

Henry Ford Health System Publication List June 2008

This is a bibliography of journal articles published by Henry Ford Health System personnel. A search was compiled in PubMed during the month of June 2008, and then imported into EndNote for formatting.

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.

You can access this page at <http://www.henryfordconnect.com/sladen.cfm?id=436>

Biostatistics & Research Epidemiology

Rybicki, B. A., C. Neslund-Dudas, et al. (2008). "Polycyclic aromatic hydrocarbon--DNA adducts in prostate and biochemical recurrence after prostatectomy." *Clin Cancer Res* **14**(3): 750-7. [PDF Full Text](#)

Departments of Biostatistics and Research Epidemiology and Surgical Pathology, Henry Ford Health System, Detroit, Michigan 48202, USA. brybick1@hfhs.org

PURPOSE: DNA adduct levels may be influenced by metabolic activity, DNA repair capabilities, and genomic integrity, all of which play a role in cancer progression. EXPERIMENTAL DESIGN: To determine if elevated DNA adducts are a marker for prostate cancer progression, we measured polycyclic aromatic hydrocarbon-DNA adducts by immunohistochemistry in prostate cells of 368 surgical prostate cancer patients treated at the Henry Ford Hospital in Detroit, Michigan, between September 1999 and July 2004. Patients were followed up to 5 years after surgery with relative risk for biochemical recurrence (BCR) estimated with a Cox proportional hazards model that adjusted for standard clinical risk factors. RESULTS: At 1 year of follow-up, patients with adduct levels above the median in tumor cells [hazard ratio (HR), 2.40; 95% confidence interval (95% CI), 1.10-5.27] and nontumor cells (HR, 3.22; 95% CI, 1.40-7.39) had significant increased risk of BCR, but these HRs decreased to 1.12 (95% CI, 0.68-1.83) and 1.46 (95% CI, 0.89-2.41) in tumor and nontumor cells at 5 years postsurgery. When we restricted our analysis to patients with advanced-stage (III+) disease, those with high adduct levels in either tumor (53.5% versus 30.2%; $P = 0.07$) or nontumor (55.2% versus 28.6%; $P = 0.02$) cells had BCR rates almost 2-fold higher. In race-stratified analyses, the greatest risk of BCR associated with high adduct levels (in nontumor cells) was for African American patients younger than 60 years old (HR, 3.79; 95% CI, 1.01-14.30). CONCLUSIONS: High polycyclic aromatic hydrocarbon-DNA adduct levels in nontumor prostate cells are most strongly associated with BCR between 1 and 2 years after surgery and in patient subsets defined by younger age, advanced tumor stage, and African American race.

...

Bone & Joint Center

Bey, M. J., S. K. Kline, et al. (2008). "Measuring dynamic in-vivo glenohumeral joint kinematics: technique and preliminary results." *J Biomech* **41**(3): 711-4. [PDF Full Text](#)

Henry Ford Hospital, Department of Orthopaedics, Bone and Joint Center; E&R 2015, 2799 W. Grand Blvd., Detroit, MI 48202, USA. bey@bjc.hfh.edu

Rotator cuff tears are a common injury that affect a significant percentage of the population over age 60. Although it is widely believed that the rotator cuff's primary function is to stabilize the humerus against the glenoid during shoulder motion, accurately measuring the three-dimensional (3D) motion of the shoulder's glenohumeral joint under in-vivo conditions has been a challenging endeavor. In particular, conventional motion measurement techniques have frequently been limited to static or two-dimensional (2D) analyses, and have suffered

2799 W Grand Blvd, K-17
Detroit, MI 48202
www.henryford.com/sladen
sladen@sladen.hfhs.org
313 916-2550 voice
313 874-4730 fax

Hours
8:30am-9:00pm M-Th
8:30am-5:00pm F
9:00am-1:00pm Sa

from limited or unknown in-vivo accuracy. We have recently developed and validated a new model-based tracking technique that is capable of accurately measuring the 3D position and orientation of the scapula and humerus from biplane X-ray images. Herein we demonstrate the in-vivo application of this technique for accurately measuring glenohumeral joint translations during shoulder motion in the repaired and contralateral shoulders of patients following rotator cuff repair. Five male subjects were tested at 3-4 months following arthroscopic rotator cuff repair. Superior-inferior humeral translation was measured during elevation, and anterior-posterior humeral translation was measured during external rotation in both the repaired and contralateral shoulders. The data failed to detect statistically significant differences between the repaired and contralateral shoulders in superior-inferior translation ($p=0.74$) or anterior-posterior translation ($p=0.77$). The measurement technique overcomes the limitations of conventional motion measurement techniques by providing accurate, 3D, in-vivo measures of glenohumeral joint motion during dynamic activities. On-going research is using this technique to assess the effects of conservative and surgical treatment of rotator cuff tears.

...

Bone & Joint Center

Johnson, C. C., R. T. Burkman, et al. (2008). "Longitudinal study of depot medroxyprogesterone acetate (Depo-Provera) effects on bone health in adolescents: study design, population characteristics and baseline bone mineral density." *Contraception* **77**(4): 239-48. [PDF Full Text](#)

Henry Ford Hospital, Detroit, MI 48202-3450, USA. cjohnso1@hfhs.org

BACKGROUND: This analysis was conducted to assess the baseline data and design methodology within an observational longitudinal comparison of use vs. nonuse of the injectable (intramuscular) contraceptive depot medroxyprogesterone acetate (DMPA-IM) and its effect on bone mass in adolescent women. **STUDY DESIGN:** A prospective, observational, open-label, unmatched-cohort, safety study in females aged 11-18 years. Participants either self-selected DMPA-IM (Depo-Provera) 150 mg to be administered every 12 weeks for up to 240 weeks with a 120-week post-treatment follow-up or were nonusers (users of nonhormonal contraception or sexually abstinent) who were to be followed up for up to 360 weeks. As each participant entered the study, bone mineral density (BMD) was measured by dual-energy X-ray absorptiometry at the lumbar spine, hip and femoral neck regions, along with total body bone mineral content; serum and urine specimens were obtained for assay of bone metabolism markers and participants' histories of parity and tobacco and alcohol use were obtained. **RESULTS:** A total of 389 participants were enrolled: 169 elected to begin DMPA-IM; 26 chose nonhormonal methods and 194 were abstinent. The baseline characteristics indicated significant disparities between DMPA-IM users and nonusers: compared with the nonusers, DMPA-IM users had more advanced chronologic and gynecologic ages, were more likely to have smoked, been pregnant and included more blacks. These factors would likely influence bone accretion rates independent of DMPA-IM exposure. Comparison of participant BMDs with standard reference data revealed that the study cohorts did not match reference populations closely enough to make a direct between-cohort comparative analysis feasible. **CONCLUSIONS:** The baseline differences in cohort characteristics preclude a meaningful comparison of mean BMD changes over time between DMPA-IM users and nonusers cohorts, and comparisons of changes in Z-scores between cohorts were also not appropriate. Therefore, within-participant BMD decreases from baseline were established as safety thresholds, and the proportion of individuals crossing those thresholds on a persistent or progressive basis was identified as the revised primary end point.

...

Bone & Joint Center

Ninh, C. C., A. Sethi, et al. (2008). "Hip Dislocation After Modular Unipolar Hemiarthroplasty." *J Arthroplasty*. Epub Ahead of Print. [PDF Full Text](#)

Department of Orthopedic Surgery, Henry Ford Hospital, Detroit, Michigan.

