

# Henry Ford Health System Publication List April 2008

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## Biostatistics & Research Epidemiology

Alexander, G. L., G. W. Divine, et al. (2008). "Effect of incentives and mailing features on online health program enrollment." *Am J Prev Med* **34**(5): 382-8. [PDF Full-Text](#)

Department of Biostatistics and Research Epidemiology, Henry Ford Hospital and Health System, Detroit, MI 48202, USA. [galexan2@hfhs.org](mailto:galexan2@hfhs.org)

**BACKGROUND:** With the growing use of Internet-based interventions, strategies are needed to encourage broader participation. This study examined the effects of combinations of monetary incentives and mailing characteristics on enrollment, retention, and cost effectiveness for an online health program. **METHODS:** In 2004, a recruitment letter was mailed to randomly selected Midwestern integrated health system members aged 21-65 and stratified by gender and race/ethnicity; recipients were randomly pre-assigned to one of 24 combinations of incentives and various mailing characteristics. Enrollment and 3-month retention rates were measured by completion of online surveys. Analysis, completed in 2005, compared enrollment and retention factors using t tests and chi-square tests. Multivariate logistic regression modeling assessed the probability of enrollment and retention. **RESULTS:** Of 12,289 subjects, 531 (4.3%) enrolled online, ranging from 1% to 11% by incentive combination. Highest enrollment occurred with unconditional incentives, and responses varied by gender. Retention rates ranged from 0% to 100%, with highest retention linked to higher-value incentives. The combination of a \$2 bill prepaid incentive and the promise of \$20 for retention (10% enrollment and 71% retention) was optimal, considering per-subject recruitment costs (\$32 enrollment, \$70 retention) and equivalent enrollment by gender and race/ethnicity. **CONCLUSIONS:** Cash incentives improved enrollment in an online health program. Men and women responded differently to mailing characteristics and incentives. Including a small prepaid monetary incentive (\$2 or \$5) and revealing the higher promised-retention incentive was cost effective and boosted enrollment.

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## Biostatistics & Research Epidemiology

Hensley Alford, S., K. Schwartz, et al. (2008). "Breast cancer characteristics at diagnosis and survival among Arab-American women compared to European- and African-American women." *Breast Cancer Res Treat*. Epub Ahead of Print. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, MI, USA.

Background Data from Arab world studies suggest that Arab women may experience a more aggressive breast cancer phenotype. To investigate this finding, we focused on one of the largest settlements of Arabs and Iraqi Christians (Chaldeans) in the US, metropolitan Detroit—a SEER reporting site since 1973. Materials and methods We identified a cohort of primary breast cancer cases diagnosed 1973-2003. Using a validated name algorithm, women were identified as being of Arab/Chaldean descent if they had an Arab last or maiden name. We compared characteristics at diagnosis (age, grade, histology, SEER stage, and marker status)

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and overall survival between Arab-, European-, and African-Americans. Results The cohort included 1,652 (2%) women of Arab descent, 13,855 (18%) African-American women, and 63,615 (80%) European-American women. There were statistically significant differences between the racial groups for all characteristics at diagnosis. Survival analyses overall and for each SEER stage showed that Arab-American women had the best survival, followed by European-American women. African-American women had the poorest overall survival and were 1.37 (95% confidence interval: 1.23-1.52) times more likely to be diagnosed with an aggressive tumor (adjusting for age, grade, marker status, and year of diagnosis). Conclusion Overall, Arab-American women have a distribution of breast cancer histology similar to European-American women. In contrast, the stage, age, and hormone receptor status at diagnosis among Arab-Americans was more similar to African-American women. However, Arab-American women have a better overall survival than even European-American women.

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### **Biostatistics & Research Epidemiology**

Lamerato, L. E., P. M. Marcus, et al. (2008). "Recruitment in the Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial: the First Phase of Recruitment at Henry Ford Health System." Cancer Epidemiol Biomarkers Prev **17**(4): 827-33. [Article Request Form/Click for Article Request Form](#)

Henry Ford Health System, One Ford Place-5C, Detroit, MI 48125. [llamera1@hfhs.org](mailto:llamera1@hfhs.org).

OBJECTIVE: Recruitment of healthy subjects to long-term randomized controlled trials (RCTs) of cancer prevention or early detection has proven to be a difficult task. To quantify recruitment yield as well as characteristics of successfully recruited participants, we examined recruitment outcomes at 1 of the 10 centers participating in the Prostate, Lung, Colorectal and Ovarian (PLCO) Cancer Screening Trial, a National Cancer Institute-funded RCT of cancer screening modalities. MATERIALS AND METHODS: During the early recruitment phase of PLCO (1993-1997), data on recruitment outcome were collected at the Henry Ford Health System (HFHS) in Detroit, Michigan. In this phase, HFHS identified potential participants using patient databases. Records were used to assess recruitment success by age, sex, race, household income (using area-based U.S. Census data), and preexisting morbidity. Logistic regression was used to assess whether enrollment success differed significantly according to these factors. RESULTS: Of 74,139 persons ages 55 to 74 invited by HFHS to participate, 8,250 (11%) ;enrolled. In multivariate analyses, the odds of enrolling were modestly but significantly higher for women, Caucasians, persons in their 60's, and persons living in census blocks with higher median household income. Persons with two or more preexisting morbidities had significantly lower odds of enrolling compared to those with one or no preexisting morbidities. CONCLUSIONS: These data suggest that only a small fraction of persons invited to enroll in long-term RCTs of cancer screening modalities actually do so. In this urban, Midwestern setting, certain characteristics including age, race, and income influenced recruitment success, albeit modestly. (Cancer Epidemiol Biomarkers Prev 2008;17(4):827-33).

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### **Biostatistics & Research Epidemiology**

Lu, M., R. L. Zhang, et al. (2008). "The linkage of neural progenitor cell cycle profiles between embryonic and adult stroke models: Analytical approach II." J Neurosci Methods **167**(2): 376-83. [PDF Full-Text](#)

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Cell kinetics employed for embryonic models was modified and used to study the neuronogenesis in the subventricular zone (SVZ) in adult rats subjected to stroke. Enhanced analytical approaches were introduced and used to compare the cell cycle length (T(C)) and length in G(1) phase, T(G1), at various times after stroke to study the correlation between T(G1) and T(C) and to compare cell cycle evolution and proliferation profiles between the stroke and embryonic models. Our data indicate that cell cycle kinetics for the embryonic model can be applied to stroke in the adult. Significant reduction of T(G1) early after stroke ( $p < 0.05$ ) corresponds to an increase of neural progenitor cells remaining in the cycle at early times and cells exiting at later times. T(G1) correlates with T(C) ( $r = 0.99$ ,  $p < 0.05$ ). In conclusion, the analytical approaches proposed can be used to study the cell proliferation profiles in adult rats subjected to stroke with and without stroke therapy. The cell kinetics the cell proliferation profile differs between the stroke and embryonic models. T(C) evolution is three-fold slower in the cells and leave the cycle earlier and more frequently in the stroke model, compared to the embryonic model. T(C) is a surrogate measure of T(G1).

