

Henry Ford Health System Publication List February 2006

This is a bibliography of journal articles published by Henry Ford Health System personnel. A search was compiled in [PubMed](#) during the month of February 2006, and then imported into [EndNote](#) for formatting.

We will be compiling this bibliography on a monthly basis. Please [contact us](#) if you would like to receive this publication list via email. If the full-text of the article is not available, you can request it from the Sladen Library by clicking on the [Article Request Form](#) or calling us at (313) 916-2550.

Barton, K. N., D. Paielli, et al. (2006). "Second-generation replication-competent oncolytic adenovirus armed with improved suicide genes and ADP gene demonstrates greater efficacy without increased toxicity." *Mol Ther* **13**(2): 347-56. **Full-Text Not Available / [Click for Article Request Form](#)**

Replication-competent adenovirus-mediated suicide gene therapy has proven to be safe in humans when delivered intraprostatically. Although signs of efficacy are emerging, it is likely that further improvements will be needed before this technology will have widespread applicability in the clinic. Toward this end, we have developed a second-generation, replication-competent adenovirus (Ad5-yCD/mutTK(SR39)rep-ADP) containing an improved yeast cytosine deaminase (yCD)/mutant(SR39) herpes simplex virus thymidine kinase fusion (yCD/mutTK(SR39)) gene and the adenovirus death protein (ADP) gene. Relative to the first-generation Ad5-CD/TKrep adenovirus, Ad5-yCD/mutTK(SR39)rep-ADP demonstrated greater tumor cell kill in vitro and significantly greater tumor control in preclinical models of human cancer. Quantification of transgene volume following direct injection of fadenovirus into human tumor xenografts and the naive canine prostate demonstrated that ADP enhanced adenoviral spread in vivo. Toxicology studies were performed to determine whether the improved yCD/mutTK(SR39) fusion and ADP genes increased toxicity. Intraprostatic injection of Ad5-yCD/mutTK(SR39)rep-ADP did not result in significantly increased toxicity relative to the parental Ad5-CD/TKrep adenovirus, the latter of which has proven to be safe in two Phase I prostate cancer clinical trials. Together, these results provide the scientific basis for evaluating the safety and efficacy of the second-generation Ad5-yCD/mutTK(SR39)rep-ADP adenovirus in humans.

Cerghet, M., R. P. Skoff, et al. (2006). "Proliferation and death of oligodendrocytes and myelin proteins are differentially regulated in male and female rodents." *J Neurosci* **26**(5): 1439-47. **[PDF Full-Text](#)**

Sexual dimorphism of neurons and astrocytes has been demonstrated in different centers of the brain, but sexual dimorphism of oligodendrocytes and myelin has not been examined. We show, using immunocytochemistry and in situ hybridization, that the density of oligodendrocytes in corpus callosum, fornix, and spinal cord is 20-40% greater in males compared with females. These differences are present in young and aged rodents and are independent of strain and species. Proteolipid protein and carbonic anhydrase-II transcripts, measured by real-time PCR, are approximately two to three times greater in males. Myelin basic protein and 2', 3'-cyclic nucleotide 3'-phosphodiesterase, measured by Western blots, are 20-160% greater in males compared with females. Surprisingly, both generation of new glia and apoptosis of glia, including oligodendrocytes, are approximately two times greater in female corpus callosum. These results indicate that the lifespan of oligodendrocytes is shorter in females than in males. Castration of males produces a female phenotype characterized by fewer oligodendrocytes and increased generation of new glia. These findings indicate that exogenous androgens differentially affect the lifespan of male and female oligodendrocytes, and they can override the endogenous production of neurosteroids. The data imply that turnover of myelin is greater in females than in males. Mu-calpain, a protease upregulated in degeneration of

myelin, is dramatically increased at both transcriptional and translational levels in females compared with males. These morphological, molecular, and biochemical data show surprisingly large differences in turnover of oligodendrocytes and myelin between sexes. We discuss the potential significance of these differences to multiple sclerosis, a sexually dimorphic disease, whose progression is altered by exogenous hormones.