An institutional review board-approved retrospective review of hip fractures in elderly patients treated with a modular unipolar implant was carried out to identify factors predisposing to dislocation of a hemiarthroplasty. The main outcome measure evaluated was dislocation vs nondislocation. Two hundred seventeen patients underwent the surgery, and 174 were available for review at 6 weeks and 144 at 1 year. The incidence of dislocation was 6%. The average time of dislocation after surgery was 19.3 days. Clinical factors significant for dislocation were male sex and mental disease. Radiographic

factors in dislocated hips included a smaller femoral neck and contralateral femoral neck offset. The center edge angle was also smaller in the dislocated patients. These patients had a higher mortality rate.

...

Cardiology

Maltsev, V. A., J. J. Kyle, et al. (2008). "Molecular identity of the late sodium current in adult dog cardiomyocytes identified by Nav1.5-antisense inhibition." *Am J Physiol Heart Circ Physiol*. Epub Ahead of Print. [PDF Full Text](#)

Henry Ford Hospital.

Late Na(+) current (INaL) is a major component of the action potential plateau in human and canine myocardium. Since INaL is increased in heart failure and ischemia, it represents a novel potential target for cardioprotection. However, the molecular identity of INaL remains unclear. Objective: We tested the hypothesis that the cardiac sodium channel (NaCh) isoform (Nav1.5) is a major contributor to INaL in adult dog ventricular cardiomyocytes (VCs). Methods: Cultured VCs were exposed to an antisense morpholino-based oligonucleotide (Nav1.5asOLIGO) targeting the region around the start codon of Nav1.5 mRNA or a control nonsense OLIGO (nsOLIGO). Both densities of transient Na(+) current (INaT) and late INaL (both in pA/pF) were monitored by whole cell patch clamp. Results: In HEK293 cells expressing Nav1.5 or Nav1.2, Nav1.5 asOLIGO silenced functional expression of Nav1.5 (up to 60 % of the initial INaT) but not Nav1.2. In both nsOLIGO-treated controls and untreated VCs, INaT and INaL remained unchanged for up to 5 days. However, both INaT and INaL exponentially decreased with a similar time course ($\tau=46$ and 56 h, respectively) after VCs were treated with Nav1.5 asOLIGO without changes in 1) decay kinetics, 2) steady-state activation and inactivation, and 3) the ratio of INaL to INaT. Four days after exposure to Nav1.5 asOLIGO, INaT and INaL amounted to $68\pm 6\%$ ($n=20$, $\text{mean}\pm\text{SE}$, $P<0.01$), and $60\pm 7\%$ ($P<0.018$, $n=11$) of those in VCs treated by nsOLIGO, respectively. Conclusion: In adult dog heart Nav1.5 sodium channels have a "functional half-life" of ~ 35 h (0.69τ) and make a major contribution to INaL. Key words: Late sodium current, molecular identity, sodium channel functional half-life, adult dog cardiomyocytes culture.

...

Cardiology

Maltsev, V. A., V. Reznikov, et al. (2008). "Modulation of late sodium current by Ca²⁺, calmodulin, and CaMKII in normal and failing dog cardiomyocytes: similarities and differences." *Am J Physiol Heart Circ Physiol* **294**(4): H1597-608. [PDF Full Text](#)

Henry Ford Hosp., Cardiovascular Research, Education & Research, Detroit, MI 48202-2689, USA.

Augmented and slowed late Na(+) current (I(NaL)) is implicated in action potential duration variability, early afterdepolarizations, and abnormal Ca(2+) handling in human and canine failing myocardium. Our objective was to study I(NaL) modulation by cytosolic Ca(2+) concentration ([Ca(2+)]_i) in normal and failing ventricular myocytes. Chronic heart failure was produced in 10 dogs by multiple sequential coronary artery microembolizations; 6 normal dogs served as a control. I(NaL) fine structure was measured by whole cell patch clamp in ventricular myocytes and approximated by a sum of fast and slow exponentials produced by burst and late scattered modes of Na(+) channel gating, respectively. I(NaL) greatly enhanced as [Ca(2+)]_i increased from "Ca(2+) free" to 1 μM : its maximum density increased, decay of both exponentials slowed, and the steady-state inactivation (SSI) curve shifted toward more positive potentials. Testing the inhibition of CaMKII and CaM revealed similarities and differences of I(NaL) modulation in failing vs. normal myocytes. Similarities include the following: 1) CaMKII slows I(NaL) decay and decreases the amplitude of fast exponentials, and 2) Ca(2+) shifts SSI rightward. Differences include the following: 1) slowing of I(NaL) by CaMKII is greater, 2) CaM shifts SSI leftward, and 3) Ca(2+) increases the amplitude of slow exponentials. We conclude that Ca(2+)/CaM/CaMKII signaling increases I(NaL) and Na(+) influx in both normal and failing myocytes by slowing inactivation kinetics and shifting SSI. This Na(+) influx provides a novel Ca(2+) positive feedback mechanism (via Na(+)/Ca(2+) exchanger), enhancing contractions at higher beating rates but worsening cardiomyocyte contractile and electrical performance in conditions of poor Ca(2+) handling in heart failure.

...

Cardiology

Sharma, N., I. C. Okere, et al. (2008). "High-sugar diets increase cardiac dysfunction and mortality in hypertension compared to low-carbohydrate or high-starch diets." *J Hypertens* **26**(7): 1402-1410. [PDF Full Text](#)

Department of Nutrition, USA, Department of Physiology and Biophysics, USA, Department of Medicine, School of Medicine, Case Western Reserve University, Cleveland, Ohio, USA, Division of Cardiovascular Medicine, Department of Medicine, Henry Ford Heart Health System, Detroit, Michigan, USA, Division of Cardiology, Department of Medicine, USA, Division of Cardiology, Department of Surgery, University of Maryland, Baltimore, Maryland, USA.

OBJECTIVE: Sugar consumption affects insulin release and, in hypertension, may stimulate cardiac signaling mechanisms that accelerate left ventricular hypertrophy and the development of heart failure. We investigated the effects of high-fructose or sucrose diets on ventricular function and mortality in hypertensive Dahl salt-sensitive rats. METHODS: Rats were fed chows that were either high starch (70% starch, 10% fat by energy), high fat (20% carbohydrates, 60% fat), high fructose (61% fructose, 9% starch, 10% fat), or high sucrose (61% sucrose, 9% starch, 10% fat). Hypertension was induced by adding 6% salt to the chow (n = 8-11/group). RESULTS: After 8 weeks of treatment, systolic blood pressure and left ventricular mass were similarly increased in all rats that were fed high-salt diets. Hypertension caused a switch in mRNA myosin heavy chain isoform from alpha to beta, and this effect was greater in the high-salt sucrose and fructose groups than in starch and fat groups. The cardiac mRNA for atrial natriuretic factor was also increased in all high-salt groups compared to respective controls, with the increase being significantly greater in the hypertensive sucrose fed group. Mortality was greater in the sucrose group (44%) compared to all the other hypertensive groups (12-18%), as was cardiomyocyte apoptosis. Left ventricular ejection fraction was lower in the high-salt sucrose group, which was due to an increase in end-systolic volume, and not increased end-diastolic volume. CONCLUSION: Diets high in sugar accelerated cardiac systolic dysfunction and mortality in hypertension compared to either a low-carbohydrate/high-fat or high-starch diet.

...