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## Biostatistics & Research Epidemiology

Wegienka, G., S. Havstad, et al. (2008). "Birth order and cord immunoglobulin E: results using a high-sensitivity immunoglobulin E protocol." *Int Arch Allergy Immunol* **145**(4): 305-12. [Article Request Form/Click for Article Request Form](#)

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BACKGROUND: Studies have shown an inverse association between birth order and allergic disease risk; some but not all have shown an inverse association between cord blood immunoglobulin E (IgE) and birth order. We further examined the relationship between birth order and cord blood IgE in a racially diverse birth cohort. METHODS: Women were interviewed about their pregnancy history, and their babies' cord blood was collected to measure total IgE using a high-sensitivity protocol (lower detection limit 0.01 IU/ml). We analyzed cord IgE as both a continuous and categorical measure. RESULTS: Of the 733 children, 171 (23%) were first born, 92 (13%) were first born with the mother having prior pregnancies but no live births, and 470 (64%) were born second or later. By birth order, the geometric means +/- standard deviations were: first born 0.26 +/- 4.2 IU/ml, first born after prior pregnancies 0.35 +/- 3.9 IU/ml, second born 0.30 +/- 4.8 IU/ml, third born 0.28 +/- 5.1 IU/ml, and fourth born or greater 0.28 +/- 4.5 IU/ml (trend p = 0.51). Other factors considered (maternal allergic disease history, age, race, exposure to smoking and cats/dogs during pregnancy, fetal gender, season of delivery) neither modified nor confounded these relationships. CONCLUSIONS: Unlike some previous reports, there was no association between total cord IgE level and birth order. Mechanisms other than cord IgE should be studied in the quest to understand the role of birth order in allergic disease risk. Categorization of a continuous measure of IgE may incorrectly create statistically significant results.

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## Biostatistics & Research Epidemiology

Strecher, V. J., J. B. McClure, et al. (2008). "Web-based smoking-cessation programs: results of a randomized trial." *Am J Prev Med* **34**(5): 373-81. [PDF Full-Text](#)

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BACKGROUND: Initial trials of web-based smoking-cessation programs have generally been promising. The active components of these programs, however, are not well understood. This study aimed to (1) identify active psychosocial and communication components of a web-based smoking-cessation intervention and (2) examine the impact of increasing the tailoring depth on smoking cessation. DESIGN: Randomized fractional factorial design. SETTING: Two HMOs: Group Health in Washington State and Henry Ford Health System in Michigan. PARTICIPANTS: 1866 smokers. INTERVENTION: A web-based smoking-cessation program plus nicotine patch. Five components of the intervention were randomized using a fractional factorial design: high- versus low-depth tailored success story, outcome expectation, and efficacy expectation messages; high- versus low-personalized source; and multiple versus single exposure to the intervention components. MEASUREMENTS: Primary outcome was 7 day point-prevalence abstinence at the 6-month follow-up. FINDINGS: Abstinence was most influenced by high-depth tailored success stories and a high-personalized message source. The cumulative assignment of the three tailoring depth factors also resulted in increasing the rates of 6-month cessation, demonstrating an effect of tailoring depth. CONCLUSIONS: The study identified relevant components of smoking-cessation interventions that should be generalizable to other cessation interventions. The study also demonstrated the importance of higher-depth tailoring in smoking-cessation programs. Finally, the use of a novel fractional factorial design allowed efficient examination of the study aims. The rapidly changing interfaces, software, and capabilities of eHealth are likely to require such dynamic experimental approaches to intervention discovery.

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## Cardiology / Cardiovascular Research

McCord, J., H. Jneid, et al. (2008). "Management of cocaine-associated chest pain and myocardial infarction: a scientific statement from the American Heart Association Acute Cardiac Care Committee of the Council on Clinical Cardiology." *Circulation* **117**(14): 1897-907. [PDF Full-Text](#)

Henry Ford Hospital.

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### **Dermatology**

Kouba, D. J., E. F. Fincher, et al. (2008). "Crescentic complex closure of perialar upper lip defects." Dermatol Surg **34**(4): 561-6. [PDF Full-Text](#)

Department of Dermatology of the Henry Ford Health System, Detroit, Michigan, USA.

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### **Dermatology**

Mahmoud, B. H. (2008). "Prospective controlled study of the efficacy of Nd:YAG for hidradenitis suppurativa." J Am Acad Dermatol: P3000. [Article Request Form/Click for Article Request Form](#)

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.

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### **Dermatology**

Mahmoud, B. H. (2008). "Impact of long wavelength UVA and visible light on melanocompetent skin." J Am Acad Dermatol: P2420. [Article Request Form/Click for Article Request Form](#)

Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.

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### **Dermatology**

Mahmoud, B. H., C. L. Hexsel, et al. (2008). "An update on new and emerging options for the treatment of vitiligo." Skin Therapy Lett **13**(2): 1-6. [Article Request Form/Click for Article Request Form](#)

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

Vitiligo is an acquired leukoderma that results from the loss of epidermal melanocytes, and is characterized by macules and patches of depigmented skin. With a relatively high rate of prevalence, vitiligo occurs in localized, generalized, or segmental patterns; it can run a rapidly progressive course or remain stationary. The pathogenesis of vitiligo is not yet fully understood, but the autoimmune hypothesis is the most commonly accepted one, based on which, many treatment modalities have been described. Although many therapeutic options exist and new modalities are still emerging, treatment challenges persist, as not all patients respond to available therapies. Variables that affect the choice of treatment include the extent, distribution, and progression rate of the lesions. Another challenge is the lack of a standardized scoring system, which hampers the production of level 1a evidence studies for the treatment of this condition.

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### **Diagnostic Radiology**

Ellika, S. K., S. C. Payne, et al. (2008). "Acute calcific tendinitis of the longus colli: an imaging diagnosis." Dentomaxillofac Radiol **37**(2): 121-4. [Article Request Form/Click for Article Request Form](#)

Division of Neuroradiology, Department of Radiology, Henry Ford Hospital, Detroit, MI 48202, USA.

Acute calcific retropharyngeal tendinitis or longus colli tendinitis is an uncommon benign condition presenting as acute neck pain. Clinically, it can be misdiagnosed as retropharyngeal abscess, traumatic injury, or infectious spondylitis. The diagnosis is made radiographically by calcification anterior to C1-C2 and prevertebral soft-tissue swelling. We present two cases of this uncommon condition to illustrate the classic findings on CT and MRI. In addition to the typical calcifications

anterior to C1-C2, we detected a retropharyngeal effusion in both patients and effusions involving both lateral atlantoaxial joints in one patient, which to our knowledge has not been published in the literature. In both patients, the correct diagnosis was established by prospective review of the radiographic studies. Recognition of the pathognomonic imaging appearance allows for easy diagnosis preventing unnecessary tests and treatment.

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## Emergency Medicine

Miller, J. B., M. W. Donnino, et al. (2008). "Relative adrenal insufficiency in post-cardiac arrest shock is under-recognized." *Resuscitation* **76**(2): 221-5. [PDF Full-Text](#)

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INTRODUCTION: Suppression of the adrenal axis may occur frequently in post-cardiac arrest patients. Physiological doses of corticosteroids have been shown to reverse hypotension and decrease mortality in other forms of shock. We sought to investigate current clinical practice pertaining to the evaluation for relative adrenal insufficiency in post-cardiac arrest shock. METHODS: We performed a retrospective analysis of post-cardiac arrest patients in an urban emergency department. Inclusion criteria included pre-hospital cardiac arrest patients over the age of 18 with a sustained return of spontaneous circulation that required vasopressor support. Exclusion criteria were traumatic arrest and cardiac arrest in the presence of healthcare personnel. The primary endpoint was the percent of patients in refractory shock that either had their adrenal axis tested or were treated for presumed relative adrenal insufficiency. Data analysis was descriptive in nature. RESULTS: A total of 79 post-cardiac arrest patients were analyzed. Of the 79 patients, 69 were vasopressor-dependent. Of this group, 13% (9/69) had a cortisol level checked (with or without cosyntropin stimulation). Of those who had a cosyntropin stimulation test performed, 86% met biochemical criteria for relative adrenal insufficiency. Seventeen percent of vasopressor-dependent patients received corticosteroids explicitly for their shock state. Overall, only 32% of patients in refractory shock had testing for relative adrenal insufficiency or received corticosteroids for shock. CONCLUSIONS: Though vasopressor-dependent shock is common in post-cardiac arrest patients, adrenal insufficiency was not considered in the majority of cases.