Fumo, M. J., C. J. Becker, et al. (2006). "Segmental renal artery dysplasia presenting as hypertension in a child." *Urology* **67**(2): 421-2. [PDF Full-Text](#)

Jin, J. Y., M. Ajlouni, et al. (2006). "A technique of using gated-CT images to determine internal target volume (ITV) for fractionated stereotactic lung radiotherapy." *Radiother Oncol* **78**(2): 177-84. [PDF Full-Text](#)

BACKGROUND AND PURPOSE: To develop and evaluate a technique and procedure of using gated-CT images in combination with PET image to determine the internal target volume (ITV), which could reduce the planning target volume (PTV) with adequate target coverage. **PATIENTS AND METHODS:** A skin marker-based gating system connected to a regular single slice CT scanner was used for this study. A motion phantom with adjustable motion amplitude was used to evaluate the CT gating system. Specifically, objects of various sizes/shapes, considered as virtual tumors, were placed on the phantom to evaluate the number of phases of gated images required to determine the ITV while taking into account tumor size, shape and motion. A procedure of using gated-CT and PET images to define ITV for patients was developed and was tested in patients enrolled in an IRB approved protocol. **RESULTS:** The CT gating system was capable of removing motion artifacts for target motion as large as 3-cm when it was gated at optimal phases. A phantom study showed that two gated-CT scans at the end of expiration and the end of inspiration would be sufficient to determine the ITV for tumor motion less than 1-cm, and another mid-phase scan would be required for tumors with 2-cm motion, especially for small tumors. For patients, the ITV encompassing visible tumors in all sets of gated-CT and regular spiral CT images seemed to be consistent with the target volume determined from PET images. PTV expanded from the ITV with a setup uncertainty margin had less volume than PTVs from spiral CT images with a 10-mm generalized margin or an individualized margin determined at fluoroscopy. **CONCLUSIONS:** A technique of determining the ITV using gated-CT images was developed and was clinically implemented successfully for fractionated stereotactic lung radiotherapy.

Joseph, C. L., L. K. Williams, et al. (2006). "Applying epidemiologic concepts of primary, secondary, and tertiary prevention to the elimination of racial disparities in asthma." *J Allergy Clin Immunol* **117**(2): 233-40; quiz 241-2. [PDF Full-Text](#)

Despite medical and scientific advances, racial and ethnic disparities persist in US asthma morbidity and mortality rates. Progress in the elimination of these disparities will involve disentangling the contribution of social constructs, such as race, socioeconomic status, and culture, from that of the physical environment and genetic susceptibility. One approach to reducing asthma disparities is through the traditional disease prevention stages of intervention. As such, primary prevention targets reductions in asthma incidence; secondary prevention is the mitigation of established disease and involves disease detection, management, and control; and tertiary prevention is the reduction of complications caused by severe disease. Once causative factors at each level of disease prevention are understood, this knowledge can be translated into clinical practice and public health policy.

Kim, D. G., X. N. Dong, et al. (2006). "Evaluation of filler materials used for uniform load distribution at boundaries during structural biomechanical testing of whole vertebrae." *J Biomech Eng* **128**(1): 161-5. [PDF Full-Text](#)

This study was designed to compare the compressive mechanical properties of filler materials, Wood's metal, dental stone, and polymethylmethacrylate (PMMA), which are widely used for performing structural testing of whole vertebrae. The effect of strain rate and specimen size on the mechanical properties of the filler materials was examined using standardized specimens and mechanical testing. Because Wood's metal can be reused after remelting, the effect of remelting on the mechanical properties was tested by comparing them before and after remelting. Finite element (FE) models were built to simulate the effect of filler material size and properties on the stiffness of vertebral body construct in compression. Modulus, yield strain, and yield strength were not different between batches (melt-remelt) of Wood's metal. Strain rate had no effect on the modulus of Wood's metal, however, Young's modulus decreased with increasing strain rate in dental stone whereas increased in PMMA. Both Wood's

metal and dental stone were significantly stiffer than PMMA (12.7 +/- 1.8 GPa, 10.4 +/- 3.4 GPa, and 2.9 +/- 0.4 GPa, respectively). PMMA had greater yield strength than Wood's metal (62.9 +/- 8.7 MPa and 26.2 +/- 2.6 MPa). All materials exhibited size-dependent modulus values. The FE results indicated that filler materials, if not accounted for, could cause more than 9% variation in vertebral body stiffness. We conclude that Wood's metal is a superior moldable bonding material for biomechanical testing of whole bones, especially whole vertebrae, compared to the other candidate materials.