Dermatology

Gold, L. S., L. E. Colon, et al. (2008). "Is switching retinoids a sound strategy for the treatment of acne vulgaris?" *J Drugs Dermatol* **7**(6 Suppl): s11-7. [PDF Full Text](#)

Henry Ford Medical Center, Detroit, MI, USA.

Topical retinoids, such as adapalene gel and tazarotene cream, are considered first-line therapy for the treatment of acne vulgaris. Dermatologists often initiate adapalene gel treatment first, due to its good tolerability, followed by a switch to tazarotene cream in an effort to improve or hasten efficacy outcomes. The goal of this study was to compare the efficacy and safety of 2 daily regimens for the treatment of acne: adapalene 0.1% gel for 12 weeks and adapalene 0.1% gel for 6 weeks followed by tazarotene 0.1% cream for 6 weeks. The primary efficacy outcome was the percent of reduction in total lesion counts posttreatment. Subjects ages 12 to 35 years with acne vulgaris were selected to participate in a 12-week, randomized, evaluator-blind study of once-daily therapy with adapalene 0.1% gel (n=101) or "switch therapy," adapalene 0.1% gel followed by tazarotene 0.1% cream (n=100). Adapalene-treated subjects achieved similar percent reductions in total lesion counts at week 12 compared to subjects receiving switch therapy, demonstrating the noninferiority of adapalene gel treatment (median difference: -3.57%; lower confidence limit [LCL]: -11.25). Adapalene gel was associated with fewer reports of cutaneous irritation, particularly for scaling and stinging/burning, and fewer treatment-related adverse events compared to switch therapy. The results of this study indicate that daily therapy with adapalene 0.1% gel for 12 weeks was noninferior to switch therapy.

...

Dermatology

Tierney, E. P., M. J. Eide, et al. (2008). "Photodynamic therapy for actinic keratoses: Survey of patient perceptions of treatment satisfaction and outcomes." *J Cosmet Laser Ther* **10**(2): 81-6. [Click for Article Request Form](#)

Department of Dermatology, Henry Ford Hospital, Detroit, MI, USA.

Background: While there are many available treatments for actinic keratoses (AKs), patient-preferred treatment options remain undefined. Objective: To quantify patient perceptions and preferences in the management of AKs, including comparison of photodynamic therapy (PDT) with other therapies. Methods: A self-administered questionnaire was mailed to 45 patients who had received PDT for AKs in 2005-2006 in the Henry Ford Health System. A series of indicators for each treatment were surveyed, including: recovery time, cosmetic appearance, patient cost, effectiveness, patient satisfaction, treatment option preference, and perceived burden of treatment. Results: A total of 39 of the 45 patients participated (86.7%). A patient's reported recovery time was significantly more likely to be 1 week or less for PDT when compared with cryotherapy ($p = 0.02$) and surgical excision ($p = 0.02$). Borderline significance was found for the improved cosmetic outcome in PDT vs. surgical excision ($p = 0.058$) and for patient satisfaction with PDT compared with 5-fluorouracil ($p = 0.058$). Patients significantly preferred PDT to 5-fluorouracil ($p < 0.001$) or imiquimod ($p = 0.031$). Conclusion: While the effectiveness of lesion clearance with PDT for AKs has been well proven in the literature, this is the first study to evaluate patient perception of the effectiveness, side-effect profile and benefits of PDT relative to several standard treatment approaches for AKs. PDT was found to have equivalent or improved recovery times, cosmetic outcomes, patient satisfaction and preference as a treatment for AKs by patients compared with other options.

...

Diagnostic Radiology

Arbab, A. S., B. Janic, et al. (2008). "Detection of migration of locally implanted AC133+ stem cells by cellular magnetic resonance imaging with histological findings." *Faseb J*. Epub Ahead of Print. [PDF Full Text](#)

Molecular and Cellular Imaging Laboratory, Department of Radiology, Henry Ford Hospital, Detroit, Michigan, USA; and Mouse Core Imaging Facility, National Heart Lung and Blood Institute; Experimental Neuroimaging Section, Laboratory of Diagnostic Radiology Research, Cell Processing Section, Department of Transfusion Medicine, and Molecular Imaging Laboratory, Clinical Center, National Institutes of Health, Bethesda, Maryland, USA.

This study investigated the factors responsible for migration and homing of magnetically labeled AC133(+) cells at the sites of active angiogenesis in tumor. AC133(+) cells labeled with ferumoxide-protamine sulfate were mixed with either rat glioma or human melanoma cells and implanted in flank of nude mice. An MRI of the tumors including surrounding tissues was performed. Tumor sections were stained for Prussian blue (PB), platelet-derived growth factor (PDGF), hypoxia-inducible factor-1 alpha (HIF-1alpha), stromal cell derived factor-1 (SDF-1), matrix metalloproteinase-2 (MMP-2), vascular endothelial growth factor (VEGF), and endothelial markers. Fresh snap-frozen strips from the central and peripheral parts of the tumor were collected for Western blotting. MRIs demonstrated hypointense regions at the periphery of the tumors where the PB(+)/AC133(+) cells were positive for endothelial cells markers. At the sites of PB(+)/AC133(+) cells, both HIF-1alpha and SDF-1 were strongly positive and PDGF and MMP-2 showed generalized expression in the tumor and surrounding tissues. There was no significant association of PB(+)/AC133(+) cell localization and VEGF expression in tumor cells. Western blot demonstrated strong expression of the SDF-1, MMP-2, and PDGF at the peripheral parts of the tumors. HIF-1alpha was expressed at both the periphery and central parts of the tumor. This work demonstrates that magnetically labeled cells can be used as probes for MRI and histological identification of administered cells.-Arbab, A. S., Janic, B., Knight, R. A., Anderson, S. A., Pawelczyk, E., Rad, A. M., Read, E. J., Pandit, S. D., Frank, J. A. Detection of migration of locally implanted AC133(+) stem cells by cellular magnetic resonance imaging with histological findings.

...

Diagnostic Radiology

Jain, R., S. K. Ellika, et al. (2008). "Quantitative estimation of permeability surface-area product in astroglial brain tumors using perfusion CT and correlation with histopathologic grade." *AJNR Am J Neuroradiol* **29**(4): 694-700. [PDF Full Text](#)

Division of Neuroradiology, Department of Radiology, Henry Ford Hospital, Detroit, MI 48202, USA. rajanj@rad.hfh.edu

BACKGROUND AND PURPOSE: Glioma angiogenesis and its different hemodynamic features, which can be evaluated by using perfusion CT (PCT) imaging of the brain, have been correlated with the grade and the aggressiveness of gliomas. Our

hypothesis was that quantitative estimation of permeability surface area product (PS), cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT) in astroglial brain tumors by using PCT will correlate with glioma grade. High-grade gliomas will show higher PS and CBV as compared with low-grade gliomas. MATERIALS AND METHODS: PCT was performed in 32 patients with previously untreated astroglial tumors (24 high-grade gliomas and 8 low-grade gliomas) by using a total acquisition time of 170 seconds. World Health Organization (WHO) glioma grades were compared with PCT parameter absolute values by using Student or nonparametric Wilcoxon 2-sample tests. Receiver operating characteristic (ROC) analyses were also done for each of the parameters. RESULTS: The differences in PS, CBV, and CBF between the low- and high-grade tumor groups were statistically significant, with the low-grade group showing lower mean values than the high-grade group. ROC analyses showed that both CBV (C-statistic 0.930) and PS (C-statistic 0.927) were very similar to each other in differentiating low- and high-grade gliomas and had higher predictability compared with CBF and MTT. Within the high-grade group, differentiation of WHO grade III and IV gliomas was also possible by using PCT parameters, and PS showed the highest C-statistic value (0.926) for the ROC analyses in this regard. CONCLUSIONS: Both PS and CBV showed strong association with glioma grading, high-grade gliomas showing higher PS and CBV as compared with low-grade gliomas. Perfusion parameters, especially PS, can also be used to differentiate WHO grade III from grade IV in the high-grade tumor group.

