersegmental flexion and extension was about 2.5°. The flexion-extension motion of the thoracic and lumbar spine moved in a wavelike pattern.

Conclusions: The lumbar spine and thoracic spine motions interacted in a reciprocal motion, with flexion-extension occurring in a balanced fashion, coronal motion occurring in the lumbar spine, and transverse plane motion occurring in the thoracic spine. Each intervertebral segment contributes just a few degrees of motion, but this could not be accurately shown by surface markers.

Reviewer's Comments: Because orthopedic surgeons often need to limit trunk mobility by fusion, this study was of significant interest. I did not know the extent of transverse plane mobility provided in the thoracic spine and that the lumbar spine contributed more coronal than sagittal motion. Since coordinated spinal-to-pelvis mobility is important for efficient gait, we should study the gait disturbances after spinal fusion with this in mind. (Reviewer-Paul D. Sponseller, MS, MD, MBA).

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Keywords: Coronal, Transverse Planes, Lumbar Motion, Gait Analysis

Print Tag: Refer to original journal article
Surgical Reduction Lowers Pseudarthrosis Rate for Spondylolisthesis

Evidence-Based Surgical Management of Spondylolisthesis: Reduction or Arthrodesis in Situ.
Longo UG, Loppini M, et al:

Among patients undergoing surgery to treat spondylolisthesis, the postoperative rate of neurologic deficits is similar for those undergoing fusion with or without reduction of the slip.

**Background:** Surgery is indicated for spondylolisthesis when the slip is >50% or pain persists despite conservative therapy. This diagnosis has one of the higher rates of neurologic complications in spine surgery. Controversy continues about whether reduction of the slip is indicated to achieve a good result and whether it is associated with an increased rate of neurologic injury.

**Objective:** To compare the results of reduction versus fusion in situ for the treatment of spondylolisthesis.

**Methods:** The authors used PRISMA methodology to conduct a rigorous evidence-based review of the literature. They included all studies that directly compared patients treated with reduction for spondylolisthesis versus those treated without reduction.

**Results:** 8 studies were included. The oldest study was published in 1992. Five studies evaluated pediatric populations, and 3 evaluated adults. Of 266 patients included in this analysis, 165 underwent reduction and fusion, and 101 underwent fusion in situ. The mean postoperative follow-up was >3 years. All reduction patients had instrumentation compared to 21% of the other patients. A greater number of the reduction patients had a circumferential fusion, including transforaminal plus posterolateral grafts. The reduction patients had significant improvement in slip angle and slip displacement, as expected. The neurologic deficit rate was 7.8% in the reduction group and 8.9% in the group fused in situ (difference not significant). Pseudarthrosis was distinctly more common in the group fused in situ (18.8%) than in the reduction group (5.5%). This outcome undoubtedly related more to the instrumentation used to perform the reduction and stabilization than to the reduction itself. The rate of deep wound infections was 3% in each group.

**Conclusions:** The rate of neurologic deficits was the same in both groups, and pseudarthrosis was more likely in the in situ group. Although the authors' preferred technique involves reduction and fusion, they state that prospective randomized studies are indicated to settle this controversy.

**Reviewer's Comments:** This study illustrates the high complication rate associated with this procedure, possibly one of the highest in spine surgery. The degree of displacement and stresses on the bony and neurologic elements predisposes to complications. Patients should be counseled about the degree of risks, but they should also be reassured that the final outcomes are generally good. (Reviewer-Paul D. Sponseller, MS, MD, MBA).

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Keywords: Spondylolisthesis, Surgical Outcomes, Reduction vs No Reduction Before Arthrodesis

Print Tag: Refer to original journal article
Height Gain May Be Added Benefit of Surgical Correction of Scoliosis

Gain in Spinal Height From Surgical Correction of Idiopathic Scoliosis.
Spencer HT, Gold ME, et al:


Patients gain a mean of 1 inch of spinal height immediately after surgical correction of idiopathic scoliosis.

**Background:** Patients commonly ask about the anticipated gain in height after spinal fusion for scoliosis. Optimizing bodily proportions is one of the goals of surgery. Patients are also concerned about the effect of spinal fusion on further growth that might occur after surgery.

**Objective:** To predict the height gain associated with spinal correction and with further growth.

**Participants:** 116 patients (91 girls and 25 boys) who underwent posterior spinal fusion at Boston Children's Hospital for idiopathic scoliosis between 2003 and 2005.

