

Henry Ford Health System Publication List December 2009

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Behavioral Services

Ylioja, S. G., A. D. Baird and K. Podell (2009). "Developing a Spatial Analogue of the Reliable Digit Span." Archives of Clinical Neuropsychology **24**(8): 729-739. [PDF Full-Text](#)

[Baird, Anne D.; Podell, Kenneth] Henry Ford Hlth Syst, Div Neuropsychol, Detroit, MI 48202 USA. [Ylioja, Shelley G.; Baird, Anne D.; Podell, Kenneth] Univ Windsor, Dept Psychol, Windsor, ON N9B 3P4, Canada.

Podell, K, Henry Ford Hlth Syst, Div Neuropsychol, 1 Ford PI 1E, Detroit, MI 48202 USA. kpodell1@hfhs.org

It is recommended that performance validity be assessed in all neuropsychological cases involving external incentive. The present study sought to develop an embedded performance validity measure based on the Spatial Span task of the Wechsler Memory Scale-III in a sample of litigating persistent postconcussion complainants. The Reliable Spatial Span (RSS) calculation had specificity, sensitivity, and predictive power values within the range of other embedded measures. This finding suggests that RSS is able to distinguish between persistent postconcussion complainants demonstrating valid and invalid performance. Other calculations involving Spatial Span scores had lower classification accuracy. Reliable Digit Span (RDS) classification accuracy within the present sample was lower than that of previous research, as well as of RSS. Potential reasons for lack of RDS replication are discussed, along with the potential use of RSS as an embedded validity performance indicator.

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Biostatistics & Research Epidemiology

Alexander, G. L., J. B. McClure, J. H. Calvi, G. W. Divine, M. A. Stopponi, S. J. Rolnick, J. B. Heimendinger, D. D. Tolsma, K. Resnicow, M. K. Campbell, V. J. Strecher and C. Cole Johnson (2009). "A Randomized Clinical Trial Evaluating Online Interventions to Improve Fruit and Vegetable Consumption." Am J Public Health. Epub Ahead of Print.

[Article Request Form](#)

Henry Ford Health System, Detroit, MI.

Objectives. We assessed change in fruit and vegetable intake in a population-based sample, comparing an online untailored program (arm 1) with a tailored behavioral intervention (arm 2) and with a tailored behavioral intervention plus motivational interviewing-based counseling via e-mail (arm 3). **Methods.** We conducted a randomized controlled intervention trial, enrolling members aged 21 to 65 years from 5 health plans in Seattle, Washington; Denver, Colorado; Minneapolis, Minnesota; Detroit, Michigan; and Atlanta, Georgia. Participants reported fruit and vegetable intake at baseline and at 3, 6,

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and 12 months. We assessed mean change in fruit and vegetable servings per day at 12 months after baseline, using a validated self-report fruit and vegetable food frequency questionnaire. Results. Of 2540 trial participants, 80% were followed up at 12 months. Overall baseline mean fruit and vegetable intake was 4.4 servings per day. Average servings increased by more than 2 servings across all study arms ($P < .001$), with the greatest increase (+2.8 servings) among participants of arm 3 ($P = .05$, compared with control). Overall program satisfaction was high. Conclusions. This online nutritional intervention was well received, convenient, easy to disseminate, and associated with sustained dietary change. Such programs have promise as population-based dietary interventions.

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Biostatistics & Research Epidemiology

Alford, S. H., S. D. Merajver, S. B. Gruber, H. O. Gad and C. G. Kleer (2009). "Epidemiology of the polycomb group protein enhancer of Zeste-2 (EZH2) in aggressive early stage breast cancer." Clinical & Experimental Metastasis **26**(7): 930-931. [PDF Full-Text](#)
(Scroll down to page 930)

[Alford, Sharon Hensley] Henry Ford Hosp, Detroit, MI 48202 USA. [Merajver, Sofia D.; Gruber, Stephen B.; Kleer, Celina G.] Univ Michigan, Ann Arbor, MI 48109 USA. [Gad, Hoda Omer] Tanta Canc Ctr, Tanta, Egypt.

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Biostatistics & Research Epidemiology

Wegienka, G., S. Havstad, E. M. Zoratti, K. J. Woodcroft, K. R. Bobbitt, D. R. Ownby and C. C. Johnson (2009). "Regulatory T cells in prenatal blood samples: variability with pet exposure and sensitization." J Reprod Immunol **81**(1): 74-81. PMC2734381. [Article Request Form](#)

Department of Biostatistics and Research Epidemiology, Henry Ford Hospital, 1 Ford Place, 3E, Detroit, MI 48202, USA.