...

Diagnostic Radiology

Janic, B., A. S. Iskander, et al. (2008). "Effects of ferumoxides-protamine sulfate labeling on immunomodulatory characteristics of macrophage-like THP-1 cells." *PLoS ONE* **3**(6): e2499. [PDF Full Text](#)

Cellular and Molecular Imaging Laboratory, Department of Radiology, Henry Ford Hospital, Detroit, Michigan, United States of America. bjanic@rad.hfh.edu

Superparamagnetic Iron Oxide (SPIO) complexed with cationic transfection agent is used to label various mammalian cells. Labeled cells can then be utilized as an in vivo magnetic resonance imaging (MRI) probes. However, certain number of in vivo administered labeled cells may be cleared from tissues by the host's macrophages. For successful translation to routine clinical application of SPIO labeling method it is important that this mode of in vivo clearance of iron does not elicit any diverse immunological effects. The purpose of this study was to demonstrate that SPIO agent ferumoxides-protamine sulfate (FePro) incorporation into macrophages does not alter immunological properties of these cells with regard to differentiation, chemotaxis, and ability to respond to the activation stimuli and to modulate T cell response. We used THP-1 cell line as a model for studying macrophage cell type. THP-1 cells were magnetically labeled with FePro, differentiated with 100 nM of phorbol ester, 12-Myristate-13-acetate (TPA) and stimulated with 100 ng/ml of LPS. The results showed 1) FePro labeling had no effect on the changes in morphology and expression of cell surface proteins associated with TPA induced differentiation; 2) FePro labeled cells responded to LPS with slightly higher levels of NFkappaB pathway activation, as shown by immunoblotting; TNF-alpha secretion and cell surface expression levels of CD54 and CD83 activation markers, under these conditions, were still comparable to the levels observed in non-labeled cells; 3) FePro labeling exhibited differential, chemokine dependent, effect on THP-1 chemotaxis with a decrease in cell directional migration to MCP-1; 4) FePro labeling did not affect the ability of THP-1 cells to down-regulate T cell expression of CD4 and CD8 and to induce T cell proliferation. Our study demonstrated that intracellular incorporation of FePro complexes does not alter overall immunological properties of THP-1 cells. The described experiments provide the model for studying the effects of in vivo clearance of iron particles via incorporation into the host's macrophages that may follow after in vivo application of any type of magnetically labeled mammalian cells. To better mimic the complex in vivo scenario, this model may be further exploited by introducing additional cellular and biological, immunologically relevant, components.

...

Diagnostic Radiology

Williams, T. R., O. J. Longoria, et al. (2008). "Incidence and imaging appearance of urethrovesical anastomotic urinary leaks following da Vinci robotic prostatectomy." *Abdom Imaging* **33**(3): 367-70. [PDF Full Text](#)

Department of Radiology, Abdominal Imaging Division, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202, USA. toddw@rad.hfh.edu

BACKGROUND: The advent of the da Vinci robotic prostatectomy has several advantages over open and laparoscopic

prostatectomy, including fewer complications, better continence and potency. We evaluate the incidence and imaging features of urinary leaks after robotic prostatectomy. **METHODS:** A retrospective study examining the anastomotic leak rates from 490 consecutive robotic prostatectomy patients. Routine postoperative cystography on day 7 was reviewed for presence and severity of urinary anastomotic leaks. **RESULTS:** A total of 490 patients were reviewed, of which 442 had cystographic imaging postoperatively (n = 442). A total of 67 urinary leaks were identified; 40 were small, limited extraperitoneal leaks confined to the surgical bed, 21 were moderate sized leaks limited to the extraperitoneal pelvic space, and six extended in to the peritoneal cavity. Two of these six patients required CT-guided drainage for peritoneal urinoma. Other cystography findings included two cases of vesicoureteral reflux and one case of colovesical fistula. **CONCLUSION:** The incidence of postoperative anastomotic urinary leaks following robotic prostatectomy (13.6%) is the same or better than laparoscopic prostatectomy and traditional radical retropubic prostatectomy. The vast majority of urethrovesical leaks are transient, requiring no follow-up intervention. The incidence of large anastomotic leaks requiring CT guided intervention is exceedingly low 2/490 (<0.5%).

...

Emergency Medicine

Boehm, K. M. and A. Pugh (2008). "A New Variant of Wiiiitis." *J Emerg Med*. EPub Ahead of Print. [PDF Full Text](#)

Department of Emergency Medicine, Henry Ford Wyandotte Hospital, Wyandotte, Michigan.

...

Endocrinology & Metabolism

Geller, D. S., J. J. Zhang, et al. (2008). "A novel form of human Mendelian hypertension featuring non-glucocorticoid remediable aldosteronism." *J Clin Endocrinol Metab*. EPub Ahead of Print. [PDF Full Text](#)

Section of Nephrology, Yale University School of Medicine; Division of Endocrinology, Henry Ford Hospital, Detroit, MI; Children's Hospital Oakland Research Institute, Oakland, CA; Department of Pathology, Yale University School of Medicine; Department of Genetics, Howard Hughes Medical Institute, Yale University School of Medicine.

Context: Primary aldosteronism is a leading cause of secondary hypertension, but the mechanisms underlying the characteristic renin-independent secretion of aldosterone remain unknown in most patients. Objective: We report a new familial form of aldosteronism in a father and 2 daughters. All were diagnosed with severe hypertension refractory to medical treatment by age 7. We performed a variety of clinical, biochemical and genetic studies to attempt to clarify the underlying molecular defect. Results: Biochemical studies revealed hyporeninemia, hyperaldosteronism, and very high levels of 18-oxocortisol and 18-hydroxycortisol, steroids that reflect oxidation by both steroid 17-alpha hydroxylase and aldosterone synthase. These enzymes are normally compartmentalized in the adrenal fasciculata and glomerulosa, respectively. Administration of dexamethasone failed to suppress either aldosterone or cortisol secretion; these findings distinguish this clinical syndrome from glucocorticoid-remediable aldosteronism (GRA), another autosomal dominant form of hypertension, and suggest a global defect in the regulation of adrenal steroid production. Genetic studies excluded mutation at the aldosterone synthase locus, further distinguishing this disorder from GRA. Because of unrelenting hypertension, all 3 subjects underwent bilateral adrenalectomy, which in each case corrected the hypertension. Adrenal glands showed dramatic enlargement, with paired adrenal weights as high as 82 grams. Histology revealed massive hyperplasia and cellular hypertrophy of a single cortical compartment which had features of adrenal fasciculata or a transitional zone, with an atrophic glomerulosa. Conclusion: These findings define a new inherited form of aldosteronism and suggest that identification of the underlying defect will provide insight into normal mechanisms regulating adrenal steroid biosynthesis.

...

Eye Care Services

Dhaliwal, J. S., B. F. Mason, et al. (2008). "Long-term use of topical tacrolimus (FK506) in high-risk penetrating keratoplasty." *Cornea* **27**(4): 488-93. [PDF Full Text](#)

Henry Ford Health System, Ophthalmology, Troy, MI, USA.