**Methods:** All patients had ≥2 years’ follow-up to determine growth. Each patient had radiographs done within 90 days preoperatively and 45 days postoperatively to separate out the effect of surgery from that of further growth. The height of the spine was measured from T1 to L5 on both coronal and sagittal images. All Lenke curve types were included. Preoperatively, the mean major Cobb angle was 61°, and the curve was corrected 60% by the surgery with a mean of 10 levels fused.

**Results:** The mean gain in spinal height due to surgery was 27.1 mm (range, 24.2 to 30.1 mm). Factors associated with height gain included preoperative curve size, amount of correction, number of levels fused, and preoperative stature. Sagittal plane changes were not associated with height gain. There was also another 5-mm gain in height until skeletal maturity. Factors related to this gain included male gender, Risser stage of ≤2, and fewer levels fused surgically. SRS-30 scores improved for the cohort, but were not proportional to the amount of height gained.

**Conclusions:** The mean spinal height gain associated with idiopathic scoliosis correction is 1 inch, and a smaller additional height gain can be expected before maturity. At Risser stage 3, only about 2 cm of growth occurs in the normal spine, so the effect of surgery to limit growth is not significant.

**Reviewer's Comments:** This article answers a few common questions asked by patients and their parents when considering scoliosis correction: "How much taller will I get?" and "Will it limit my growth in the future?" Because most patients end up with surgical correction of idiopathic scoliosis at a Risser stage of 2 or 3, the answer is that they will likely gain an inch of height and will not lose more than an additional cm of potential height growth due to surgery (which they would not have obtained under normal circumstances due to worsening scoliosis). (Reviewer-Paul D. Sponseller, MS, MD, MBA).

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Keywords: Idiopathic Scoliosis, Correction of Scoliosis, Height Gain, Predictive Factors

Print Tag: Refer to original journal article
Predictors of estimated blood loss after posterior spinal fusion for adolescent idiopathic scoliosis include kyphosis, gender, and levels fused.

**Background:** Blood loss is an important issue in the surgical management of adolescent idiopathic scoliosis (AIS). Reduced blood loss can be associated with a reduced rate of infection as well as a shorter hospital stay.

**Objective:** To predict blood loss during AIS surgery using preoperatively known variables.

**Methods:** The authors reviewed the results of AIS treated surgically by a single surgeon during an 8-year study interval. They analyzed preoperative laboratory values, radiographic parameters, and surgical planning issues (such as anterior vs posterior and levels fused). Multivariate regression analysis was performed, and a predictive formula was developed.

**Results:** Of 340 patients reviewed, 124 were fused anteriorly and 188 were treated posteriorly. The mean blood loss was 1024 mL for the entire series, 323 mL for anterior fusion, and 987 mL for posterior fusion. Blood loss during a few circumferential fusions included in the series raised the overall group mean. Only 15% of patients had rib graft harvest. Important factors regarding blood loss during posterior fusion were number of levels fused, preoperative kyphosis, gender, and operative time. For anterior fusion, important variables regarding blood loss were operative time and mean arterial pressure (MAP) at incision. The authors developed a formula to predict estimated blood loss (EBL) for each approach.

**Conclusions:** The authors call attention to the variables that can guide surgical decision-making. This, in turn, may guide the use of Cell Saver® or antifibrinolytic drug use, and perhaps even the dosing of antifibrinolytic drugs. The authors now state that they only start a case when the MAP is between 65 and 75 mm Hg. They also stress that each surgeon may have different numbers, so that EBL may need to be calculated by each surgeon.

**Reviewer's Comments:** This interesting paper may have clinical relevance. It was interesting that INR and PT/PTT did not correlate with blood loss. This was an important way of looking at a set of variables. Since AIS surgery is typically done on high-functioning individuals, the standard for care should be very high. (Reviewer-Paul D. Sponseller, MS, MD, MBA).

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Keywords: Scoliosis, Blood Loss, Fusion

Print Tag: Refer to original journal article
Background: There is high morbidity associated with brachial plexus injuries, some of which can be difficult to diagnose clinically. The radiologist's awareness of brachial plexus anatomy and pathology becomes critical.