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## Emergency Medicine

Rivers, E. P. (2008). "Volume therapy and innate immune response during systemic inflammation or sepsis." *Crit Care Med* **36**(3): 1028-9. [PDF Full-Text](#)

Department of Emergency Medicine, Emergency Medicine and Surgery (Critical Care), Henry Ford Health Systems, Detroit, MI.

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## Endocrinology & Metabolism

Zee, R. Y., S. Germer, et al. (2008). "C-reactive protein gene variation and type 2 diabetes mellitus: a case-control study." *Atherosclerosis* **197**(2): 931-6. [Article Request Form/Click for Article Request Form](#)

Center for Cardiovascular Disease Prevention, Brigham and Women's Hospital and Harvard Medical School, 900 Commonwealth Avenue East, Boston, MA 02215, USA. [rzee@rics.bwh.harvard.edu](mailto:rzee@rics.bwh.harvard.edu)

OBJECTIVE: C-reactive protein (CRP) gene variation, in particular an rs2794521 variant was recently associated with type 2 diabetes mellitus (T2DM) in Pima Indians. RESEARCH DESIGN AND METHODS: The present investigation was conducted to replicate this previous association, and to further examine the potential association of a set of common CRP gene variants with the prevalence of T2DM in a case-control investigation. A total of 629 T2DM cases (476 Whites, and 153 Blacks), and 579 controls (481 Whites, and 98 Blacks) were examined. Seven CRP variants were evaluated: rs3093059, rs2794521, rs3091244, rs1417938, rs1800947, rs1130864, and rs1205. RESULTS: Using a marker-by-marker logistic regression analysis, adjusting for age, smoking, gender, and body mass index, we found an association of rs3093059 (recessive: OR, 7.01; 95% CI, 1.16-42.22; p=0.03) with T2DM in the white study population, and an association, albeit not statistically significant, of rs2794521 with T2DM in the Black study population. Moreover, further analysis using a haplotype-based analysis showed no evidence

for an association of the haplotypes tested with T2DM. CONCLUSION: Further studies are needed to examine the possible involvement of C-reactive protein gene variation in the pathogenesis of type 2 diabetes mellitus.

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### **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): 488-493. [PDF Full-Text](#)

Henry Ford Health System, Ophthalmology, Troy, MI; and Department of Ophthalmology, University of Minnesota, Minneapolis, MN.

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.

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### **Hematology, Medical Oncology & Josephine Ford Cancer Center**

Dabak, V., P. Kuriakose, et al. (2007). "Successful management of a Jehovah's Witness with thrombotic thrombocytopenic purpura unwilling to be treated with therapeutic plasma exchange." *J Clin Apher* **22**(6): 330-2. [PDF Full-Text](#)

Department of Hematology-Oncology, Henry Ford Hospital, Detroit, Michigan 48202, USA. [vdabak1@hfhs.org](mailto:vdabak1@hfhs.org)

Thrombotic thrombocytopenic purpura (TTP) is a life-threatening disease treated successfully with plasma exchange. Jehovah's Witnesses whose religious beliefs preclude them from accepting plasma exchange may require alternative forms of therapy. We report a case of one such patient who presented with TTP, whom we successfully managed with vincristine and responded favorably without the need for plasma exchange.

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### **Hematology, Medical Oncology & Josephine Ford Cancer Center**

Hammoud, R., S. H. Patel, et al. (2008). "Examining margin reduction and its impact on dose distribution for prostate cancer patients undergoing daily cone-beam computed tomography." *Int J Radiat Oncol Biol Phys* **71**(1): 265-73. [PDF Full-Text](#)

Josephine Ford Downriver Center for Oncology, Henry Ford Health System, Brownstown, MI.

PURPOSE: To examine the dosimetric impact of margin reduction and quantify residual error after three-dimensional (3D) image registration using daily cone-beam computed tomography (CBCT) for prostate cancer patients. METHODS AND MATERIALS: One hundred forty CBCTs from 5 prostate cancer patients were examined. Two intensity-modulated radiotherapy plans were generated on CT simulation on the basis of two planning target volume (PTV) margins: 10 mm

all around the prostate and seminal vesicles except 6 mm posteriorly (10/6) and 5 mm all around except 3 mm posteriorly (5/3). Daily CBCT using the Varian On-Board Imaging System was acquired. The 10/6 and 5/3 simulation plans were overlaid onto each CBCT, and each CBCT plan was calculated. To examine residual error, PlanCT/CBCT intensity-based 3D image registration was performed for prostate localization using center of mass and maximal border displacement. RESULTS: Prostate coverage was within 2% between the 10/6 and 5/3 plans. Seminal vesicle coverage was reduced with the 5/3 plan compared with the 10/6 plan, with coverage difference within 7%. The 5/3 plan allowed 30-50% sparing of bladder and rectal high-dose regions. For residual error quantification, center of mass data show that 99%, 93%, and 96% of observations fall within 3 mm in the left-right, anterior-posterior, and superior-inferior directions, respectively. Maximal border displacement observations range from 79% to 99%, within 5 mm for all directions. CONCLUSION: Cone-beam CT dosimetrically validated a 10/6 margin when soft-tissue localization is not used. Intensity-based 3D image registration has the potential to improve target localization and to provide guidelines for margin definition.

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### **Hematology, Medical Oncology & Josephine Ford Cancer Center**

Yood, M. U., C. P. Quesenberry, Jr., et al. (2008). "Incidence of hepatocellular carcinoma among individuals with hepatitis B virus infection identified using an automated data algorithm." *J Viral Hepat* **15**(1): 28-36. [PDF Full-Text](#)

Josephine Ford Cancer Center, Henry Ford Health System, Detroit, MI, USA. [muyood@muyood.com](mailto:muyood@muyood.com)

The purpose of this study was to develop an algorithm for identifying patients with chronic hepatitis B virus (HBV) using automated data sources from two US health systems and evaluate the algorithm's performance by quantifying the incidence of hepatocellular carcinoma (HCC) among chronic HBV patients. To allow comparisons with estimates from automated databases that may not contain all data elements used in this algorithm, we created three definitions of chronic HBV infection and used these definitions to create three overlapping cohorts. We compared the incidence of HCC in each cohort with the incidence of HCC in a matched general population comparison cohort with no evidence of HBV. Patients who met the most stringent criteria for chronic HBV infection (based on the standard definition of 6 months of infection using repeat laboratory tests and record review) were 146 times more likely to develop HCC than matched comparison patients (adjusted hazard ratio = 146.5, 95% CI: 74.0-289.8). Those not meeting the stringent criteria, but who met the criterion of at least one positive hepatitis B surface antigen test were 30 times more likely to develop HCC than comparison patients (adjusted hazard ratio = 29.8, 95% CI: 16.5-53.6). Finally, patients who met the criterion based on at least one HBV diagnosis were 38 times more likely to develop HCC than matched comparison patients (adjusted hazard ratio = 37.8, 95% CI: 25.9-55.1). The magnitude of the relative increase in HCC risk seen using different criteria used to define HBV infection indicate that these automated data algorithms can identify patients with chronic HBV infection.

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### **Hypertension & Vascular Research**

Zhuo, J. L. (2008). "Intrarenal Perfusion and Angiotensin II Levels Regulate In Vivo Angiotensin II Type 1 Receptor Imaging in the Kidney." *Hypertension*. [Article Request Form/Click for Article Request Form](#)

Laboratory of Receptor and Signal Transduction, Division of Hypertension and Vascular Research, Department of Internal Medicine, Henry Ford Hospital, Detroit, Mich.