Kugelmass, A. D., D. J. Cohen, et al. (2006). "Hospital resources consumed in treating complications associated with percutaneous coronary interventions." *Am J Cardiol* **97**(3): 322-7. [PDF Full-Text](#)

Nearly 9.5% of all Medicare beneficiaries who undergo a percutaneous coronary intervention (PCI) procedure develop > or =1 of 7 acute complications. This study used 2 approaches (regression analysis and propensity-matched samples) to estimate the cost of selected complications, based on administrative data from 335,477 Medicare beneficiaries who underwent PCI during a hospitalization in fiscal year 2002. Selected complications included hospital mortality, emergency/urgent coronary artery bypass surgery, postoperative stroke, acute renal failure, vascular complications, septicemia, and adult respiratory distress syndrome. The observed average cost of a PCI hospitalization for patients who did not develop complications was 13,861 dollars +/- 9,635 dollars, with an average length of stay of 3.0 +/- 3.2 days, compared with 26,807 dollars +/- 27,596 dollars and 8.0 +/- 8.9 days for patients who did develop complications. Estimates of the adjusted incremental hospital cost of treating any acute complication except death varied from a high of 33,030 dollars for patients who developed septicemia to a low of 4,278 dollars for those who developed vascular complications, whereas estimates of the incremental length of stay ranged from a high of 12.3 days for patients who had septicemia to a low of 1.8 days for patients who had vascular complications. In conclusion, we found that the incremental hospital resources that are consumed to treat patients with acute PCI complications are large compared with the cost of an uncomplicated PCI hospitalization.

Kummer, J. L., R. Nair, et al. (2006). "Images in cardiovascular medicine. Bidirectional ventricular tachycardia caused by digitalis toxicity." *Circulation* **113**(7): e156-7. [PDF Full-Text](#)

Li, S., D. Liu, et al. (2006). "Real-time 3D-surface-guided head refixation useful for fractionated stereotactic radiotherapy." *Med Phys* **33**(2): 492-503. **Full-Text Not Available / [Click for Article Request Form](#)**

Accurate and precise head refixation in fractionated stereotactic radiotherapy has been achieved through alignment of real-time 3D-surface images with a reference surface image. The reference surface image is either a 3D optical surface image taken at simulation with the desired treatment position, or a CT/MRI-surface rendering in the treatment plan with corrections for patient motion during CT/MRI scans and partial volume effects. The real-time 3D surface images are rapidly captured by using a 3D video camera mounted on the ceiling of the treatment vault. Any facial expression such as mouth opening that affects surface shape and location can be avoided using a new facial monitoring technique. The image artifacts on the real-time surface can generally be removed by setting a threshold of jumps at the neighboring points while preserving detailed features of the surface of interest. Such a real-time surface image, registered in the treatment machine coordinate system, provides a reliable representation of the patient head position during the treatment. A fast automatic alignment between the real-time surface and the reference surface using a modified iterative-closest-point method leads to an efficient and robust surface-guided target refixation. Experimental and clinical results demonstrate the excellent efficacy of <2 min set-up time, the desired accuracy and precision of <1 mm in isocenter shifts, and <1 degree in rotation.

Li, X. C., O. A. Carretero, et al. (2006). "AT1 Receptor-Mediated Accumulation of Extracellular Angiotensin II in Proximal Tubule Cells: Role of Cytoskeleton Microtubules and Tyrosine Phosphatases." *Am J Physiol Renal Physiol*. [PDF Full-Text](#)

Long-term angiotensin II (Ang II) administration is associated with increased Ang II accumulation in the kidney, but intrarenal compartment(s) involved in this response remains to be determined. We tested the hypothesis that a) extracellular Ang II is taken up by proximal tubule cells (PTCs) through AT1 receptor-mediated endocytosis, b) this process is regulated by cytoskeleton microtubule- and tyrosine phosphatase-dependent mechanisms, and c)

AT1 receptor-mediated endocytosis of Ang II has a functional relevance by modulating intracellular cAMP signaling. In cultured PTCs, $[(125)\text{I}]\text{-Tyr-Ang II}$ and fluorescein labeled-Ang II were internalized in a time-dependent manner and colocalized with the endosome marker Alexa Fluor 594-transferrin. Endocytosis of extracellular Ang II was inhibited by the AT1 receptor blocker losartan (16.5 +/- 4.6%, $p < 0.01$ vs. Ang II: 78.3 +/- 6.2%) and by the tyrosine phosphatase inhibitor phenylarsine oxide (PAO) (30.0 +/- 3.5%, $p < 0.05$ vs. Ang II). Intracellular Ang II levels were increased by ~ 58% (basal: 229.8 +/- 11.4 vs. Ang II: 361.3 +/- 11.8 pg Ang II/mg protein, $p < 0.01$), and the responses were blocked by losartan ($p < 0.01$), the cytoskeleton microtubule inhibitor colchicine ($p < 0.05$), and PAO ($p < 0.01$), whereas depletion of clathrin-coated pits with hyperosmotic sucrose had no effect (356.1 +/- 25.5 pg Ang II/mg protein, n.s.). Ang II accumulation was associated with significant inhibition of both basal (control: 15.5 +/- 2.8 vs. Ang II: 9.1 +/- 2.4 pmol/mg protein, $p < 0.05$) and forskolin-stimulated cAMP signaling (forskolin: 68.7 +/- 8.6 vs. forskolin+Ang II: 42.8 +/- 13.8 pmol/mg protein, $p < 0.01$). These effects were blocked by losartan and PAO. We conclude that extracellular Ang II is internalized in PTCs through AT1 receptor-mediated endocytosis and that internalized Ang II may play a functional role in proximal tubule cells by inhibiting intracellular cAMP signaling.