PURPOSE: To evaluate the long-term efficacy and side effects of off-label topical tacrolimus 0.03% ointment (Protopic; Fujisawa Health, Deerfield, IL) as a sole second-line immunosuppressive agent in the management of high-risk corneal grafts. **METHODS:** Four consecutive patients underwent high-risk penetrating keratoplasty (4 grafts) with a prior diagnosis of corneal scar secondary to herpetic keratitis, keratoconus, acanthamoeba keratitis, and Fuchs endothelial dystrophy, respectively. All 4 patients developed steroid-induced glaucoma and failed traditional immunosuppressant therapy. Patients were started on topical tacrolimus ointment 0.03%, twice daily, which was tapered to the lowest possible therapeutic dose that maintained its antirejection efficacy. Patients were monitored for adverse treatment effects. The mean follow-up was 33 months (range, 26-48 months), and the mean treatment duration was 22.6 months (range, 13-32 months). **RESULTS:** All 4 high-risk corneal transplant patients experienced episodes of acute rejection that was successfully reversed with topical tacrolimus treatment. During tacrolimus treatment, there were no further episodes of graft rejection and no incidents of herpes simplex virus infection or reactivation, with the longest follow-up being 4 years. Two patients have been successfully tapered off tacrolimus, and 2 patients are currently on once-daily dosing. No adverse effects were observed. **CONCLUSIONS:** Topical tacrolimus 0.03% ointment seems to be a promising second-line immunosuppressant in management of high-risk grafts.

...

Eye Care Services

Ruttig, N. J., M. Jancevski, et al. (2008). "Evaluating wavefront analysis application in intraocular lens placement." Curr Opin Ophthalmol **19**(4): 309-13. [PDF Full Text](#)

Henry Ford Hospital, Detroit, Michigan 48202-2689, USA.

PURPOSE OF REVIEW: New advances in wavefront analysis offer an opportunity for greater refinement of cataract surgery. In this article, we critically review the recent advances in wavefront technology with specific attention to its application in customizing cataract surgery. **RECENT FINDINGS:** Historically, wavefront analysis has been implemented in corneal refractive procedures. Expansion of this technology may soon allow surgeons to choose the most optically appropriate intraocular lens for a patient's individualized wavefront pattern, thus allowing for a 'custom-fitted' intraocular lens. The benefit of full correction of all higher-order aberrations measured by wavefront analysis remains controversial. Additionally, in certain subsets of patients with specific anterior chamber pathology, wavefront intraocular lenses may not be appropriate. **SUMMARY:** The application of wavefront technology continues to expand the surgical options available to the practicing ophthalmologist. Significant advances have been made in our understanding of wavefront analysis and its usefulness in vision correction. Careful consideration of the optics of the whole eye must be considered when implementing wavefront analysis.

...

Gastroenterology

Krishnan, P., S. Asfandiyar, et al. (2008). "Aortogastric fistula formation 3 days after endovascular stent placement." Gastrointest Endosc. Epub Ahead of Print. [PDF Full Text](#)

Division of Gastroenterology, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA.

...

Hypertension & Vascular Research

Li, X. C. and J. L. Zhuo (2008). "Intracellular ANG II directly induces in vitro transcription of TGF-beta1, MCP-1, and NHE-3 mRNAs in isolated rat renal cortical nuclei via activation of nuclear AT1a receptors." Am J Physiol Cell Physiol **294**(4): C1034-45. [PDF Full Text](#)

Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.

The present study tested the hypothesis that intracellular ANG II directly induces transcriptional effects by stimulating AT(1a) receptors in the nucleus of rat renal cortical cells. Intact nuclei were freshly isolated from the rat renal cortex, and transcriptional responses to ANG II were studied using in vitro RNA transcription assays and semiquantitative RT-PCR. High-

power phase-contrast micrographs showed that isolated nuclei were encircled by an intact nuclear envelope and stained strongly by the DNA marker 4',6-diamidino-2-phenylindole, but not by the membrane or endosomal markers. Fluorescein isothiocyanate-labeled ANG II and [(125)I]Val(5)-ANG II binding confirmed the presence of ANG II receptors in the nuclei with a predominance of AT(1) receptors. RT-PCR showed that AT(1a) mRNA expression was threefold greater than AT(1b) receptor mRNAs in these nuclei. In freshly isolated nuclei, ANG II increased in vitro [α -(32)P]CTP incorporation in a concentration-dependent manner, and the effect was confirmed by autoradiography and RNA electrophoresis. ANG II markedly increased in vitro transcription of mRNAs for transforming growth factor-beta1 by 143% ($P < 0.01$), macrophage chemoattractant protein-1 by 89% ($P < 0.01$), and the sodium and hydrogen exchanger-3 by 110% ($P < 0.01$). These transcriptional effects of ANG II on the nuclei were completely blocked by the AT(1) receptor antagonist losartan ($P < 0.01$). By contrast, ANG II had no effects on transcription of angiotensinogen and glyceraldehyde-3-phosphate dehydrogenase mRNAs. Because these transcriptional effects of ANG II in isolated nuclei were induced by ANG II in the absence of cell surface receptor-mediated signaling and completely blocked by losartan, we concluded that ANG II may directly stimulate nuclear AT(1a) receptors to induce transcriptional responses that are associated with tubular epithelial sodium transport, cellular growth and hypertrophy, and proinflammatory cytokines.

...

Hypertension & Vascular Research

Liao, T. D., X. P. Yang, et al. (2008). "Role of Inflammation in the Development of Renal Damage and Dysfunction in Angiotensin II-Induced Hypertension." Hypertension. [Click for Article Request Form](#)

Hypertension and Vascular Research Division, Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich; and PDL BioPharma, Inc, Fremont, Calif.

Angiotensin II (Ang II)-induced hypertension is associated with an inflammatory response that may contribute to the development of target organ damage. We tested the hypothesis that, in Ang II-induced hypertension, CC chemokine receptor 2 (CCR2) activation plays an important role in the development of renal fibrosis, damage, and dysfunction by causing oxidative stress, macrophage infiltration, and cell proliferation. To test this hypothesis, we used CCR2 knockout mice (CCR2^{-/-}). The natural ligand of CCR2 is monocyte chemoattractant protein-1, a chemokine important for macrophage recruitment and activation. CCR2^{-/-} and age-matched wild-type (CCR2^{+/+}) C57BL/6J mice were infused continuously with either Ang II (5.2 ng/10 g per minute) or vehicle via osmotic minipumps for 2 or 4 weeks. Ang II infusion caused similar increases in systolic blood pressure and left ventricular hypertrophy in both strains of mice. However, in CCR2^{-/-} mice with Ang II-induced hypertension, oxidative stress, macrophage infiltration, albuminuria, and renal damage were significantly decreased, and glomerular filtration rate was significantly higher than in CCR2^{+/+} mice. We concluded that, in Ang II-induced hypertension, CCR2 activation plays an important role in the development of hypertensive nephropathy via increased oxidative stress and inflammation.

...

Infectious Diseases

Chua, T., C. L. Moore, et al. (2008). "Molecular Epidemiology of Methicillin-Resistant *Staphylococcus aureus* (MRSA) Bloodstream Isolates in Urban Detroit." J Clin Microbiol. [Click for Article Request Form](#)

Henry Ford Health System, Detroit, MI; Boston University School of Medicine, Boston, MA; Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University School of Medicine, Detroit, MI.