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### **Nephrology**

Kilpatrick, R. D., C. W. Critchlow, et al. (2008). "Greater Epoetin alfa Responsiveness Is Associated With Improved Survival in Hemodialysis Patients." *Clin J Am Soc Nephrol*. [Article Request Form/Click for Article Request Form](#)

Departments of Biostatistics & Epidemiology, Clinical Development, and Medical Affairs, Amgen Inc, Thousand Oaks, California; Division of Nephrology & Hypertension, Department of Medicine, SUNY at Stony

Brook, Stony Brook, New York; and Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, Michigan.

**BACKGROUND AND OBJECTIVES:** Among hemodialysis patients, achieved hemoglobin is associated with Epoetin alfa dose and erythropoietin responsiveness. A prospective erythropoietin responsiveness measure was developed and its association with mortality evaluated. **DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:** Data from 321 participants were used and randomized to the hematocrit normalization arm of the Normal Hematocrit Cardiac Trial. Subjects were to receive a 50% Epoetin alfa dose increase at randomization. The prospective erythropoietin responsiveness measure was defined as the ratio of weekly hematocrit change (over the 3 wk after randomization) per Epoetin alfa dose increase (1000 IU/wk) corresponding to the mandated 50% dose increase at randomization. The distribution of responsiveness was divided into quartiles. Over a 1-yr follow-up, Cox proportional hazard modeling evaluated associations between this responsiveness measure and mortality. **RESULTS:** Erythropoietin responsiveness values ranged from -2.1% to 2.4% per week per 1000 IU. Although subjects were similar across response quartiles, mortality ranged between 14% and 34% among subjects in the highest and lowest response quartiles ( $P = 0.0004$ ), respectively. After adjusting for baseline prognostic indicators, highest versus lowest responsiveness was associated with a hazard ratio of 0.41 (95% confidence interval, 0.20 to 0.87). **CONCLUSION:** Lower erythropoietin responsiveness is a strong, independent predictor of mortality risk and should be considered when evaluating associations between clinical outcomes and potential prognostic indicators, such as Epoetin alfa dose and achieved hemoglobin values.

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### **Nephrology**

Yee, J. (2008). "From research to practice: Diabetic kidney disease: Chronic kidney disease and diabetes: Preface." *Diabetes Spectrum* **21**(1): 8-10. [PDF Full-Text](#)

Chief, Division of Nephrology and Hypertension, Henry Ford Hospital, Detroit, Michigan.

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### **Neurology**

Chopp, M., Y. Li, et al. (2008). "Plasticity and remodeling of brain." *J Neurol Sci* **265**(1-2): 97-101. [PDF Full-Text](#)

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The injured brain can be stimulated to amplify its intrinsic restorative processes to improve neurological function. Thus, after stroke, both cell and pharmacological neurorestorative treatments, amplify the induction of brain neurogenesis and angiogenesis, and thereby reduce neurological deficits. In this manuscript, we describe the use of bone marrow mesenchymal cells (MSCs) and erythropoietin (EPO) as examples of cell-based and pharmacological neurorestorative treatments, respectively, for both stroke and a mouse model of experimental autoimmune encephalomyelitis (EAE). We demonstrate that these therapies significantly improve neurological function with treatment initiated after the onset of injury and concomitantly promote brain plasticity. The application of MRI to monitor changes in the injured brain associated with reduction of neurological deficit is also described.

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### **Neurology**

Ding, G., Q. Jiang, et al. (2008). "Magnetic resonance imaging investigation of axonal remodeling and angiogenesis after embolic stroke in sildenafil-treated rats." *J Cereb Blood Flow Metab*. **Article Request Form/Click for Article Request Form**

Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA.

Interaction between angiogenesis and axonal remodeling after stroke was dynamically investigated by MRI in rats with or without sildenafil treatments. Male Wistar rats were subjected to embolic stroke and treated daily with saline ( $n=10$ ) or with sildenafil ( $n=11$ ) initiated at 24 h and subsequently for 7 days after onset of ischemia. T(2)(\*)-weighted imaging,

cerebral blood flow (CBF), and diffusion tensor imaging (DTI) measurements were performed from 24 h to 6 weeks after embolization. T2(\*) and fractional anisotropy (FA) maps detected angiogenesis and axonal remodeling after stroke, respectively, starting from 1 week in sildenafil-treated rats. Areas demarcated by MRI with enhanced angiogenesis, elevated local CBF, and augmented axonal remodeling were spatially and temporally matched, and FA values were significantly correlated with the corresponding CBF values ( $R=0.66$ ,  $P<4 \times 10^{-5}$ ) at 6 weeks after stroke. Axonal projections were reorganized along the ischemic boundary after stroke. These MRI measurements, confirmed by histology, showed that sildenafil treatment simultaneously enhanced angiogenesis and axonal remodeling, which were MRI detectable starting from 1 week after stroke in rats. The spatial and temporal consistency of MRI metrics and the correlation between FA and local CBF suggest that angiogenesis, by elevating local CBF, promotes axonal remodeling after stroke. *Journal of Cerebral Blood Flow & Metabolism* advance online publication, 16 April 2008; doi:10.1038/jcbfm.2008.33.

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## Neurology

Katramados, A., R. Rabah, et al. (2008). "Longitudinal myelitis, aseptic meningitis, and conus medullaris infarction as presenting manifestations of pediatric systemic lupus erythematosus." *Lupus* **17**(4): 332-6. [PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA.

A healthy boy developed subacutely progressive quadriplegia, complicated by sudden paraplegia, fever, and meningeal signs, diagnosed as longitudinal myelitis, aseptic meningitis, and conus medullaris infarction and identified as the presenting manifestations of neuropsychiatric systemic lupus erythematosus. Rapid expansion of the conus on serial neuroimaging led to emergent decompressive laminectomy and cord biopsy showing vasculitis and cord infarction. The patient had partial recovery after treatment with high-dose steroids. Increased vigilance is required when pediatric patients develop a similar subacute presentation on the ground of active systemic lupus erythematosus because it may herald the onset of a catastrophic neurological syndrome.

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## Neurology

LeWitt, P. A., M. Guttman, et al. (2008). "Adenosine A2A receptor antagonist istradefylline (KW-6002) reduces "off" time in Parkinson's disease: a double-blind, randomized, multicenter clinical trial (6002-US-005)." *Ann Neurol* **63**(3): 295-302. [PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, Southfield, MI 48034, USA. [palewitt@ameritech.net](mailto:palewitt@ameritech.net)

**OBJECTIVE:** Based on new understanding of nondopaminergic pathways involved in Parkinson's disease (PD) pathophysiology, a selective adenosine A<sub>2A</sub> receptor antagonist, istradefylline, shows promise for the treatment of PD. **METHODS:** Istradefylline (40mg/day) was studied in levodopa-treated PD subjects experiencing prominent wearing-off motor fluctuations. At 23 North American sites, 196 subjects were randomized in a double-blind, 12-week outpatient clinical trial of istradefylline (114 completing the trial) or placebo (58 completing the trial). The primary efficacy measure was change from baseline to end point in the percentage of daily awake "off" time, recorded by subjects using a patient PD diary. Secondary end points evaluated "on" time (including "on time with dyskinesia"), the Unified Parkinson's Disease Rating Scale, and a Clinical Global Impression-Improvement of Illness score. Clinical laboratory, electrocardiograms, vital signs, and adverse event monitoring comprised the safety monitoring. **RESULTS:** After randomization, approximately 88% of subjects completed the double-blind period. Compared with baseline, the decrease of daily awake "off" time for istradefylline was a mean (+/- standard deviation) of -10.8 +/- 16.6% (95% confidence interval, -13.46 to -7.52) and for placebo, -4.0 +/- 15.7% (95% confidence interval, -7.73-0.31;  $p = 0.007$  using two-way analysis of variance). This effect corresponded to changes from baseline in total daily awake "off" time of -1.8 +/- 2.8 hours for istradefylline and -0.6 +/- 2.7 hours for placebo ( $p = 0.005$ ). Treatment-emergent adverse effects with istradefylline were generally mild. **INTERPRETATION:** Istradefylline was safe, well tolerated, and offered a clinically meaningful reduction in "off" time without increased troublesome dyskinesia.