Mahmood, A., D. Lu, et al. (2006). "Long-term recovery after bone marrow stromal cell treatment of traumatic brain injury in rats." *J Neurosurg* **104**(2): 272-7. [PDF Full-Text \(ID=sladen / Password = library1\)](#)

OBJECT: This study was designed to follow the effects of bone marrow stromal cell (BMSC) administration in rats after traumatic brain injury (TBI) for a 3-month period. METHODS: Forty adult female Wistar rats were injured by a controlled cortical impact and, 1 week later, were injected intravenously with one of three different doses of BMSCs (2 x 10(6), 4 x 10(6), or 8 x 10(6) cells per animal) obtained in male rats. Control rats received phosphate-buffered saline (PBS). Neurological function in these rats was studied using a neurological severity scale (NSS). The rats were killed 3 months after injury, and immunohistochemical stains were applied to brain samples to study the distribution of the BMSCs. Additional brain samples were analyzed by quantitative enzyme-linked immunosorbent assays to measure the expression of the growth factors brain-derived neurotrophic factor (BDNF) and nerve growth factor (NGF). Three months after injury, BMSCs were present in the injured brain and their number was significantly greater in animals that received 4 x 10(6) or 8 x 10(6) BMSCs than in animals that received 2 x 10(6) BMSCs. The cells were primarily distributed around the lesion boundary zone. Functional outcome was significantly better in rats that received 4 x 10(6) or 8 x 10(6) BMSCs, compared with control animals, although no improvement was seen in animals that received 2 x 10(6) BMSCs. All doses of BMSCs significantly increased the expression of BDNF but not that of NGF; however, this increase was significantly larger in animals that received 4 x 10(6) or 8 x 10(6) BMSCs than in controls or animals that received 2 x 10(6) BMSCs. CONCLUSIONS: In summary, when injected in rats after TBI, BMSCs are present in the brain 3 months later and significantly improve functional outcome.

Mitsias, P. D., N. M. Ramadan, et al. (2006). "Factors determining headache at onset of acute ischemic stroke." *Cephalalgia* **26**(2): 150-7. [PDF Full-Text](#)

Headache is a frequent accompaniment of acute ischaemic stroke. The predisposing factors and underlying mechanisms are currently incompletely defined. We analysed prospectively collected data relevant to headache occurring at ischaemic stroke onset in consecutive patients included in the Henry Ford Hospital Stroke Data Bank. Patients with headache (HA+) and without headache (HA-) were compared for demographic factors, medical history, medications, examination findings, laboratory findings, and stroke localization and subtype. Group comparisons for categorical data were performed with chi(2) test, and for continuous variables with two-sample t-tests. Stepwise logistic regression analysis, including all variables with $P < 0.25$, was used to define the independent predictors of onset headache. Three hundred and seventy-five patients had complete headache and clinical datasets and were included in the analysis (HA+, N=118; HA-, N=257). Multivariate analysis revealed that the independent predictors of HA+ were: infarct in the distribution of the posterior circulation [$P=0.0076$, odds ratio (OR) 2.15, 95% confidence interval (CI) 1.23, 3.77], absence of history of hypertension ($P=0.0106$, OR 0.48, 95% CI 0.27, 0.84), and treatment with warfarin at the time of the index stroke ($P=0.0135$, OR 4.89, 95% CI 1.39, 17.21). The occurrence of headache at onset of ischaemic stroke is determined by posterior circulation distribution of the ischaemic event, absence of history of hypertension and treatment with warfarin at the time of the index stroke. These results suggest that preserved elasticity and maintenance of the intracranial vasculature in a relaxed state, in

combination with coagulation system derangements, and activation of dense perivascular afferent nerves, play a role in the pathogenesis of onset headache.