To gain a better understanding of epidemiology of resistance in *Staphylococcus aureus*, we describe the molecular epidemiology of methicillin-resistant *Staphylococcus aureus* bloodstream isolates in Urban Detroit. Bloodstream isolates from July 2005 to February 2007 were characterized. Two hundred and ten bloodstream isolates from 201 patients were evaluated. Patient characteristics were: median age 54 years, 56% male, 71% African-American. Seventy-six percent of infections were health care-associated, with 55% community onset and 21% hospital acquired, and 24% were community-associated. The most common sources were skin/wound (25%), central venous catheters (24%), unknown source (20%) and endocarditis (9%). Ninety percent and 5% of isolates had MIC to vancomycin of ≤ 1.0 mg/L, using automated dilution testing and E-test, respectively. Six percent of isolates showed heteroresistance to vancomycin, all occurring with isolates having vancomycin E-test MIC ≥ 1.5 mg/L. Results of PFGE showed seventeen strain types. The predominant strains were

USA100 (104 isolates) and USA300 (74 isolates). Forty-nine percent of the isolates were SCCmec II and 56% were agr II. All USA300 isolates were positive for the PVL toxin genes and agr I. Forty-seven percent of USA300 bloodstream infections were health care-associated (35% community onset and 12% hospital onset). USA300 strains were more common in injection drug users with skin/wound as the predominant source of infection. Thirty percent of the USA100 strains were closely related to vancomycin-resistant *Staphylococcus aureus* isolates. The results of this study show that vancomycin MICs using automated dilution testing with Vitek-2 and E-test is highly discordant. Most MRSA causing bacteremia are health care-associated, commonly have MICs to vancomycin that are high within the susceptible range, and are not detected by routine automated dilution testing and have significant diversity of molecular characteristics. USA100 strains that are closely related to VRSA isolates and USA300 strains are common as causes of both hospital and community onset infection. Infection control measures should focus not only on prevention of spread of community strains in the hospital but also prevention of spread of hospital strains associated with VRSA into the community.

...

Infectious Diseases

Vazquez, J. A., J. A. Schranz, et al. (2008). "A Phase 2, Open-Label Study of the Safety and Efficacy of Intravenous Anidulafungin as a Treatment for Azole-Refractory Mucosal Candidiasis." *J Acquir Immune Defic Syndr* **48**(3): 304-309. [PDF Full Text](#)

From the Division of Infectious Diseases, Henry Ford Hospital and Wayne State University School of Medicine, Detroit, MI; Vicuron Pharmaceuticals, King of Prussia, PA; Division of Infectious Diseases, Cooper University Hospital, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, Camden, NJ; and Division of Infectious Diseases, University of Cincinnati College of Medicine, Cincinnati, OH.

BACKGROUND:: Azole-refractory mucosal candidiasis is a debilitating disease frequently seen in patients who are immunosuppressed as a result of HIV, malignancy, posttransplant immunosuppressive therapy, persistent neutropenia, steroid use, or diabetes. Anidulafungin has potent activity against a broad spectrum of *Candida* species, including strains resistant to azoles and amphotericin B. We performed an open-label, noncomparative study to examine efficacy and safety of anidulafungin in patients with azole-refractory oropharyngeal and esophageal candidiasis. **METHODS::** Patients enrolled met diagnostic criteria for azole-refractory mucosal candidiasis. They received intravenous anidulafungin 100 mg on day 1 followed by daily 50-mg doses on day 2 through day 14 or for a maximum of 21 days. Primary efficacy variables were clinical response (for oropharyngeal candidiasis) and endoscopic and clinical response (for esophageal candidiasis) at the end of therapy. **RESULTS::** Nineteen patients were enrolled; 89% had advanced HIV infection. Clinical success was observed in 95% of patients at end of therapy, and endoscopic success was observed in 92% of patients with esophageal candidiasis. At follow-up, clinical success was maintained in 47% of patients. The most common adverse event, experienced by 4 patients, was nausea and/or vomiting. **CONCLUSIONS::** Anidulafungin was well tolerated and efficacious in the treatment of patients with azole-refractory esophageal and oropharyngeal candidiasis.

...

Internal Medicine

Prihar, B. J. and S. Katz (2008). "Patient education as a tool to increase screening for osteoporosis." *J Am Geriatr Soc* **56**(5): 961-2. [PDF Full Text](#)

Internal Medicine, Henry Ford Hospital, Detroit, MI

...

Nephrology

Besarab, A., M. Allon, et al. (2008). "Resolved: Fistulas Are Preferred to Grafts as Initial Vascular Access for Dialysis." *J Am Soc Nephrol*. Epub Ahead of Print. [PDF Full Text](#)

Division of Nephrology and Hypertension, Henry Ford Health System, Detroit, Michigan.

There is growing concern that the Fistula First Initiative, KDOQI guidelines, and subsequent pressure from the Centers for Medicare and Medicaid Services lack reasonableness regarding likely success for fistula maturation in a heterogeneous, new-onset dialysis population. Here the various positions are examined from multiple perspectives.

...

Neurology

Bagher-Ebadian, H., Q. Jiang, et al. (2008). "A modified Fourier-based phase unwrapping algorithm with an application to MRI venography." *J Magn Reson Imaging* **27**(3): 649-52. [PDF Full Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI 48202, USA.

PURPOSE: To present a single-step deterministic procedure for unwrapping MRI phase maps. **MATERIALS AND METHODS:** Using an algorithm previously developed for optical applications, Laplacian operators were applied in the Fourier space of the MRI phase map. The original Fourier-based phase unwrapping algorithm was modified so that demodulation accomplished the required signal symmetrization in Fourier space. To evaluate the method's performance in the presence of thermal noise, a set of wrapped phase maps were simulated at different levels of noise in k-space, and the response of the algorithm at different levels of signal-to-noise ratio (SNR) was evaluated for stability. To demonstrate its utility in MRI, the algorithm was applied to the wrapped phase maps of susceptibility-weighted imaging (SWI) studies, which were then used to generate venograms. **RESULTS:** In simulated phase wrapping, the algorithm correctly reproduced the original phase for a wide range of phase gradients and noise. The procedure was fast and produced useful maps of venous structures in SWI images. **CONCLUSION:** A fast and stable single-step deterministic method for unwrapping MRI phase maps is available for such applications as SWI and mapping of static magnetic field inhomogeneity.

...

Neurology

Cerghet, M., B. Redman, et al. (2008). "Prolonged survival after multifocal brain radiation necrosis associated with whole brain radiation for brain metastases: case report." *J Neurooncol*. Epub Ahead of Print. [PDF Full Text](#)

Department of Neurology, Henry Ford Health System, Detroit, MI, USA, mirela@neuro.hfh.edu.

Radiation necrosis of the brain is a well documented adverse effect of radiation therapy. The authors report an unusual case of relapsing multifocal radiation necrosis following whole brain radiation therapy (WBRT) for brain metastases from a systemic germ cell tumor. Anticoagulation with warfarin may have had therapeutic benefit. The patient is alive without a neurological deficit 10 years after the diagnosis of radiation necrosis.

...

Neurology

Chen, J., X. Cui, et al. (2008). "Increasing Ang1/Tie2 expression by simvastatin treatment induces vascular stabilization and neuroblast migration after stroke." *J Cell Mol Med*. Epub Ahead of Print. [PDF Full Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI, 48202 USA.