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## Neurology

LeWitt, P. A. and D. C. Taylor (2008). "Protection against Parkinson's disease progression: clinical experience." *Neurotherapeutics* 5(2): 210-25. **Article Request Form/Click for Article Request Form**

Department of Neurology, Henry Ford Hospital, Detroit, Michigan, USA. [palewitt@ameritech.net](mailto:palewitt@ameritech.net)

Treatments with potential neuroprotective capability for Parkinson's disease (PD) have been investigated in randomized, controlled, clinical trials and other studies since the mid-1980s. Although promising leads have arisen, no therapy has been proven to halt or slow disease progression. Several large-scale studies have highlighted progress in methodology, as well as the frustrations of translating laboratory science to practical applications. This review summarizes findings from clinical trials with several classes of compounds, including monoamine oxidase-B inhibitors (selegiline, lazabemide, rasagiline), dopaminergic drugs (ropinirole, pramipexole, levodopa), antioxidant strategies (alpha-tocopherol), mitochondrial energy enhancers (coenzyme Q(10), creatine), antiapoptotic agents (TCH346, minocycline, CEP-1347), and antiglutamatergic compounds (riluzole). Beyond small-molecule pharmacology, gene therapy approaches, such as delivering neurotrophic substances (e.g., neurturin) by viral vector, are the next generation of treatment options.

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## Neurology

Liu, Z., Y. Li, et al. (2008). "Evaluation of corticospinal axon loss by fluorescent dye tracing in mice with experimental autoimmune encephalomyelitis." *J Neurosci Methods* 167(2): 191-7. **Article Request Form/Click for Article Request Form**

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

In both multiple sclerosis (MS) patients and experimental autoimmune encephalomyelitis (EAE) animals, axon loss has been demonstrated to correlate with neurological disability. However, it is difficult to accurately determine the location and severity of axonal damage since the lesion in MS or EAE is disseminated and is frequently in a relapsing-remitting mode. The corticospinal system is the only direct pathway from the motor sensory cortex to the spinal cord, and the major neural pathway for control of voluntary movement. Moreover, it is frequently involved in the pathological process of the disease. To evaluate corticospinal tract (CST) axon loss in EAE mice, we developed a direct tracing method with a fluorescent neuronal tracer Dil which was injected into the primary motor cortex and sensorimotor cortex to label the pyramidal neurons. The lesion location in the spinal cord and axon disruption were indicated by dye leakage. Using the EAE induced axon reduction as an index of the extent of axonal damage, our data showed a high correlation between the axonal loss and the behavioral outcome score in the EAE mice. The results were consistent with the axonal Bielschowsky silver staining. Thus, this CST tracing method permits monitoring of the axonal damage in EAE.

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## Neurology

Wang, L., M. Chopp, et al. (2008). "Neural progenitor cells treated with EPO induce angiogenesis through the production of VEGF." *J Cereb Blood Flow Metab.* **Article Request Form/Click for Article Request Form**

Department of Neurology, Henry Ford Health Sciences Center, Detroit, Michigan, USA.

Recombinant human erythropoietin (rhEPO) induces neurogenesis and angiogenesis. Using a coculture system of mouse brain endothelial cells (MBECs) and neural progenitor cells derived from the subventricular zone of adult mouse, we investigated the hypothesis that neural progenitor cells treated with rhEPO promote angiogenesis. Treatment of neural progenitor cells with rhEPO significantly increased their expression and secretion of vascular endothelial growth factor (VEGF) and activated phosphatidylinositol 3-kinase/Akt (PI3K/Akt) and extracellular signal-regulated kinase (ERK1/2). Selective inhibition of the Akt and ERK1/2 signaling pathways significantly attenuated the rhEPO-induced VEGF expression in neural progenitor cells. The supernatant harvested from neural progenitor cells treated with rhEPO significantly increased the capillary-like tube formation of MBECs. SU1498, a specific VEGF type-2 receptor (VEGFR2) antagonist, abolished the supernatant-enhanced angiogenesis. In addition, coculture of MBECs with neural progenitor cells treated with rhEPO substantially increased VEGFR2 mRNA and protein levels in MBECs. These in vitro results suggest that EPO enhances VEGF

secretion in neural progenitor cells through activation of the PI3K/Akt and ERK1/2 signaling pathways and that neural progenitor cells treated with rhEPO upregulate VEGFR2 expression in cerebral endothelial cells, which along with VEGF secreted by neural progenitor cells promotes angiogenesis. *Journal of Cerebral Blood Flow & Metabolism* advance online publication, 16 April 2008; doi:10.1038/jcbfm.2008.32.

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## Neurosurgery

Darbar, A., P. D. Kim, et al. (2008). "Use of grotenhuis perforator in endoscopic third ventriculostomy and cyst fenestration." *Minim Invasive Neurosurg* **51**(2): 126-9. **Article Request Form/Click for Article Request Form**

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

We performed a retrospective review of consecutive patients at our institution who underwent endoscopic third ventriculostomy (E3 V) or fenestration of intraventricular cysts using the Grotenhuis endoscopic perforator. The procedure was performed on 23 patients between 2001 and 2006, and included 20 E3Vs and three intraventricular cyst fenestrations. The Grotenhuis perforator was effective in accomplishing a fenestration with multiple attempts. When the floor of the third ventricle was translucent, the perforator was effective with the least amount of effort. The instrument was less effective and additional instruments were necessary in patients with arachnoid cysts or when the floor of the third ventricle was thick. The main advantage in using the Grotenhuis perforator was in displacing the floor of the third ventricle away from the basilar artery during perforation. No basilar artery injury or other serious complications occurred in patients who underwent E3 V or cyst fenestration using the Grotenhuis perforator.

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## Neurosurgery

Lee, H. K., C. Xiang, et al. (2008). "GRP78 is overexpressed in glioblastomas and regulates glioma cell growth and apoptosis." *Neuro Oncol*. **Article Request Form/Click for Article Request Form**

Department of Neurosurgery and Hermelin Brain Tumor Center, Henry Ford Health System, Detroit, MI, USA.

We characterized the expression and function of the endoplasmic reticulum protein GRP78 in glial tumors. GRP78 is highly expressed in glioblastomas but not in oligodendrogliomas, and its expression is inversely correlated with median patient survival. Overexpression of GRP78 in glioma cells decreases caspase 7 activation and renders the cells resistant to etoposide- and cisplatin-induced apoptosis, whereas silencing of GRP78 decreases cell growth and sensitizes glioma cells to etoposide, cisplatin, and Upsilon-radiation. Thus, GRP78 contributes to the increased apoptosis resistance and growth of glioma cells and may provide a target for enhancing the therapeutic responsiveness of these tumors.

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## Neurosurgery

Lomonaco, S. L., S. Kahana, et al. (2008). "Phosphorylation of PKCdelta on distinct tyrosine residues induces sustained activation of Erk1/2 via downregulation of MKP-1: role in the apoptotic effect of etoposide." *J Biol Chem*. Epub Ahead of Print. **PDF Full-Text**

Neurosurgery, Henry Ford Hospital, Detroit, MI 48202.