Nathanson, S. D., R. Slater, et al. (2006). "Her-2/neu expression in primary breast cancer with sentinel lymph node metastasis." *Ann Surg Oncol* **13**(2): 205-13. **Full-Text Not Available** / [Click for Article Request Form](#)

BACKGROUND: Amplification of the protein product of the HER-2/neu oncogene in primary breast cancer specimens is associated with an adverse prognosis. We hypothesized that overexpression of HER-2/neu would predict metastases to the sentinel lymph nodes (SLNs). **METHODS:** A retrospective review of a prospective nonrandomized evaluation of 1055 clinically node-negative breast cancer patients undergoing 1063 SLN biopsies was performed. HER-2/neu analysis was performed by immunohistochemistry and, in selected cases, by fluorescence in situ hybridization. Clinical, demographic, surgical, radiological, and pathologic data were analyzed by using generalized estimating equations logistic regression models. **RESULTS:** Two hundred thirty-two (23.6%) of 985 operations in which the SLN was found at operation resulted in positive nodes. In a multivariate analysis, size ($P < .0001$) and HER-2/neu overexpression ($P = .026$) were independent predictors of SLN metastasis. **CONCLUSIONS:** Size is a known predictor of SLN metastasis in the modern SLN era, as it was in the pre-SLN eras. HER-2/neu was found to be significantly predictive of SLN metastasis in our study. We anticipate a future when even the relatively minor procedure of SLN biopsy might be avoided with the predictive information gained from studying the pathology and molecular markers of primary breast cancers.

Roehrs, T., M. Hyde, et al. (2006). "Sleep loss and REM sleep loss are hyperalgesic." *Sleep* **29**(2): 145-51. [PDF Full-Text](#)

STUDY OBJECTIVES: Disturbed sleep is observed in association with acute and chronic pain, and some data suggest that disturbed and shortened sleep enhances pain. We report the first data showing, in healthy, pain-free, individuals, that modest reductions of sleep time and specific loss of rapid eye movement (REM) sleep produces hyperalgesia the following morning. **DESIGN:** Two repeated-measures design protocols were conducted: (1) a sleep-loss protocol with 8 hours time-in-bed, 4 hours time-in-bed, and 0 hours time-in-bed conditions and (2) a REM sleep-loss protocol with 8 hours time-in-bed, 2 hours time-in-bed, REM deprivation, and non-REM yoked-control conditions. **SETTING:** The studies were conducted in an academic hospital sleep laboratory. **PARTICIPANTS:** Healthy pain-free normal sleepers, 7 in the sleep-loss protocol and 6 in the REM sleep-loss protocol, participated. **MEASUREMENTS:** Finger-withdrawal latency to a radiant heat stimulus tested at 10:30 AM and 2:30 PM and the Multiple Sleep Latency Test conducted at 10:00 AM, noon, 2:00 PM, and 4:00 PM were measured. **RESULTS:** Finger-withdrawal latency was shortened by 25% after 4 hours of time in bed the previous night relative to 8 hours of time in bed ($p < .05$), and REM sleep deprivation relative to a non-REM yoked-control sleep-interruption condition shortened finger-withdrawal latency by 32% ($p < .02$). **CONCLUSION:** These studies showed that the loss of 4 hours of sleep and specific REM sleep loss are hyperalgesic the following day. These findings imply that pharmacologic treatments and clinical conditions that reduce sleep and REM sleep time may increase pain.

Rubowitz, A. and U. Desai (2006). "Nontraumatic macular holes associated with Terson syndrome." *Retina* **26**(2): 230-2. [PDF Full-Text](#)

Santra, M., M. Katakowski, et al. (2006). "Protection of adult mouse progenitor cells and human glioma cells by de novo decorin expression in an oxygen- and glucose-deprived cell culture model system." *J Cereb Blood Flow Metab.* **Full-Text Not Available** / [Click for Article Request Form](#)

We employed an in vitro hypoxia cell culture model system and gene transfer technology to examine the effect of the decorin gene on cell survival against oxygen and glucose deprivation (OGD). Ectopic expression of decorin in subventricular zone (SVZ) cells from adult male mouse brain and human glioblastoma U-87 cells kept the cells viable against 24 h of OGD. Fewer than 1% of decorin-synthesizing cells were apoptotic after 12 h of OGD. In contrast, 100% of the control cells were apoptotic even after 4 h of OGD. De novo decorin synthesis in SVZ and U-87 cells induced expression of p21, p27 and Ras, AKT (acutely transforming retrovirus AKT8 in rodent T-cell lymphoma), and phosphorylated AKT. Blocking of phosphoinositide 3-kinase (PI-3K), Ras, and the epidermal

growth factor receptor with specific inhibitors had no effect on induction of Ras, p21, and p27 at the messenger RNA level in decorin-synthesizing SVZ and U-87 cells. PI-3K inhibitors significantly increased apoptosis in decorin-expressing cells. Our data indicate that induction of p21, p27, Ras, AKT, and phosphorylated AKT by decorin inhibits apoptosis and protects U-87 and SVZ cells against OGD. Therefore, our data suggest that decorin is a potent trophic factor that protects neuronal progenitor cells and glioma cells from OGD.