Fetal exposures have come under investigation as risk factors of early life allergic disease. In this study we aimed to examine the relationships between dog or cat exposure and naturally occurring regulatory T cells (Treg cells), thought to play an important role in immune tolerance, in pregnant women. A cross-sectional analysis was conducted among 204 pregnant women who were queried regarding dog and cat exposure. Treg cells (CD4+CD25+Foxp3+ lymphocytes) and allergen-specific IgE were measured in venous blood samples. Atopy was defined as allergen-specific IgE $>$ or $= 0.35$ kU/l reactive with common allergens including dust mite, dog, cat, Timothy grass, ragweed, *Alternaria alternata*, egg white or cockroach. Nonparametric Wilcoxon rank sum tests and linear regression models of log transformed Treg cell levels were used in analyses. Among women sensitized to dog, those who had a dog or cat in the home had lower Treg cell levels compared with those who had no dog or cat. However, among women not sensitized to dog, those with a dog or cat in the home had higher Treg cell levels compared with those who did not. Among women sensitized to cat, those who had a dog or cat in the home had lower Treg cell levels compared with those who had no dog or cat. Gestational age at blood draw did not affect the associations. We conclude that Treg cell levels during pregnancy vary in association with both dog and cat exposure and atopic status.

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Bone & Joint Center

Ciarelli, T. E., C. Tjhia, D. S. Rao, S. Qiu, A. M. Parfitt and D. P. Fyhrie (2009). "Trabecular packet-level lamellar density patterns differ by fracture status and bone formation rate in white females." Bone **45**(5): 903-8. [PDF Full-Text](#)

Bone and Joint Center, Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, MI, USA.

Spatial patterns of mineralization for human iliac crest cancellous bone were measured from images obtained by quantitative backscattered electron microscopy. Biopsies collected from vertebral fracture patients and healthy individuals with high or low bone formation rate (BFR(s)) were examined (fracture/low BFR(s): N=12, fracture/high BFR(s): N=10, normal/low BFR(s): N=12, normal/high BFR(s): N=15). 20 by 20 pixel square areas or smaller were sampled from superficial and deep remodeling packets. Mean ($Z(\text{mean})$) and standard deviation (SD) of mineralization were measured, and coefficients of variation ($CV = SD/Z(\text{mean})$) were

calculated. Fast Fourier transform analysis was used to quantify the distribution of the mineral in the packets. "FFT_ratio" was defined as the ratio magnitude of the principal spatial frequency to the average atomic number density. A higher FFT_ratio occurred in specimens with more pronounced alternating layers of light and dark as visible in the backscattered electron image, which was defined as lamellar patterning. Two-way ANOVA revealed that the coefficients of variation of mineralization for both superficial and deep packets were significantly lower in fracture patients than in normal individuals. However, the interaction between turnover rate and group (fracture/non-fracture) indicated that the difference in packet CV occurred among the low turnover individuals and not among those with high turnover. Mean mineralization levels and CV between deep and superficial packets were highly correlated. Regressions of packet CV of mineralization and FFT_ratio were highly significant ($p < 0.001$) for all packets pooled and for packets divided by group (fracture/normal). However, analyses of packet CV and FFT_ratio by individual were variable (R^2 from 0.00338 to 0.700). Packet-level mineralization variability may be associated with fracture toughness, and fracture patients had less variable packet-level mineralization. The result that the packet CV varied significantly between fracture and non-fracture individuals with low turnover suggests that for low turnover subjects without fracture, high variability in mineralization may have a protective effect. In high turnover patients, the accelerated turnover may prevent the lamellar variability from developing over time. Strong correlations between CV and Z(mean) for both superficial and deep packets imply that newly formed bone is created similarly to older bone within an individual. Fourier transform results show that the mineralization variability found within packets is associated with lamellar patterning. Lamellar structure has been hypothesized to guide microcrack propagation in order to optimize bone strength and toughness. Osteoporotics with fracture had less pronounced lamellation than healthy normals and may be more prone to fracture.