The mechanism underlying the important role of protein kinase Cdelta in the apoptotic effect of etoposide in glioma cells is incompletely understood. Here, we examined the role of PKCdelta in the activation of Erk1/2 by etoposide. We found that etoposide induced persistent activation of Erk1/2 and nuclear translocation of phospho-Erk1/2. MEK1 inhibitors decreased the apoptotic effect of etoposide, whereas inhibitors of p38 and JNK did not. The activation of Erk1/2 by etoposide was downstream of PKCdelta since the phosphorylation of Erk1/2 was inhibited by a PKCdelta-KD mutant and PKCdelta siRNA. We recently reported that phosphorylation of PKCdelta on tyrosines 64 and 187 was essential for the apoptotic effect of etoposide. Using PKCdelta tyrosine mutants, we found that the phosphorylation of PKCdelta on these tyrosine residues, but not on tyrosine 155, was also essential for the activation of Erk1/2 by etoposide. In contrast, nuclear translocation of PKCdelta was independent of its tyrosine phosphorylation and not necessary for the phosphorylation of Erk1/2. Etoposide

induced down-regulation of MKP-1 which correlated with persistent phosphorylation of Erk1/2 and was dependent on the tyrosine phosphorylation of PKCdelta. Moreover, silencing of MKP-1 increased the phosphorylation of Erk1/2 and the apoptotic effect of etoposide. Etoposide induced polyubiquitylation and degradation of MKP-1 that was dependent on PKCdelta and on its tyrosine phosphorylation. These results indicate that distinct phosphorylation of PKCdelta on tyrosines 64 and 187 specifically activates the Erk1/2 pathway by the down-regulation of MKP-1, resulting in the persistent phosphorylation of Erk1/2 and cell apoptosis.

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### Neurosurgery

Qu, C., A. Mahmood, et al. (2008). "Treatment of traumatic brain injury in mice with marrow stromal cells." Brain Res **1208**: 234-9. [PDF Full-Text](#)

Department of Neurosurgery, Henry Ford Health System, Detroit, MI, USA; Department of Neurology, Henry Ford Health System, Detroit, MI, USA.

This study was designed to investigate the potential beneficial effects of bone marrow stromal cell (MSC) treatment of traumatic brain injury (TBI) in mice. Twelve female C57BL/6J mice (weight, 21-26 g) were injured with controlled cortical impact and divided into 2 groups (n=6 each). The experimental group was injected with MSCs ( $0.3 \times 10^6$ ) intravenously one day after TBI, whereas the control group was injected with saline. MSCs were harvested from male mice, and male to female transplantation was performed to identify male donor cells within female recipient animals. This was achieved by localizing Y chromosomes within the female mice. Neurological function was assessed using the Morris water maze and foot fault tests. All mice were sacrificed 35 days after TBI. Brain sections were stained using in situ hybridization and immunohistochemistry to identify MSCs as well as to analyze vascular density following MSC treatment. Both modalities of testing demonstrated significant improvement in neurological function in the MSC-treated group compared to the saline-treated control group ( $p < 0.05$ ). Histologically, Y chromosome labeled MSCs were easily identified in the injured brain, localized primarily around the lesion boundary zone. There was also a significant increase in vascular density in the lesion boundary zone and hippocampus of MSC-treated mice compared to control mice. This is the first study to show beneficial effects of MSC treatment after TBI in mice.

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### Other

Sircy, R. A. and A. Stojanoski (2008). "ADHD treatment and the risk of substance abuse." Nurse Pract **33**(4): 33-6. [PDF Full-Text](#)

Ruth A. Sircy is a Staff Nurse at Henry Ford Health System, Sterling Heights, Mich. Aco Stojanoski is a Staff Nurse at Henry Ford Health System, West Bloomfield, Mich.

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### Other

Szpunar, S., P. Williams, et al. (2008). "Improving the documentation of vital signs: a business reengineering efficiency study." Jt Comm J Qual Patient Saf **34**(3): 171-8, 125. [PDF Full-Text](#)

Clinical Systems Research & Integration, Information Technology, Henry Ford Health System, Detroit, USA.  
[Susan.Szpunar@stjohn.org](mailto:Susan.Szpunar@stjohn.org)

By upgrading its electronic medical record to include a Quick Vitals screen, the Henry Ford Health System increased the mean rate of entry of vital signs from 0.7% to 58.5%.

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### Otolaryngology

Seidman, M. D., D. D. Ridder, et al. (2008). "Direct electrical stimulation of Heschl's gyrus for tinnitus treatment." Laryngoscope **118**(3): 491-500. [PDF Full-Text](#)

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, MI 48323, USA.  
[mseidma1@hfhs.org](mailto:mseidma1@hfhs.org)

OBJECTIVES/HYPOTHESIS: The purpose of the study was to determine the effect of electrical stimulation of the auditory cortex in patients with tinnitus. STUDY DESIGN: Nonrandomized clinical trial. METHODS: Two patients with debilitating tinnitus refractory to conventional therapies were treated. Patients were evaluated with validated questionnaires and psychoacoustic measures to determine the frequency and pitch of their tinnitus. Tones at these frequencies were then presented to the first patient (RP) under magnetoencephalography (MEG) and functional magnetic resonance imaging (fMRI) to determine the tonotopic map for these frequencies in Heschl's gyrus. These tonotopic sites were targeted for implant with a quadripolar electrode. In the second patient (MV), only the fMRI tonotopic map was performed. These fMRI results detected an area of increased activity, which was selected as the site for the implanted bipolar electrode. RESULTS: Patient RP (bilateral tinnitus for 2 years) has experienced a sustained reduction to near elimination of tinnitus with intracerebral implanted electrodes, whereas patient MV (unilateral tinnitus for 7 years) had an unsustained reduction in her tinnitus. CONCLUSION: These findings suggest that the perception and annoyance of tinnitus may be modulated or reduced through electrical stimulation of the auditory cortex. These unsustained effects for patient MV may have been influenced by the longstanding nature of her tinnitus or by another reason as yet undetermined.

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### Pathology

Stark, A., L. Gregoire, et al. (2008). "Human papillomavirus, cervical cancer and women's knowledge." Cancer Detect Prev **32**(1): 15-22. [Article Request Form/Click for Article Request Form](#)

Department of Pathology and Laboratory Medicine, Henry Ford Health System, 2799 West Grand Blvd, Detroit, MI 48202, United States. [Astark1@hfhs.org](mailto:Astark1@hfhs.org)

BACKGROUND: Human papillomavirus (HPV) is the major risk factor for cervical cancer. METHODS: We implemented a retrospective case-series study to discern HPV knowledge accuracy among women diagnosed with and treated for cervical cancer. Cases (n=1174), identified from the Pathology database, were diagnosed and treated for cervical cancer at the same institution. Data were collected using self-administered questionnaires and by reviewing medical records. RESULTS: A total of 328 (27.9%) women returned the completed forms. Only 19% of the respondents had identified HPV as the primary risk factor for cervical cancer. Environmental pollutants, radiation exposure, poor dietary habits, excessive physical activity and family history of cervical cancer were listed as risk factors among many others. Multivariate analysis was performed to determine variables that were best associated with HPV knowledge accuracy. Age and education were the two variables that were statistically associated with the outcome. Younger and more educated women who participated in this study were more likely to know about the association between HPV infection and the risk of cervical cancer. CONCLUSIONS: Cervical cancer risk factor knowledge, especially knowledge about HPV is low, even among women with the history of cervical cancer. Younger and more educated women are more likely to have HPV and cervical cancer knowledge accuracy. The importance of personal health practices and the focus on health education should be equally emphasized to achieve successful cancer prevention through vaccination.