Seyfried, D., J. Ding, et al. (2006). "Effects of intravenous administration of human bone marrow stromal cells after intracerebral hemorrhage in rats." *J Neurosurg* **104**(2): 313-8. [PDF Full-Text \(ID=sladen / Password = library1\)](#)

OBJECT: The goal of this study was to investigate whether human bone marrow stromal cells (hBMSCs) administered by intravenous injection have a beneficial effect on outcome after intracerebral hemorrhage (ICH) in rats. **METHODS:** An ICH was induced in 54 adult male Wistar rats by a stereotactically guided injection of autologous blood into the right striatum. Intravenous infusion of the hBMSCs (3, 5, or 8 million cells) was performed 1 day after ICH, and for each dose group there was a control group that received injections of vehicle. Neurological function, which was evaluated using the Neurological Severity Score (NSS) and the corner turn test, was tested before and at 1, 7, and 14 days after ICH. After 14 days of survival, the area of encephalomalacia was calculated and histochemical labeling was performed. For all three groups, there were no statistical differences in either the NSS or corner turn tests after 1 day. After 7 and 14 days, however, the three groups that received the hBMSCs showed significant improvement in functional scores compared with the control group. In addition, after 14 days there was significantly more striatal tissue loss in the placebo groups compared with each of the three treatment groups. The region of injury in the treated animals demonstrated a significantly increased presence of hBMSCs, immature neurons, neuronal migration, synaptogenesis, and newly formed DNA. **CONCLUSIONS:** Intravenous administration of hBMSCs significantly improves neurological function in rats subjected to ICH. This improvement in the treated animals is associated with reduced tissue loss and increased local presence of the hBMSCs, mitotic activity, immature neurons, synaptogenesis, and neuronal migration.

Tessler, D. A., A. Catanzaro, et al. (2006). "Predictors of cancer in patients with suspected pancreatic malignancy without a tissue diagnosis." *Am J Surg* **191**(2): 191-7. [PDF Full-Text](#)

BACKGROUND: The aim of this study was to identify predictive factors for malignancy in patients undergoing surgery for suspected pancreatic cancer without a preoperative tissue diagnosis. **METHODS:** Patients were identified by International Classification of Diseases Ninth Revision and current procedural terminology codes, respectively, for pancreatic cancer and pancreaticoduodenectomy at a single tertiary referral center between January 1998 and May 2004. Data were collected retrospectively by chart review. Multivariate analysis of potential predictive factors was performed. **RESULTS:** A total of 150 patients underwent surgery for documented or suspected pancreatic malignancy; 102 did not have a preoperative tissue diagnosis of cancer. Of these, 75 had neoplastic disease at surgery. Average weight loss was greater for those with malignancy (13.5 vs. 4.8 lbs; $P = .014$) as was mean bilirubin (6.1 vs. 3.3 mg/dL; $P = .006$). In multivariate analysis, a combination of weight loss >20 lbs, bilirubin >3 mg/dL, and CA 19-9 >37 U/mL had both a specificity and positive predictive value of 100% for predicting malignancy regardless of bile duct abnormalities or mass lesions on endoscopic retrograde cholangiopancreatography or endoscopic ultrasound, respectively. The positive predictive value decreased to 89.5% when any 2 of these findings were present. The presence of a mass on CT or EUS alone had a sensitivity of 84%; however, no other single finding had a sensitivity >65%. **CONCLUSIONS:** In patients suspected of having a pancreatic malignancy, weight loss, hyperbilirubinemia, and increased CA 19-9 level may be predictive of a final cancer diagnosis. Surgical exploration should be considered in these patients even in the absence of a preoperative tissue diagnosis.