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Cardiology

Alsheikh-Ali, A. A., M. H. Al-Mallah, W. Al-Mahmeed, N. Albustani, J. Al Suwaidi, K. Sulaiman and M. Zubaid (2009). "Heart failure in patients hospitalized with acute coronary syndromes: observations from the Gulf Registry of Acute Coronary Events (Gulf RACE)." European Journal of Heart Failure **11**(12): 1135-1142. [PDF Full-Text](#)

[Alsheikh-Ali, Alawi A.; Al-Mahmeed, Wael; Albustani, Nazar] Sheikh Khalifa Med City, Inst Cardiac Sci, Div Cardiol, Abu Dhabi, U Arab Emirates. [Alsheikh-Ali, Alawi A.] Tufts Med Ctr, Tufts Clin & Translat Sci Inst, Boston, MA USA. [Al-Mallah, Mouaz H.] Henry Ford Hosp, Dept Cardiol, Detroit, MI 48202 USA. [Al Suwaidi, Jassim] Hamad Med Corp, Dept Cardiol, Doha, Qatar. [Sulaiman, Kadhim] Royal Hosp, Muscat, Oman. [Zubaid, Mohammad] Kuwait Univ, Fac Med, Dept Med, Kuwait, Kuwait. Alsheikh-Ali, AA, Sheikh Khalifa Med City, Inst Cardiac Sci, Div Cardiol, POB 51900, Abu Dhabi, U Arab Emirates. aalsheikhali@alum.mit.edu

We describe the prevalence and prognostic significance of heart failure (HF) complicating acute coronary syndromes (ACS) in patients enrolled in the Gulf Registry of Acute Coronary Events (Gulf RACE). Gulf RACE is a prospective, multi-national study of all patients hospitalized with ACS in 65 centres in six Arab countries. Data were analysed based on HF on presentation (Killip class II/III) or during hospital stay. The study endpoint was all-cause in-hospital mortality. Of 8000 patients with ACS, 2009 (25%) had HF on presentation or during the hospital stay. Patients with HF were older, more often with co-morbid conditions, and less often treated with evidence-based therapies. Heart failure was associated with higher in-hospital mortality (7.9 vs. 0.9%, $P < 0.001$), which persisted after adjusting for age, gender, and presentation and treatment characteristics [adjusted odds ratio 4.1 (1.8-9.4)]. There was a significant interaction between age and the prognostic effect of HF on in-hospital mortality, such that younger patients had a significantly higher increase in mortality related to HF (P for interaction = 0.002). Heart failure complicates a substantial proportion of ACS admissions in the Arab Middle East and is associated with higher in-hospital death. Younger patients with ACS have a higher relative increase in mortality related to HF.

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Cardiology

Gupta, R. C., S. Mishra, S. Rastogi, M. J. Wang, B. Rousso, Y. Mika, A. Remppis and H. N. Sabbah (2009). "Ca²⁺-Binding Proteins in Dogs with Heart Failure: Effects of Cardiac Contractility Modulation Electrical Signals." Cts-Clinical and Translational Science **2**(3): 211-215. [Article Request Form](#)

[Gupta, Ramesh C.; Mishra, Sudhish; Rastogi, Sharad; Wang, Mengjum; Sabbah, Hani N.] Henry Ford Hosp, Dept Med, Div Cardiovasc Med, Henry Ford Heart & Vasc Inst, Detroit, MI 48202 USA. [Rouso, Benny; Mika, Yuval] Impulse Dynam USA Inc, Orangeburg, NY 10962 USA. [Remppis, Andrew] Univ Heidelberg, Med Clin 3, Heidelberg, Germany.

Sabbah, HN, Henry Ford Hosp, Dept Med, Div Cardiovasc Med, Henry Ford Heart & Vasc Inst, Detroit, MI 48202 USA. hsabbah1@hfhs.org

Background: In dogs with heart failure (HF), chronic therapy with cardiac contractility modulation (CCM) electrical signals delivered to left ventricular (LV) muscle during the absolute refractory period improves LV function. This study examined the effects of CCM therapy on the expression of calcium (Ca²⁺)-binding proteins (CBPs) in dogs with HF. **Methods and Results:** Studies were performed in LV tissue from seven CCM-treated HF dogs, seven untreated HF dogs, and six normal (NL) dogs. mRNA expression of S100A1, sorcin, presenillin-1 (PS1), PS2, histidine-rich Ca²⁺-binding protein (HRC), and 18S ribosomal RNA (18S), a housekeeping gene, was measured using RT-PCR. Protein levels of CBPs and calsequestrin (CSQ) were determined by Western blotting. No difference was observed in the expression of 18S and CSQ among study groups. Compared with NL, the expression of S100A1, sorcin, and HRC was decreased, whereas the expression of PS2 was increased in untreated HF dogs. CCM therapy normalized the expression of S100A1, sorcin, and PS2 but not of HRC. No change was seen in the expression of PS1 among study groups. **Conclusion:** CCM therapy restores LV expression of S100A1, PS2, and sorcin. Normalization of CBPs may partly contribute to improved LV function in HF following CCM therapy.