Background: In this study, we tested the hypothesis that the Angiopoietin 1 (Ang1)/Tie2 pathway mediates simvastatin induced vascular integrity and migration of neuroblasts after stroke. **Methods and Results:** Rats were subjected to 2 hours of middle cerebral artery occlusion (MCAo) and treated, starting 1 day after stroke with or without simvastatin (1 mg/kg, daily) for 7 days. Simvastatin treatment significantly decreased blood brain barrier (BBB) leakage and concomitantly, increased Ang1, Tie2, and Occludin expression in the ischemic border (IBZ) compared to the MCAo control group. Simvastatin also significantly increased doublecortin (DCX, a marker of migrating neuroblasts) expression in the IBZ compared to control MCAo rats. DCX was highly expressed around vessels. To further investigate the signaling pathway of simvastatin induced vascular stabilization and angiogenesis, rat brain microvascular endothelial cell (RBMEC) culture was employed. The data show that simvastatin treatment of RBMEC increased Ang1 and Tie2 gene and protein expression and promoted phosphorylated-Tie2 activity. Simvastatin significantly increased endothelial capillary tube formation, an index of angiogenesis, compared to non-treated control. Inhibition of Ang1 or knockdown of Tie2 gene expression in endothelial

cells significantly attenuated simvastatin-induced capillary tube formation. In addition, simvastatin significantly increased subventricular zone (SVZ) explant cell migration compared to non treatment control. Inhibition of Ang1 significantly attenuated simvastatin-induced SVZ cell migration. Conclusion: Simvastatin treatment of stroke increases Ang1/Tie2 expression and thereby reduces BBB leakage and promotes vascular stabilization. Ang1/Tie2 expression induced by simvastatin treatment promotes neuroblast micro-vascular coupling after stroke.

...

Neurology

Ding, G., Q. Jiang, et al. (2008). "Angiogenesis detected after embolic stroke in rat brain using magnetic resonance T2*WI." *Stroke* **39**(5): 1563-8. [PDF Full Text](#)

Henry Ford Hospital, Neurology Department, Detroit, MI 48202, USA.

BACKGROUND AND PURPOSE: This study uses T(2)* weighted imaging (T2*WI) to measure the temporal evolution of cerebral angiogenesis in rats subjected to embolic stroke up to 6 weeks after stroke onset with or without sildenafil treatment. Method- Male Wistar rats were subjected to embolic stroke and treated with saline (n=10) or with sildenafil (n=11), with treatment initiated at 24 hours and continued daily for 7 days after onset of ischemia. T2*WI measurements were performed at 24 hours after embolization and weekly up to 6 weeks using a 7-Tesla system. Histological measurements were obtained at 6 weeks after MRI scans. RESULTS: Using T2*WI, cerebral angiogenesis was detected starting from 4 weeks and from 2 weeks after onset of embolic stroke in saline and sildenafil treated rats, respectively. Significant differences in the temporal and spatial features of angiogenesis after embolic stroke up to 6 weeks after onset of stroke were found between saline and sildenafil treated rats and were identified with T2*WI. MRI permeability parameter, K(i), complementarily detected angiogenesis after ischemia in embolic stroke rats. Sildenafil treatment of stroke rats significantly enhanced the angiogenesis, as confirmed histologically. CONCLUSIONS: T2*WI can quantitatively measure the temporal evolution of angiogenesis in rats subjected to embolic stroke. Compared to control rats, sildenafil treatment significantly increased angiogenesis in treated animals up to 6 weeks after stroke.

...

Neurology

Ewing, J. R., S. L. Brown, et al. (2008). "MRI measurement of change in vascular parameters in the 9L rat cerebral tumor after dexamethasone administration." *J Magn Reson Imaging* **27**(6): 1430-8. [PDF Full Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, Michigan 48202, USA. jre@neurnis.neuro.hfh.edu

PURPOSE: To demonstrate in the rat 9L cerebral tumor model that repeated MRI measurements can quantitate acute changes in the blood-brain distribution of Gadomer after dexamethasone administration. MATERIALS AND METHODS: A total of 16 Fischer 344 rats were studied at 7T, 15 days after cerebral implantation of a 9L tumor. MRI procedures employed a T-One by Multiple Read Out Pulses (TOMROP) sequence to estimate R(1) ($R(1) = 1/T(1)$) at 145-second intervals before and after administration of Gadomer (Bayer), a macromolecular contrast agent (CA). Two baseline studies preceded Gadomer administration and 10 subsequent R(1) maps tracked CA concentration in blood and brain for 25 minutes. Thereafter, either dexamethasone (N = 10) or normal saline (N = 6) was administered intravenously. A total of 90 minutes later a second series of 12 TOMROP measurements of Gadomer distribution was performed. The influx constant, K(1), plasma distribution volume, v(D), backflux constant, k(b), and interstitial space, v(e), were determined, and the test-retest differences of each of four vascular parameters were calculated. RESULTS: Dexamethasone decreased K(1) approximately 60% (P = 0.02), lowered k(b) and v(D) (P = 0.03 and P < 0.01, respectively), and marginally but insignificantly decreased v(e). CONCLUSION: This noninvasive MRI technique can detect drug effects on blood-brain transfer constants of CAs within two hours of administration.

...

Neurology

Teng, H., Z. G. Zhang, et al. (2008). "Coupling of angiogenesis and neurogenesis in cultured endothelial cells and neural progenitor cells after stroke." *J Cereb Blood Flow Metab* **28**(4): 764-71. [Click for Article Request Form](#)

Department of Neurology, Henry Ford Health System, Detroit, Michigan 48202, USA.

Angiogenesis and neurogenesis are coupled processes. Using a coculture system, we tested the hypothesis that cerebral endothelial cells activated by ischemia enhance neural progenitor cell proliferation and differentiation, while neural progenitor cells isolated from the ischemic subventricular zone promote angiogenesis. Coculture of neural progenitor cells isolated from the subventricular zone of the adult normal rat with cerebral endothelial cells isolated from the stroke boundary substantially increased neural progenitor cell proliferation and neuronal differentiation and reduced astrocytic differentiation. Conditioned medium harvested from the stroke neural progenitor cells promoted capillary tube formation of normal cerebral endothelial cells. Blockage of vascular endothelial growth factor receptor 2 suppressed the effect of the endothelial cells activated by stroke on neurogenesis as well as the effect of the supernatant obtained from stroke neural progenitor cells on angiogenesis. These data suggest that angiogenesis couples to neurogenesis after stroke and vascular endothelial growth factor likely mediates this coupling.

...

Neurosurgery

Seyfried, D. M., Y. Han, et al. (2008). "*Mannitol enhances delivery of marrow stromal cells to the brain after experimental intracerebral hemorrhage.*" *Brain Res.* EPub Ahead of Print. [PDF Full Text](#)

Department of Neurosurgery, Henry Ford Health System, 2799 W Grand Boulevard, Detroit, MI 48202, USA.

Previous studies show that intravascular injection of human bone marrow stromal cells (hBMSCs) significantly improves neurological functional recovery in a rat model of intracerebral hemorrhage (ICH). In the present study, we tested the hypothesis that mannitol improves the efficiency of intraarterial MSC delivery (i.e., fewer injected cells required for therapeutic efficacy) after ICH. There were four post-ICH groups (N=9): group 1, negative control with only intraarterial injection of 1 million human fibroblasts in phosphate-buffered saline (PBS); group 2, intravenous injection of mannitol alone in PBS (1.5 g/kg); group 3, intraarterial injection of 1 million hBMSCs alone in PBS; and group 4, intravenous injection of mannitol (1.5 g/kg) in PBS followed by intraarterial injection of 1 million hBMSCs in PBS. Group 4 exhibited significantly improved neurological functional outcome as assessed by neurological severity score (NSS) and corner test scores. Immunohistochemical staining of group 4 suggested increased synaptogenesis, proliferating immature neurons, and neuronal migration. The number of hBMSCs recruited to the injured region increased strikingly in group 4. Tissue loss was notably reduced in group 4. In summary, the beneficial effects of intraarterial infusion of MSCs are amplified with intravenous injection of mannitol. Preadministration of mannitol significantly increases the number of hBMSCs located in the ICH region, improves histochemical parameters of neural regeneration, and reduces the anatomical and pathological consequences of ICH.