Velanovich, V. and N. Mohlberg (2006). "The split-stomach fundoplication after esophagogastrectomy." *J Gastrointest Surg* **10**(2): 178-85. **Full-Text Not Available / [Click for Article Request Form](#)**

Two complications associated with esophagogastrectomy are anastomotic leak and gastroesophageal reflux. We describe here a modification of an intrathoracic esophagogastrostomy using the gastric fundus to address these issues. After completion of the esophagogastrectomy, the fundus is divided to produce "wings." After the esophagogastrostomy is performed, the wings are used to form a wrap around the anastomosis. This wrap is secured to the esophagus and to the stomach. All patients undergoing the split-stomach fundoplication were compared with

all patients undergoing standard esophagogastrectomies. End points were in-hospital mortality, anastomotic leak, and postoperative endoscopic dilation. All living patients were contacted and questioned about refluxlike symptoms and completed the Gastroesophageal Reflux Disease-Health Related Quality of Life (GERD-HRQL) symptom severity questionnaire. Twenty-six patients underwent the split-stomach fundoplication (wrap group), compared to 54 patients undergoing standard resection (no wrap group). Occurrence of end points in the wrap vs. no wrap groups were, respectively, in-hospital mortality, 3.8% vs. 7.4% ($P = \text{NS}$); anastomotic leak, 0% vs. 17% ($P = 0.03$); reflux symptoms 20% vs. 60% ($P < 0.001$); postoperative dilation, 40% vs. 30% ($P = \text{NS}$). The median total GERD-HRQL score was 5 for the wrap group vs. 14 for the no wrap group ($P = 0.03$). The addition of the split-stomach fundoplication to esophagogastrectomy may decrease the incidence of anastomotic leak and postoperative refluxlike symptoms.

Velanovich, V., P. Shadduck, et al. (2006). "Analysis of the SAGES Outcomes Initiative groin hernia database." *Surg Endosc* **20**(2): 191-8. **Full-Text Not Available** / [Click for Article Request Form](#)

BACKGROUND: In 1999, the Society of American Gastrointestinal Endoscopic Surgeons (SAGES) introduced the SAGES Outcomes Initiative as a way for its members to track their own outcomes. It contains perioperative and postoperative data on nearly 20,000 operations. This report provides a descriptive analysis of the groin hernia database. **METHODS:** The SAGES Outcomes Initiative database was accessed for all groin hernia cases from September 1999 to February 2005. The data from the preoperative, intraoperative, and postoperative entries were summarized. These data are purely descriptive and no statistical analysis was done. **RESULTS:** The hernia registry contains 1,607 entries, with 1,070 follow-up entries. Males comprised 85% of patients, 63% were employed, 62% had at least one comorbidity, with 84% ASA class I or II. Primary, unilateral hernia accounted for 86% of cases, whereas 14% were recurrent, 11% bilateral, 6% incarcerated, and 3% required emergency repair. The operating surgeon was the attending surgeon in 83% of cases. Anesthetic techniques were general anesthesia in 74% of cases, regional in 7%, and local in 34%, with only 16% of cases local only. Most patients had symptomatic hernias and symptoms were improved in more than 95% of patients. Most repairs were open, although 45% were endoscopic. The most frequently cited postoperative event was significant bruising (6%), with more than 99% of complications being class I or II. More than 95% of patients were able to return to work by the first postoperative visit. Patients who underwent endoscopic repair were reported to have fewer days of narcotic use than patients undergoing open repairs (0 vs 3). **CONCLUSIONS:** First analysis of the SAGES Outcomes Initiative groin hernia database demonstrates that (a) this is one of the largest prospective; voluntary hernia registries; (b) missing data are infrequent; and (c) the data are similar to published data from national, mandatory registries and randomized trials. Although the SAGES Outcomes Initiative is a voluntary registry, initially designed for surgeon self-assessment, and it therefore has the potential for methodological concerns inherent to voluntary registries, the findings from this first analysis are encouraging. Efforts are ongoing to simplify data entry (PDA), refine data parameters, increase surgeon participation, and determine the role of data audit and thereby the potential for clinical research.

Yeni, Y. N., D. G. Kim, et al. (2006). "Do sacrificial bonds affect the viscoelastic and fracture properties of bone?" *Clin Orthop Relat Res* **443**: 101-8. [PDF Full-Text](#)

Sacrificial bonds have been suggested as a toughening mechanism for bone tissue. Ionic bridges formed by divalent calcium ions between collagen molecules have been proposed as candidates for sacrificial bonds. If this mechanism is active at the macroscopic level, we should observe changes in mechanical properties of bone when calcium ions are maintained or removed from the tissue. To test this hypothesis, we measured viscoelastic and monotonic mechanical properties of cortical bone subjected to differing ionic environments. Storage modulus of bone could be changed up to 3.8% by the presence or absence of Na^+ or Ca^{++} in the environment in a reversible fashion when bones were monitored continuously during treatments. A long-term one-time treatment increased the viscoelastic properties of bone soaked in Na^+ solutions whereas the viscoelastic properties of bones soaked in Ca^{++} solutions were maintained. However, the strength and toughness of bone specimens soaked and fractured in treatment solutions were not improved. The presence of Ca^{++} affected the mechanical behavior of mineralized bone tissue at the macro scale. These effects were reversible, consistent with the original proposal. However, these effects may not necessarily indicate an increase in strength or toughness of the tissue at the macro scale.