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Cardiology

Jaffery, Z., A. B. Greenbaum, M. F. Siddiqui, N. Mahendraker, V. Gupta, V. Mokkal, U. Kanakadandi, A. Robbins and J. McCord (2009). "Predictors of Mortality in Patients with Lower Extremity Peripheral Arterial Disease: 5-Year Follow-up." Journal of Interventional Cardiology **22**(6): 564-570. [PDF Full-Text](#)

[Jaffery, Zehra] Ochsner Med Ctr, Dept Cardiol, New Orleans, LA USA. [Siddiqui, Mohammad F.; Mahendraker, Neetu; Gupta, Vikesh; Mokkal, Vidu; Kanakadandi, Uday; Robbins, Andrew] VA Illiana Hlth Care Syst, Dept Internal Med, Danville, IL USA. [Siddiqui, Mohammad F.; Mahendraker, Neetu; Gupta, Vikesh; Mokkal, Vidu; Kanakadandi, Uday; Robbins, Andrew] Univ Illinois Urbana Champaign, Urbana, IL USA. [Greenbaum, Adam B.; Mccord, James] Henry Ford Hosp, Inst Heart & Vasc, Detroit, MI 48202 USA. Jaffery, Z, 1514 Jefferson Hwy, New Orleans, LA 70120 USA. zjaffery@ochsner.org

Methods: Two hundred and eighty-three patients with an ankle brachial index (ABI) < 0.9 were identified at the Veterans Administration Hospital, Danville, Illinois, and rates of LE arterial revascularization and all-cause mortality were measured at 5 years. **Results:** Of 283 patients identified, 42 (15%) underwent LE revascularization including 39 surgical procedures and 18 percutaneous interventions for symptomatic PAD. Eleven (26%) patients underwent repeat procedures over the 5 years of follow-up. Those undergoing revascularization were more often Caucasian (95% vs. 79%, P = 0.01) and had lower ABIs (ABI < 0.4, 45% vs. 17%, P = < 0.001). At 44 +/- 19 months follow-up, there were fewer deaths in patients that underwent revascularization compared to patients who did not undergo revascularization; 10/42 (24%) versus 107/241 (44%) patients, P = 0.012. In a multivariate model LE arterial revascularization was associated with a trend toward lower all-cause mortality (HR 0.51 [95% CI 0.26-1.02], P = 0.056). Independent predictors of mortality were age >= 65 years (HR 2.42 [95% CI 1.52-3.85], P < 0.001), history of coronary artery disease (HR 1.67 [95% CI 1.13-2.46], P = 0.010), chronic kidney disease (HR 1.75 [95% CI 1.15-2.67], P = 0.010), and an ABI < 0.4 (HR 1.88 [95% CI 1.19-2.96], P = 0.006). **Conclusion:** Few patients at this center with LE-PAD underwent arterial revascularization. After adjusting for baseline differences, there is a trend toward lower 5-year mortality in those undergoing LE arterial revascularization when compared to those who do not. (J Interven Cardiol 2009;22:564-570).

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Cardiology

Saval, M. A., D. J. Kerrigan, K. M. Ophaug, J. K. Ehrman and S. J. Keteyian (2009). "Relationship Between Leg Muscle Endurance and $\dot{V}O_2$ Slope in Patients With Heart Failure." J Cardiopulm Rehabil Prev. Epub Ahead of Print. [Article Request Form](#)

Henry Ford Hospital, Detroit, Michigan (Mr Saval and Drs Kerrigan, Ehrman, and Keteyian); and Wayne State University, Detroit, Michigan (Ms Ophaug).

PURPOSE: Ventilatory efficiency, as measured by the slope of the relationship between minute ventilation and carbon dioxide production (&OV0312;E/&OV0312;CO2 slope) during cardiopulmonary exercise (CPX) testing, is an important prognostic measure in patients with heart failure (HF). An abnormal slope is linked to the skeletal muscle metaboreflex. In addition, skeletal muscle endurance is reduced in patients with HF. However, the relationship between &OV0312;E/&OV0312;CO2 slope and skeletal muscle endurance is not known. This investigation tests the hypothesis that reduced knee extensor muscle endurance is inversely related to an elevated &OV0312;E/&OV0312;CO2 slope during CPX testing in patients with HF and that these variables are not related in normal subjects. **METHODS:** Patients with HF (n = 32) and 6 age-matched normal subjects performed CPX testing and isokinetic dynamometry to determine the &OV0312;E/&OV0312;CO2 slope and knee extensor muscle endurance, respectively. **RESULTS:** The &OV0312;E/&OV0312;CO2 slope and leg muscle endurance percentage were significantly related in patients with HF (r = -0.68, P < .001), but not in normal subjects (r = -0.11, P = .83). **DISCUSSION:** Based on these data, abnormalities of skeletal muscle endurance of patients with HF partially account for (r = 0.46; standard error estimate = 6.6) abnormalities of ventilatory efficiency, as measured by the &OV0312;E/&OV0312;CO2 slope. This finding helps explain, in part, the factors that influence an established prognostic indicator, elevated &OV0312;E/&OV0312;CO2 slope. Future research is needed to determine whether the relationship between skeletal muscle dysfunction and ventilatory efficiency is directly mediated through the skeletal muscle ergoreflex.