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### Pathology

Tuthill, M. (2008). "Automating anatomic pathology. Implementing an AP solution that integrates with your hospital's LIS can improve workflow and productivity." Health Manag Technol **29**(3): 18, 20. [PDF Full-Text](#)

Division of Pathology Informatics, Henry Ford Health System, Detroit, USA. [mtuthil1@hfhs.org](mailto:mtuthil1@hfhs.org)

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### Pharmacy

Austin, R. (2008). "An ounce of prevention." Diabetes Spectrum **21**(1): 5-6. [PDF Full-Text](#)

Henry Ford Health System, Detroit, Michigan.

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## Pharmacy

Villareal, C. (2007). "Amantadine therapy in traumatic brain injury patients." *J Pharm Technol* **23**(2): 95-103.

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Pharmacy Specialist, Surgical Intensive Care Unit, Department of Pharmacy Services, Henry Ford Hospital, [cschnei1@hfhs.org](mailto:cschnei1@hfhs.org)

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## Radiation Oncology

Freytag, S. O., H. Stricker, et al. (2007). "Five-year follow-up of trial of replication-competent adenovirus-mediated suicide gene therapy for treatment of prostate cancer." *Mol Ther* **15**(3): 636-42. **Article Request Form/**[Click for Article Request Form](#)

Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan, USA.

Replication-competent adenovirus-mediated suicide gene therapy is an investigational cancer treatment that combines the oncolytic actions of human adenoviruses with the cytotoxic effects of chemo-radiosensitizing genes. Previously, we reported the short-term effects of this therapy in men with local recurrence of prostate cancer after definitive radiotherapy. With a median prostate-specific antigen (PSA) follow-up of 5 years, we report here the effect of the gene therapy on prostate-specific antigen doubling time (PSADT), a surrogate end point with significant prognostic power. When considering all evaluable subjects, the PSADT increased following the gene therapy from a mean of 17 to 31 months (median 16 to 22 months) (P=0.014). Assuming that salvage androgen suppression therapy (AST) was uniformly initiated at a PSA of 15 ng/mL, the gene therapy would have delayed the projected onset of salvage therapy by an average of 2 years. The results indicate that replication-competent adenovirus-mediated suicide gene therapy may provide a potential long-term benefit to patients, as shown by a lengthening of the PSADT, and delay in when salvage therapy is indicated. Given the high morbidity associated with AST, we believe this approach could provide an attractive treatment option for selection of patients experiencing PSA relapse following definitive therapy.

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## Radiation Oncology

Jin, J. Y., M. Ajlouni, et al. (2007). "Quantification of incidental dose to potential clinical target volume (CTV) under different stereotactic body radiation therapy (SBRT) techniques for non-small cell lung cancer - tumor motion and using internal target volume (ITV) could improve dose distribution in CTV." *Radiother Oncol* **85**(2): 267-76. **Article Request Form/**[Click for Article Request Form](#)

Department of Radiation Oncology, Henry Ford Hospital, 2799 W. Grand Boulevard, Detroit, MI 48202, USA. [jjin1@hfhs.org](mailto:jjin1@hfhs.org)

**PURPOSE:** Clinical target volume (CTV), although present, is usually not considered during stereotactic body radiation therapy (SBRT) for non-small cell lung cancer. This study aimed to quantify the incidental dose to the potential CTV under different SBRT techniques. **MATERIALS AND METHODS:** Ten patients with various tumor motions were included in the study. Gated-4DCT was performed for all patients. Three treatment plans were generated. Plan A was based on free breathing gross tumor volume (GTV) from a regular CT. Plan B was based on internal target volume (ITV) from gated 4DCT. Plan C was a perfect gated treatment at the exhale phase. The hypothetical CTV was represented by three CTV shells (5, 10, and 15 mm). Time-averaged dose for different respiratory phases was calculated for 18 representative points in each shell. **RESULTS:** The minimum doses for plans A, B, and C were 84+/-20%, 94+/-3%, and 80+/-17% of the isocenter dose to the 5mm shell, 72+/-27%, 64+/-7%, and 20+/-11% to the 10mm shell, and 38+/-27%, 27+/-17%, and 6+/-7% to the 15 mm shell, respectively. The caudal and cranial ends of each shell usually had lower dose compared to the other points on the shell. Plan B had the most uniform and reasonable doses to the CTV shells, and patients with large respiratory motion had significantly higher minimum dose than patients with less motion. **CONCLUSION:** The potential CTV may incidentally receive adequate and relatively homogeneous doses when ITV is used and the patients have large respiratory motion. However, it could be underdosed for gated treatment or for patients with little motion.

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## Radiation Oncology

Jin, J. Y., S. Ryu, et al. (2008). "Evaluation of residual patient position variation for spinal radiosurgery using the Novalis image guided system." *Med Phys* **35**(3): 1087-93. [Article Request Form/Click for Article Request Form](#)

Department of Radiation Oncology, Henry Ford Hospital, Detroit, Michigan 48202, USA. [jjin1@hfhs.org](mailto:jjin1@hfhs.org)

**PURPOSE:** The Novalis system has been demonstrated to achieve accurate target localization on anthropomorphic phantoms. However, other factors, such as rotational deviation, patient intrafraction motion, and image fusion uncertainty due to patient body deformation, could contribute additional position uncertainty for actual patients. This study evaluates such position uncertainty for spinal radiosurgery patients. **MATERIALS AND METHODS:** Fifty-two consecutive spinal radiosurgery patients were included in the study. Rotational deviation was evaluated from 6-deg of freedom (6D) fusion results for all patients. The combined uncertainty of patient motion and image fusion was determined from fusion results of additional kV x-ray images acquired before, during, and after treatment for 25 of the 52 patients. The uncertainty of image fusion was also evaluated by performing 6D fusion ten different times with various regions of interest in the images selected for fusion. This was performed for two patients with L3 and T2 lesions, respectively, for comparison. **RESULTS:** The mean rotational deviation was 0.7 +/- 1.8, 0.7 +/- 1.5, and 0.7 +/- 1.6 deg along the yaw, roll, and pitch directions, respectively. The combined uncertainty from patient motion and image fusion was 0.1 +/- 0.9, 0.2 +/- 1.2, and 0.2 +/- 1.0 mm in the anteroposterior (AP), longitudinal, and lateral directions, respectively. The uncertainty (standard deviation) due to image fusion was less than 0.28 mm in any direction for the L3 lesion and 0.8 mm in the AP direction for the T2 lesion. **CONCLUSION:** Overall position uncertainty for spinal radiosurgery patients has been evaluated. Rotational deviation and patient motion were the main factors contributed to position uncertainty for actual patient treatment.

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## Radiation Oncology

Ryu, S., R. Jin, et al. (2008). "Pain control by image-guided radiosurgery for solitary spinal metastasis." *J Pain Symptom Manage* **35**(3): 292-8. [PDF Full-Text](#)

Department of Radiation Oncology, Henry Ford Hospital, Detroit, MI 48202, USA. [sryu1@hfhs.org](mailto:sryu1@hfhs.org)

Precision and accuracy of image-guided spinal radiosurgery has been previously demonstrated. This study was carried out to determine the clinical efficacy of spine radiosurgery for the treatment of solitary spinal metastases with or without cord compression. A total of 49 patients with 61 separate spinal metastases were treated with radiosurgery. All patients had pathologically proven primary cancers and had either synchronous or metachronous metastasis to the spine. The majority of the patients presented with back pain. All patients received single-dose radiosurgery to the involved spine only. The radiosurgery dose ranged from 10 to 16Gy. The primary endpoint was pain control, but outcomes in neurological status and radiological tumor control also were assessed. The median time to pain relief was 14 days and the earliest time of pain relief was within 24hours. Complete pain relief was achieved in 46%, partial relief in 18.9%, and stable symptoms in 16.2%. Relapse of pain at the treated spinal segment was 6.9%. Median duration of pain relief at the treated spine was 13.3 months. Overall pain control rate for one year was 84%. This experience demonstrates that spinal radiosurgery can achieve rapid and durable pain relief. Single-dose radiosurgery has a potential to be a viable treatment option for single spinal metastasis.