Objective: To review brachial plexus anatomy and common causes of brachial plexopathies. Discussion: The authors review the anatomy of the brachial plexus, giving a useful mnemonic for the roots, trunks, divisions, cords, and branches as "Radiology technicians drink cold beverages." Each root is subdivided into preganglionic and postganglionic with the anterior rami of the postganglionic roots continuing as the brachial plexus. The trunks are located between the anterior and middle scalene muscles, the divisions above the clavicle, the cords below the clavicle, and branches lateral to the lateral border of pectorals minor. The authors also review the proper MR protocol and search pattern. Axial T2-weighted sequences are best for evaluating the nerve rootlets, which should be contiguous, and the postganglionic roots, which should be low in signal intensity. The coronal sequences are best for evaluating the trunks through the branches as well as the clavicles, ribs, and muscles and nerves, which should be homogenous in signal intensity. The sagittal plane is best for evaluation of the cords and for evaluation of the perivascular and perineural fat, as subclavian artery aneurysms, for example, can exert mass effect. Next, the authors review etiologies for nontraumatic and traumatic plexopathy. Nontraumatic causes include masses, mainly nerve sheath tumors and lung tumors or cervical ribs, and inflammatory causes such as radiation or infection in which the plexus is thickened, hyperintense, and enhancing. Traumatic causes are divided by age, with children presenting with birth injuries and young men presenting with gunshot wounds, etc. In the latter, imaging detects causes such as nerve root avulsion and becomes critical, as many of these patients are nonverbal. The importance of the distinction of preganglionic and postganglionic is made as well. Preganglionic injuries require more complex repair with the sacrificing of a nerve and attachment to its root, while postganglionic injuries require repair only if fascicles are disrupted, in which case a nerve autograft, usually from the sural or phrenic, is used.

Conclusions: Knowledge of the anatomy and imaging characteristics of common pathologies can make assessment of the brachial plexus much easier.

Reviewer's Comments: I thought this was an excellent review article. The authors chose a topic that is important, but not well known or regularly addressed. They provided a mnemonic for the breakdown of the plexus as well as beautiful diagrams, and supplied a chart that very concisely and systematically depicted what to assess on each sequence. Finally, they discussed common pathologies, their appearances, and how management is affected by their diagnosis. (Reviewer-Uma Thakur, MD, MSK).
Is Staged Epilepsy Surgery Safe for Children?

Safety of Staged Epilepsy Surgery in Children.

Roth J, Carlson C, et al:

Neurosurgery 2014; 74 (February): 154-162

Repeat-staged epilepsy surgery with invasive monitoring is a safe procedure when it is necessary in children with medically refractory epilepsy.

**Background:** Accurate localization of seizure focus is the key to achieving successful surgical intervention of medically intractable seizures. Some neurosurgeons dislike staged procedures due to concerns about complications from multiple surgical interventions.

**Objective:** To review morbidity and mortality in staged procedures for medically intractable seizures in pediatric patients.

**Design:** Single-institution retrospective study.

**Methods:** Staged procedures with at least 2 operations were performed. At first stage, invasive electrodes, including subdural strips, grids, and depth electrodes, were placed unilaterally or bilaterally. The patients were monitored in the pediatric intensive care unit with video electroencephalography (VEEG) until enough information was recorded. Bedside functional mappings were performed on a case-by-case basis. If there was any sign of central nervous system infection, VEEGs were terminated. Second-stage surgery involved removal of invasive electrodes and epilepsy focus resection. Some patients had additional electrodes to confirm complete removal and/or identify additional foci. Third stage was performed using similar methods, except with no placement of additional invasive electrodes. Patients rarely underwent the fourth stage. At each stage, a Jackson-Pratt subgaleal drain was left. Perioperative antibiotics were used until the following stage surgery. Decadron® was given and tapered over 1 week. Screening epidural and subdural cultures were obtained in the following stage.

**Results:** 161 children underwent staged epilepsy surgery from 1996 to 2009. Mean patient age was 7.1 years (8.0 months to 16.5 years); 25 had single foci and 136 with multifocal epilepsy. In total, 200 admissions were recorded; average admissions per patient were 1.2 ± 0.5 (1.0 to 4.0 admissions). Of patients, 139 (69.5%) had unilateral, and 61 (30.5%) had bilateral monitoring. Of admissions, 20% were only monitoring without resection, and 80% included monitoring with resection. Overall, 496 surgeries were performed (250 resection and electrode placement, 189 electrode placement only, and 57 electrode removal only). Average duration of monitoring was 10 ± 4 (1 to 30) days. Length of hospital stay was 6 to 38 days (16 ± 5). Positive screening cultures with asymptomatic patients, noninfectious fevers, bone absorption, wound complication, and hydrocephalus represented 50% of all complications. Permanent neurological deficit, which included hemiparesis, was seen 4 cases. Thirty surgical interventions were required to treat complications, including shunt placement, cranioplasty, evacuation of subdural hemorrhage, cerebrospinal fluid leak repair, wound revision, drainage of abscess or fluid collection, and removal of the remaining strip electrode.