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Dermatology

Eide, M. J., R. Krajenta, D. Johnson, J. J. Long, G. Jacobsen, M. M. Asgari, H. W. Lim and C. C. Johnson (2010). "Identification of patients with nonmelanoma skin cancer using health maintenance organization claims data." *Am J Epidemiol* **171**(1): 123-8. PMC2796985. [PDF Full-Text](#)

Department of Dermatology, Henry Ford Hospital, 3031 West Grand Boulevard, Suite 800, Detroit, MI 48202, USA. meide1@hfhs.org

Cancer registries usually exclude nonmelanoma skin cancers (NMSC), despite the large population affected. Health maintenance organization (HMO) and health system administrative databases could be used as sampling frames for ascertaining NMSC. NMSC patients diagnosed between January 1, 1988, and December 31, 2007, from such defined US populations were identified by using 3 algorithms: NMSC International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes, NMSC treatment Current Procedural Terminology (CPT) codes, or both codes. A subset of charts was reviewed to verify NMSC diagnosis, including all records from HMO-enrollee members in 2007. Positive predictive values for NMSC ascertainment were calculated. Analyses of data from 1988-2007 ascertained 11,742 NMSC patients. A random sample of 965 cases was selected for chart review, and NMSCs were validated in 47.0% of ICD-9-CM-identified patients, 73.4% of CPT-identified patients, and 94.9% identified with both codes. All charts from HMO-health plan enrollees in 2007 were reviewed (n = 1,116). Cases of NMSC were confirmed in 96.5% of ICD-9-CM-identified patients, 98.3% of CPT-identified patients, and 98.7% identified with both codes. HMO administrative data can be used to ascertain NMSC with high positive predictive values with either ICD-9-CM or CPT code, but both codes may be necessary among non-HMO patient populations.

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Dermatology

Hood, A. F. (2010). "Dermatopathology calendar." *Journal of Cutaneous Pathology* **37**(1): 105-105. [PDF Full-Text](#)

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Dermatology

Martin, J. M., J. M. Ghaferi, D. L. Cummins, A. J. Mamelak, C. D. Schmults, M. Parikh, L. A. Speyer, A. Chuang, H. V. Richardson, D. Stein and N. J. Liegeois (2009). "CHANGES in SKIN TANNING ATTITUDES Fashion Articles and Advertisements in the Early 20th Century." *American Journal of Public Health* **99**(12): 2140-2146. [PDF Full-Text](#)

[Chuang, Alice; Richardson, Hazel V.; Liegeois, Nanette J.] Johns Hopkins Univ Hosp, Dept Dermatol, Div Dermatol Surg, Baltimore, MD 21287 USA. [Stein, David] Johns Hopkins Univ, Sch Med, Dept Dermatol, Baltimore, MD 21205 USA. [Ghaferi, Jessica M.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA. [Cummins, Deborah L.] Harvard Univ, Dept Dermatol, Boston, MA 02115 USA. [Mamelak, Adam J.] Methodist Hosp, Dept Dermatol, Houston, TX 77030 USA. [Schmults, Chrys D.; Speyer, Lark-Aeryn] Harvard Univ, Brigham & Womens Hosp, Dept Dermatol, Boston, MA 02115 USA. [Parikh, Mona] Columbia Presbyterian Med Ctr, Dept Med, New York, NY 10032 USA. [Stein, David] Johns Hopkins Univ, Bloomberg Sch Publ Hlth, Baltimore, MD 21218 USA.