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## Surgery

Lin, J. C., D. Eun, et al. (2008). "Total Robotic Ligation of Inferior Mesenteric Artery for Type II Endoleak after Endovascular Aneurysm Repair." *Ann Vasc Surg*. [Article Request Form/Click for Article Request Form](#)

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

We present a case of totally robotic ligation of the inferior mesenteric artery (IMA) for treatment of a persistent endoleak from the IMA into the aneurysm sac after endovascular aneurysm repair (EVAR). An 84-year-old male underwent EVAR with a Gore Excluder stent graft for an asymptomatic infrarenal abdominal aortic aneurysm. Follow-up computed tomographic (CT) scan showed persistent type II endoleak from the IMA, with progressive enlargement of the aneurysm sac from 5 to 6.1 cm over an 18-month period. In this case, the patient underwent ligation of the IMA using the da Vinci Surgical System for the treatment of retrograde flow into the aneurysm sac. The total operating time was 249 min; of this, the robotic assistance

time was approximately 180 min. No intraoperative complications occurred. The estimated blood loss was 50 mL and the urine output 650 mL. The patient was extubated immediately after the procedure and tolerated a regular diet the following day. He was discharged home with a urinary catheter on postoperative day 2. CT scan postoperatively and at 3-month follow-up demonstrated an occluded IMA and stabilization of the aneurysm sac size.

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## **Surgery**

Rao, S., L. van Holsbeeck, et al. (2008). "A pilot study of comprehensive ultrasound education at the wayne state university school of medicine: a pioneer year review." *J Ultrasound Med* **27**(5): 745-9. [PDF Full-Text](#)

Department of Surgery, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202 USA. [sdulcha1@hfhs.org](mailto:sdulcha1@hfhs.org).

**OBJECTIVE:** Ultrasound is a versatile diagnostic modality used in a variety of medical fields. Wayne State University School of Medicine (WSUSOM) is one of the first medical schools in the United States to integrate an ultrasound curriculum through both basic science courses and clinical clerkships. **METHODS:** In 2006, 25 portable ultrasound units were donated to WSUSOM. First-year medical students were provided an ultrasound curriculum consisting of 6 organ-system sessions that addressed the basics of ultrasound techniques, anatomy, and procedural skills. After the last session, students were administered 2 anonymous and voluntary evaluations. The first assessed their overall experience with the ultrasound curriculum, and the second assessed their technical skills in applying ultrasound techniques. **RESULTS:** Eighty-three percent of students agreed or strongly agreed that their experience with ultrasound education was positive. On the summative evaluation, nearly 91% of students agreed or strongly agreed that they would benefit from continued ultrasound education throughout their 4 years of medical school. Student performance on the technical assessment was also very positive, with mean class performance of 87%. **CONCLUSIONS:** As residency programs adopt ultrasound training, medical school faculty should consider incorporating ultrasound education into their curriculum. Portable ultrasound has the potential to be used in many different settings, including rural practice sites and sporting events. The WSUSOM committee's pilot ultrasound curriculum will continue to use student feedback to enhance the ultrasound experience, helping students prepare for challenges that they will face in the future.

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## **Surgery**

Velanovich, V. (2008). "Innovative Use of Quality-of-Life Data: Correlating Physiologic Parameters With Patient-Centered Symptoms-- The Example of Anemia on the Vitality of Surgical Oncology Patients." *Surg Innov* **15**(1): 47-51. [Article Request Form/Click for Article Request Form](#)

Division of General Surgery, Henry Ford Hospital, Detroit, Michigan. [vvelano1@hfhs.org](mailto:vvelano1@hfhs.org).

**BACKGROUND:** It has been difficult to correlate quality of life with physiologic parameters. This may be because of the multitude of factors that lead to a symptom. An example of a cause of fatigue, lassitude, and lack of vitality is anemia. This study explores whether a generic quality-of-life instrument's measure of vitality is correlated with anemia. **METHODS:** Surgical oncology patients were asked to complete the SF-36. One of the domains is vitality (VT), which is a measure of fatigue (best possible score 100, worst possible score 0). Hemoglobin (Hb, gm/dL) and hematocrit (Hct, %) levels from the same period were recorded. **RESULTS:** A total of 319 patients were assessed, 114 postoperative patients with no evidence of disease (NED) and 205 patients with active disease. There were no differences in Hb or Hct levels, but VT was slightly higher in NED patients. Linear regression analysis demonstrated that for overall VT, VT in patients with active malignant disease, and VT in NED patients the regression slopes were statistically significantly different from 0, although the regression coefficients (r) were all less than .5. **CONCLUSIONS:** There are direct correlations between Hb and Hct levels and the VT domain of the SF-36. This correlation was stronger in NED patients. The low r(2) values reflect that anemia is one of many factors affecting VT.

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## **Urology**

Bhandari, M. and S. Siva (2008). "Re: the effects of bladder neck incision on urodynamic abnormalities of children with posterior urethral valves a. M. Kajbafzadeh, s. Payabvash and g. Karimian j urol 2007; 178: 2142-2149." *J Urol*

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan.

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### **Urology**

Elder, J. S. (2008). "Therapy for vesicoureteral reflux: antibiotic prophylaxis, urotherapy, open surgery, endoscopic injection, or observation?" *Curr Urol Rep* **9**(2): 143-50. [Article Request Form/Click for Article Request Form](#)

Vattikuti Urology Institute, Henry Ford Health System, 2799 West Grand Boulevard K-9, Detroit, MI 48202, USA. [jelder1@hfhs.org](mailto:jelder1@hfhs.org)

Vesicoureteral reflux (VUR) refers to the retrograde flow of urine from the bladder into the ureter and renal pelvis. It generally results from congenital maldevelopment of the ureterovesical junction, although VUR may develop in individuals with abnormally high detrusor pressure. VUR increases a child's susceptibility to pyelonephritis and renal scarring. Treatment goals include the prevention of pyelonephritis, reflux nephropathy, and other complications of reflux. Treatment alternatives include antibiotic prophylaxis, urotherapy (correction of voiding dysfunction), and surgical correction (open, injection therapy, or laparoscopic). Recent studies have challenged the presumed benefit of prophylaxis in children with VUR, while long-term retrospective studies have documented a high rate of hypertension in adults with reflux nephropathy. In addition, the risk of persistent VUR in adulthood is unresolved. These reports have stimulated a reevaluation of the role of various treatment options in children with VUR.

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### **Urology**

Malley, D., R. Boris, et al. (2008). "Synchronous Bilateral Adrenalectomy for Adrenocorticotrophic-Dependent Cushing's Syndrome." *Jsls* **12**(2): 198-201. [Article Request Form/Click for Article Request Form](#)

Vattikuti Urology Institute, Henry Ford Health System, Detroit, Michigan, USA.

Select patients with ACTH-dependent Cushing's syndrome, such as patients with persistent Cushing's disease after failed hypophysectomy or patients with ectopic ACTH production, may require bilateral adrenalectomy. Laparoscopic bilateral adrenalectomy has been described, offering definitive treatment with reduced morbidity compared with open techniques. We report on the performance of synchronous bilateral adrenalectomy treated using the da Vinci robot (Intuitive Surgical, Sunnyvale, CA). To our knowledge, the usage of this minimally invasive approach for this operation has yet to be reported in literature. The details of the case and a brief review of the literature are described herein.

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