...

Radiation Oncology

Siddiqui, F., P. R. Avery, et al. (2008). "*Induction of the human heat shock promoter HSP70B by nutritional stress: implications for cancer gene therapy.*" *Cancer Invest* **26**(6): 553-61.

Department of Environmental, Colorado State University, Fort Collins, Colorado, USA. fsiddiq1@hfhs.org

BACKGROUND: We designed and tested, in vitro, an adenoviral construct containing the feline interleukin-12 (IL-12) gene under control of the heat-inducible promoter HSP70B. This construct, AdhspIL12, was used in a phase I trial in feline soft tissue sarcomas. During the course of our experiments, we noted that IL-12 was being produced in the transfected Crandell Feline Kidney (CrFK) cells under certain conditions even in the absence of hyperthermia. This observation was further explored to identify the cause of this unintended HSP70B induction. **MATERIALS AND METHODS:** We used real-time PCR as a sensitive method to quantitatively detect the presence of even small amounts of IL-12 mRNA. This served as a surrogate indicator of HSP70B induction. Various conditions were tested to induce the heat shock promoter, including nutritional deprivation, radiation and changes in pH. **RESULTS:** Nutritional stresses, specifically the absence of glucose and glutamine, could induce the heat shock promoter, thus, resulting in production of the downstream gene product. Other factors known to trigger the heat shock response, pH change, and reactive oxygen species production were also studied but were not found to contribute to heat shock promoter induction in our setting. **CONCLUSIONS:** The human heat shock promoter (HSP70B) is reported to be an efficient and tightly regulated promoter. We discovered, using sensitive real-time PCR

techniques, that it can also be induced in response to cellular nutrient stresses. The pros and cons of this phenomenon and its implications for cancer gene therapy are discussed.

...

Surgery

Kakkos, S. K. and A. D. Shepard (2008). "Delayed presentation of aortic injury by pedicle screws: report of two cases and review of the literature." *J Vasc Surg* **47**(5): 1074-82. [PDF Full Text](#)

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI 48202, USA.

OBJECTIVES: Perforation of the aorta by pedicle screws is a rare but serious complication of spine fixation surgery. This article reviews the clinical presentation and management of this complication. **METHODS:** Presented are two cases of thoracic aorta perforation by a pedicle screw and a review of the appropriate literature performed using a MEDLINE search. **RESULTS:** Literature review identified eight additional patients. In most cases, aortic perforation was recognized and managed within 18 months of the spine surgery. Clinical presentation included acute bleeding, necessitating urgent exploration in two patients, and pseudoaneurysm formation in five cases, two of which were infected. Depending on the extent of aortic damage and the presence or absence of infection, management ranged from endovascular grafting, to screw burring with closure of the perforation site, to aortic reconstruction with a tube graft and complete orthopedic hardware removal. Outcome was favorable in all patients who were operated on. **CONCLUSIONS:** The small number of reported cases indicates either the rarity of this complication or unawareness of its existence. The true incidence of this complication is probably under-reported. Orthopedic and vascular surgeons should be aware of this potentially fatal problem. Prevention remains the best treatment. Once encountered, a variety of techniques are available to manage this complication with reasonable outcome.

...

Surgery

Wei, B., M. R. Hemmila, et al. (2008). "Angioembolization reduces operative intervention for blunt splenic injury." *J Trauma* **64**(6): 1472-7. [PDF Full Text](#)

Department of Surgery, Henry Ford Health System Detroit, Michigan, USA.

BACKGROUND: Nonoperative management for blunt splenic injury (BSI) has become gold standard, but the role of angiographic embolization (AE) is still controversial for bleeding. We postulated that splenic AE for BSI would have superior outcomes compared with operation and increase our splenic salvage rate. **METHODS:** This was a retrospective study of all adult trauma patients admitted to our Level I center from 2000 through 2006. Multivariate analysis adjusting for age, Injury Severity Score, and Glasgow Coma Scale score was performed. Only patients who had a computed tomographic (CT) scan before surgery (CT + OR) were compared with those who had CT scans then AE. **RESULTS:** Eighty-seven of 317 patients required initial intervention for their BSI, for a no intervention rate (no OR or AE) of 73% and a nonoperative rate of 89%. The groups had similar Injury Severity Score, mortality, and lengths of stay. The AE group was older ($p < 0.01$), had higher spleen Abbreviated Injury Score ($p = 0.02$), and required significantly fewer packed RBC transfusions, $p < 0.01$. The overall hospitalization costs were not different, but the number of intraabdominal complications was higher for the CT + OR group (36% vs. 6%, $p < 0.01$). Pneumonia, thromboembolic events, and pleural effusions were equivalent. There were no deaths from splenic hemorrhage. **CONCLUSION:** Despite recent concerns that AE may be overutilized for BSI, this study showed a lower incidence of abdominal complications and blood utilization in the AE group despite an older age and higher splenic Abbreviated Injury Score. Use of AE decreased operative intervention by 16%.

...

Urology

Kim, S. H., A. R. Davalos, et al. (2008). "Telomere dysfunction and cell survival: roles for distinct TIN2-containing complexes." *J Cell Biol* **181**(3): 447-60. [PDF Full Text](#)

Life Sciences Division, Lawrence Berkeley National Laboratory, Berkeley, CA 94720, USA. skim3@hfhs.org

Telomeres are maintained by three DNA-binding proteins (telomeric repeat binding factor 1 [TRF1], TRF2, and protector of telomeres 1 [POT1]) and several associated factors. One factor, TRF1-interacting protein 2 (TIN2), binds TRF1 and TRF2 directly and POT1 indirectly. Along with two other proteins, TPP1 and hRap1, these form a soluble complex that may be the core telomere maintenance complex. It is not clear whether subcomplexes also exist in vivo. We provide evidence for two TIN2 subcomplexes with distinct functions in human cells. We isolated these two TIN2 subcomplexes from nuclear lysates of unperturbed cells and cells expressing TIN2 mutants TIN2-13 and TIN2-15C, which cannot bind TRF2 or TRF1, respectively. In cells with wild-type p53 function, TIN2-15C was more potent than TIN2-13 in causing telomere uncapping and eventual growth arrest. In cells lacking p53 function, TIN2-15C was more potent than TIN2-13 in causing telomere dysfunction and cell death. Our findings suggest that distinct TIN2 complexes exist and that TIN2-15C-sensitive subcomplexes are particularly important for cell survival in the absence of functional p53.

...

HFHS Publication List Sladen Library

<http://www.henryfordconnect.com/sliden.cfm?id=436>

If you are interested in receiving this list of HFHS Publications on a monthly basis, please fill out the following information:

Name _____

Department _____

Phone Number _____

Email _____

Do you want to receive it:

_____ Via email (Recommended format – includes links to full-text if available)

_____ Via interdepartmental mail

Please return to:

Valerie Reid
HFH Sladen Library, K-17
(313) 916-2550
(313) 874-4730 Fax
vreid1@sladen.hfhs.org