Liegeois, NJ, Johns Hopkins Univ Hosp, Dept Dermatol, Div Dermatol Surg, 601 N Caroline St, JHOC 6054, Baltimore, MD 21287 USA. nliegeo1@jhmi.edu

Historical reviews suggest that tanning first became fashionable in the 1920s or 1930s. To quantitatively and qualitatively examine changes in tanning attitudes portrayed in the popular women's press during the early 20th century, we reviewed summer issues of *Vogue* and *Harper's Bazaar* for the years 1920, 1927, 1928, and 1929. We examined these issues for articles and advertisements promoting skin tanning or skin bleaching and protection. We found that articles and advertisements promoting the fashionable aspects of tanned skin were more numerous in 1928 and 1929 than in 1927 and 1920, whereas those promoting pale skin (by bleaching or protection) were less numerous. These findings demonstrate a clear shift in attitudes toward tanned skin during this period. (*Am J Public Health*. 2009;99:2140-2146. doi:10.2105/AJPH.2008.144352)

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Dermatology

Tang, N., H. Gibson, T. Germeroth, P. Porcu, H. W. Lim and H. K. Wong (2009). "T-plastin (PLS3) gene expression differentiates Sezary syndrome from mycosis fungoides and inflammatory skin diseases and can serve as a biomarker to monitor disease progression." *Br J Dermatol*. Epub Ahead of Print. [PDF Full-Text](#)

Department of Dermatology, Henry Ford Hospital, Detroit, MI, U.S.A.

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Dermatology

Tierney, E. and D. J. Kouba (2009). "A subcutaneous corset plication rapidly and effectively relieves tension on large linear closures." *Dermatol Surg* **35**(11): 1806-8. [PDF Full-Text](#)

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

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Diagnostic Radiology

Ali, M. M., B. Yoo and M. D. Pagel (2009). "Tracking the relative in vivo pharmacokinetics of nanoparticles with PARACEST MRI." *Mol Pharm* **6**(5): 1409-16. [Article Request Form](#)

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

A noninvasive assay that tracks the relative in vivo pharmacokinetics of two nanoparticles may accelerate the development of nanoparticles for biomedical applications, and may provide a method to select personalized nanomedicines for individual patients. To develop an in vivo competitive assay, two MRI contrast agents that could be selectively detected through paramagnetic chemical exchange saturation transfer (PARACEST) were conjugated to a second generation and fifth generation polyamidoamine (PAMAM) dendrimer. The CEST effects of each agent was calibrated relative to concentration. The effects of T(1) relaxivities of these dendritic PARACEST magnetic resonance imaging (MRI) contrast agents were found to be negligible relative to their CEST effects with respect to changes in image contrast, which facilitated the measurement of the ratios of

their chemical exchange lifetimes. Injection of both contrast agents into a mouse model of mammary carcinoma resulted in a temporal increase in the CEST effect from each agent in the flank tumor. Although the in vivo CEST effects could not be used to determine the absolute concentrations of each agent within the tumor, the ratio of the in vivo CEST effects was used to measure the ratio of the concentrations of the agents. This result demonstrated that the relative in vivo pharmacokinetics of two nanoparticles may be evaluated using PARACEST MRI.

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Diagnostic Radiology

Jafari-Khouzani, K., K. Elisevich, S. Patel, B. Smith and H. Soltanian-Zadeh (2010). "FLAIR signal and texture analysis for lateralizing mesial temporal lobe epilepsy." Neuroimage **49(2)**: 1559-1571. [Article Request Form](#)

[Jafari-Khouzani, Kourosh; Patel, Suresh; Soltanian-Zadeh, Hamid] Henry Ford Hosp, Dept Diagnost Radiol, Detroit, MI 48202 USA. [Elisevich, Kost] Henry Ford Hosp, Dept Neurosurg, Detroit, MI 48202 USA. [Smith, Brien] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Soltanian-Zadeh, Hamid] Univ Tehran, Control & Intelligent Proc Ctr Excellence, Dept Elect & Comp Engn, Tehran 14395515, Iran. Jafari-Khouzani, K, Henry Ford Hosp, Dept Diagnost Radiol, Detroit, MI 48202 USA. kjafari@rad.hfh.edu