**Conclusions:** The complication rate was not affected by number of surgeries per admission. There were significantly lower complications in the last 100 admissions compared to the first 100 admissions.

**Reviewer's Comments:** Repeat invasive monitoring and their complications were reviewed in this study. This study demonstrated that complications were not statistically related to the number of repeated procedures. When epilepsy is not well controlled, repeat invasive monitoring should be considered as a management option. (Reviewer-Tomoko Tanaka, MD).

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Keywords: Complications, Epilepsy Surgery, Monitoring, Staged Procedures

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After CSF Diversion, Patients With Tectal Plate Gliomas Still Require Observation

Pediatric Tectal Plate Gliomas: Clinical and Radiological Progression, MR Imaging Characteristics, and Management of Hydrocephalus.

Griessenauer CJ, Rizk E, et al:

J Neurosurg Pediatr 2014; 13 (January): 13-20

Tectal plate gliomas seldom need any intervention except for cerebrospinal fluid diversion.

**Background:** Incidence of tectal plate glioma account for 10% to 20% of pediatric central nervous system tumors. Most often, the pathology is low-grade astrocytoma and prognosis is favorable. Observation of tumor, cerebrospinal fluid (CSF) diversion, including endoscopic third ventriculostomy (ETV) and ventriculoperitoneal (VP) shunts, and biopsy have been favored treatment options. Adjuvant therapies are indicated for progressive disease.

**Objective:** To review progression of tectal plate gliomas and management.

**Design:** 2-institution retrospective study.

**Methods:** Medical records and imaging studies were reviewed. Tumor volume was measured at the time of diagnosis and follow-up. Tumor volume was defined as the largest dimensions in all 3 dimensions divided by 2. Hydrocephalus was determined by frontal and occipital horn ratio (FOHR) and width of the third ventricle.

**Results:** 44 patients (27 boys, 17 girls) with tectal plate glioma were identified between 1995 and 2012. Average age at diagnosis was 10.2 ± 4.3 years (2.0 to 19.0 years). Headache was the most common presenting symptom in 22 patients (50%). Eleven patients (25%) were diagnosed incidentally. Visual complaints, balance problems, nausea, vomiting, and cognitive changes were less common presenting symptoms. Only 4 patients (9.1%) underwent biopsy. Two patients had pilocytic astrocytoma and 2 others were inconclusive. One patient with pilocytic astrocytoma had neurofibromatosis type 1 and received chemotherapy in another institution. The other pilocytic patient underwent endoscopic biopsy of a large cystic lesion and received Gamma Knife surgery, which was complicated with remote mesencephalic hemorrhage and subsequent neurological deficit. One patient with pilocytic astrocytoma underwent resection and radiotherapy after developing enlargement of the residual tumor. One patient with neurofibromatosis received chemotherapy without biopsy and another had radiation and chemotherapy without biopsy. Most patients' MRIs showed T1 iso- and T2 hyperintensity. However, about 30% of patients had T1 hyper- or hypointensity. Only 20% demonstrated enhancement; otherwise, lesions were nonenhanced or cystic. Mean tumor volume was 1.6 ± 2.2 cm³ at presentation and 2.0 ± 4.4 cm³ at follow-up. Patients who had resection without follow-up imaging were excluded. Significant tumor growth was seen in patients without neurofibromatosis compared to patients with neurofibromatosis. In total, 36 patients underwent CSF diversion (18 ETV, 16 shunt). Two patients who underwent both ETV and shunt were excluded. FOHR was decreased in all patients with ETV, but 11 of 15 patients who had VP shunt placement had unchanged FOHR on follow-up MRI. Patients with higher FOHR had headache (P<0.01).

**Conclusions:** The results of this study support the notion that tectal plate gliomas rarely require any intervention except CSF diversion.

**Reviewer's Comments:** Tectal plate gliomas are known to have favorable outcomes. The results demonstrated supportive data, which included MRI findings, CSF diversion, and tumor volume. However, the study shows that some tectal plate gliomas still progress. Therefore, after CSF diversion, patients still require observation. (Reviewer-Tomoko Tanaka, MD).

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Keywords: Gliomas, Lesion, Brain Tumor, Tectal Plate, Pediatric, Hydrocephalus, MRI, Oncology

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