Yood, M. U., C. P. Quesenberry, Jr., et al. (2006). "An observational study examining the impact of capecitabine on warfarin antithrombotic activity and bleeding complications." *Curr Med Res Opin* 22(2): 307-14. **Full-Text Not Available / [Click for Article Request Form](#)**

OBJECTIVE: The objectives of this study are to quantify the frequency of concomitant use of capecitabine and warfarin, and to quantify the rate of bleeding events and elevated international normalized ratio (INR) among concomitant users of warfarin and capecitabine. **RESEARCH DESIGN AND METHODS:** We conducted a retrospective population-based study within the Henry Ford Health System (Detroit, MI) and the Kaiser Permanente Medical Care Program of Northern California (Oakland, CA). The study population included patients prescribed concomitant capecitabine and warfarin from 1 April 1997 through 31 July 2002. Data from the medical records of concurrent users were extracted through 31 August 2002. **MAIN OUTCOME MEASURES:** Concomitant use of capecitabine and warfarin, bleeding events, and INR laboratory results, collected from computerized databases and medical record review. **RESULTS:** Overall, 11% of capecitabine users also received warfarin (99 / 883). Among 17 patients who received warfarin for venous access device prophylaxis, one bleeding event occurred during concomitant capecitabine/warfarin use (rate = 35.7 bleeding events per 100 person-years, 95% confidence interval [CI] 0.9-198.9), and no events occurred during use of warfarin alone (95% CI 0.0-136.2) ($p = 0.50$). Among patients prescribed warfarin for indications other than port prophylaxis, no bleeding events occurred during concomitant use of capecitabine and warfarin (95% CI 0.0-34.6), and one event occurred during warfarin use alone (rate = 9.2 bleeding events per 100 person-years, 95% CI 0.2-51.3) ($p = 0.54$). We found one INR elevation > 3.0 among concomitant capecitabine/warfarin users receiving warfarin for port prophylaxis (rate = 35.7 per 100 person-years) and no INR elevations > 3.0 during use of warfarin alone ($p = 0.46$). Among patients using warfarin for indications other than port prophylaxis, the rates of INR > 3.0 were 309.7 per 100 person-years (95% CI 213.2-434.9) during concomitant capecitabine/warfarin use and 193.5 events per 100 person-years (95% CI 119.8-295.8) during use of warfarin alone ($p = 0.09$). **CONCLUSIONS:** The results of our study show a low prevalence of capecitabine and warfarin concomitant use. We did not find large differences in the rates of bleeding events and elevated INR in patients receiving concomitant capecitabine and warfarin when compared with use of warfarin alone. While these results do not imply a lack of biologic interaction, our findings indicate that patients appear to be appropriately managed in clinical practice.

ZaueI, R., Y. N. Yeni, et al. (2006). "Comparison of the linear finite element prediction of deformation and strain of human cancellous bone to 3D digital volume correlation measurements." *J Biomech Eng* 128(1): 1-6. **[PDF Full-Text](#)**

The mechanical properties of cancellous bone and the biological response of the tissue to mechanical loading are related to deformation and strain in the trabeculae during function. Due to the small size of trabeculae, their motion is difficult to measure. To avoid the need to measure trabecular motions during loading the finite element method has been used to estimate trabecular level mechanical deformation. This analytical approach has been empirically successful in that the analytical models are solvable and their results correlate with the macroscopically measured stiffness and strength of bones. The present work is a direct comparison of finite element predictions to measurements of the deformation and strain at near trabecular level. Using the method of digital volume correlation, we measured the deformation and calculated the strain at a resolution approaching the trabecular level for cancellous bone specimens loaded in uniaxial compression. Smoothed results from linearly elastic finite element models of the same mechanical tests were correlated to the empirical three-dimensional (3D) deformation in the direction of loading with a coefficient of determination as high as 97% and a slope of the prediction near one. However, real deformations in the directions perpendicular to the loading direction were not as well predicted by the analytical models. Our results show, that the finite element modeling of the internal deformation and strain in cancellous bone can be accurate in one direction but that this does not ensure accuracy for all deformations and strains.