Standard magnetic resonance (MR) imaging analysis in several cases of mesial temporal lobe epilepsy (mTLE) either fail to show an identifiable hippocampal asymmetry or provide only subtle distinguishing features that remain inconclusive. A retrospective analysis of hippocampal fluid-attenuated inversion recovery (FLAIR) MR images was performed in cases of mTLE addressing, particularly, the mean and standard deviation of the signal and its texture. Preoperative T1-weighted and FLAIR MR images of 25 nonepileptic control subjects and 36 mTLE patients with Engel class Ia outcomes were analyzed. Patients requiring extraoperative electrocorticography (ECoG) with intracranial electrodes and thus judged to be more challenging were studied as a separate cohort. Hippocampi were manually segmented on T1-weighted images and their outlines were transposed onto FLAIR studies using an affine registration. Image intensity features including mean and standard deviation and wavelet-based texture features were determined for the hippocampal body. The right/left ratios of these features were used with a linear classifier to establish laterality. Whole hippocampal within-subject volume ratios were assessed for comparison. Mean and standard deviation of FLAIR signal intensities lateralized the site of epileptogenicity in 98% of all cases, whereas analysis of wavelet texture features and hippocampal volumetry each yielded correct lateralization in 94% and 83% of cases, respectively. Of patients requiring more intensive study with extraoperative ECoG, 17/18 were lateralized effectively by the combination of mean and standard deviation ratios despite a ratio of mean signal intensity near one in some. The analysis of mean and standard deviation of FLAIR signal intensities provides a highly sensitive method for lateralizing the epileptic focus in mTLE over that of volumetry or texture analysis of the hippocampal body. (C) 2009 Elsevier Inc. All rights reserved.

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Diagnostic Radiology

Lee, K. S., M. T. van Holsbeeck and A. Abbud (2010). "Atypical rapid progression of osteoarticular amyloidosis involving the hip in a patient on hemodialysis using polyacrylonitrile membranes." Skeletal Radiology **39(1)**: 79-83. [PDF Full-Text](#)

[Lee, Kenneth S.] Univ Wisconsin, Sch Med & Publ Hlth, Univ Wisconsin Hosp & Clin, Dept Radiol, Madison, WI 53792 USA. [van Holsbeeck, Marnix T.] Henry Ford Hosp, Dept Radiol, Wayne State Sch Med, Detroit, MI 48202 USA. [Abbud, Alexander] Henry Ford Hosp, Dept Pathol, Wayne State Sch Med, Detroit, MI 48202 USA. Lee, KS, Univ Wisconsin, Sch Med & Publ Hlth, Univ Wisconsin Hosp & Clin, Dept Radiol, 600 Highland Ave, CSC E3-311, Madison, WI 53792 USA. klee2@uwhealth.org

Amyloidosis related to dialysis is a well-known complication affecting many organ systems, in particular the musculoskeletal system. In 1985 Shirahama et al. (Biochem Biophys Res Commun 53:705-709, 1985) identified beta-2 microglobulin (MG) as the offending constituent by using protein purification techniques. Amyloidosis has been increasing in prevalence because of longer life spans and increased chronic medical conditions such as end-stage renal disease. When dialysis-related amyloidosis involves the musculoskeletal system, it affects the shoulder girdle, the so called shoulder pad sign, the wrist, hip, knee, and spine (Resnick,

Diagnosis of bone and joint disorders, 4th edn., pp. 2054-2058 and 2176-2183, 2002). Other osteoarticular manifestations of amyloidosis include osteoporosis, lytic lesions, and pathologic fractures. It has been well documented that the prevalence of amyloid is dependent on duration of dialysis-over 90% in patients on dialysis for over 7 years (Jadoul, *Nephrol Dial Transplant* 13:61-64, 1998). However, a recent changeover to high-flux membranes used in hemofiltration has been reported to delay its onset (Campistol et al., *Contrib Nephrol* 125:76-85, 1999). We report on the radiographic, nuclear medicine, and computed tomography (CT) findings of osteoarticular amyloidosis involving the hip, and sequence its atypical rapid onset. The imaging, histopathological findings, and differential diagnosis are discussed.

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Diagnostic Radiology

Shalchian, B., H. Rajabi and H. Soltanian-zadeh (2009). "Fusion of PET and CT images using wavelet transform." *Hellenic Journal of Nuclear Medicine* 12(3): 238-243. [Article Request Form](#)

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While information about anatomy is available in CT images, information about physiology and metabolism is available in PET images. To integrate both information, the two images are fused. Image fusion methods include simple methods like pixel averaging and sophisticated methods like wavelet transformation. An advantage of using wavelet transformation is that it preserves significant parts of each image. After creating lesions of 10, 8, 6 mm in a NURBS (non-uniform rational B-splines) based cardiac torso (NCAT) phantom, PET images were simulated using SimSET simulator. Attenuation maps of the activity phantom were used as CT images. Each of the PET and CT images was divided into an approximation image and three detailed images by the wavelet transform. The corresponding transformed images generated from the PET and CT images were fused in nine different ways to generate composite images, which were compared to the original images. The basis of comparison is the lesion-to-tissue contrast in the fused image in comparison to the lesion-to-tissue contrast in the original PET and CT images. Our results showed that except for one method, the lesion-to-tissue contrast in the fused image was higher than that of the CT images. In the first six methods, the lesion-to-tissue contrast in the fused image was less than the contrast, in the PET image. In the other three methods, the contrast in the fused image was higher than in the PET image. This was true in cases of 10, 8,6 mm lesions. In conclusion, we have show that the approximation image produced a better ultimate image and that the lesion-to-tissue contrast in the fused image was also better than that of the original PET and CT images. This is because the approximation image is comprised of fundamental information of the signal (low frequency) that directly affects the image contrast.

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Emergency Medicine

Uebbing, C., J. Miller, C. Arnold and M. Walsh (2010). "Soccer player whiplash maculopathy." *Am J Emerg Med* 28(1): 120 e7-8. [PDF Full-Text](#)

Department of Emergency Medicine, Henry Ford Hospital, Detroit, MI 48202, USA.

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Endocrinology & Metabolism

Rubin, R. R., M. Peyrot, D. F. Kruger and L. B. Travis (2009). "Barriers to Insulin Injection Therapy Patient and Health Care Provider Perspectives." *Diabetes Educator* 35(6): 1014-1022. [Article Request Form](#)

[Rubin, Richard R.; Peyrot, Mark] Johns Hopkins Univ, Dept Med, Baltimore, MD 21218 USA. [Rubin, Richard R.] Johns Hopkins Univ, Dept Pediat, Baltimore, MD 21218 USA. [Peyrot, Mark] Loyola Univ Maryland, Dept Sociol, Baltimore, MD USA. [Kruger, Davida F.] Henry Ford Hlth Syst, Div Endocrinol Diabet Bone & Mineral Disorders, Detroit, MI USA. [Travis, Luther B.] Univ Texas Med Branch, Dept Pediat, Galveston, TX USA. [Travis, Luther B.] Univ Texas Med Branch, Dept Nephrol & Diabet, Galveston, TX USA.

Rubin, RR, Johns Hopkins Univ, Dept Med, Baltimore, MD 21218 USA.

Objective To compare patients' perceptions of injection-related problems with clinicians' estimates of those problems. **Methods** Data were obtained through 2 Internet surveys, one of US adults self-identified as taking insulin to treat diabetes and the second of health care professionals who treat people with diabetes who inject insulin, including primary care physicians, endocrinologists, and diabetes educators. **Results** A substantial majority of patients would like to reduce the number of injections they take each day; almost half said that they would be more likely to take their insulin injections regularly if a product were available to ease the pain. A much smaller proportion of patients reported that (1) injections were a serious burden, (2) they were dissatisfied with the way they took insulin, (3) injections had a substantial negative impact on quality of life, (4) they skipped injections they should take, or (5) injection-related problems affected the number of injections they were willing to take. Half of the patients said they mentioned injection-related problems to their provider; a similar number reported that their providers had not given them a solution to problems with injection-related pain and bruising. Although awareness of products to ease injection pain was high among providers (especially diabetes educators), this information was not effectively transmitted to patients. **Conclusions** Patients should be encouraged to discuss their injection-related concerns, and providers should regularly ask about injection-related problems. Providers should offer patients information about tools to reduce injection-related worries, preferably by having them available to show and demonstrate.

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Gastroenterology

Kang, H., J. K. K. Greenson, M. A. Y. Huang, J. Omo and H. S. Conjeevaram (2009). "Portal Inflammation Is an Independent Predictor of Severe Liver Disease in Patients with Nonalcoholic Fatty Liver Disease." *Hepatology* **50**(4): 1011. [PDF Full-Text](#) (Scroll down to abstract 1011)

[Kang, Hellan; Greenson, Joel K. K.; Omo, Jason; Conjeevaram, Hari S.] Univ Michigan, Ann Arbor, MI 48109 USA. [Huang, Mary Ann Y.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Gastroenterology

Kwo, P. Y., E. Lawitz, J. McCone, E. R. Schiff, J. M. Vierling, D. Pound, M. Davis, J. S. Galati, S. C. Gordon, N. Ravendhran, L. Rossaro, F. H. Anderson, I. M. Jacobson, R. Rubin, K. Koury, N. Boparai, E. I. Chaudhri, C. A. Brass and J. K. Albrecht (2009). "High Sustained Virologic Response (Svr) in Genotype 1 (G1) Null Responders to Peg-Interfeon Alfa-2b (P) Plus Ribavirin (R) When Treated with Boceprevir (Boc) Combination Therapy." *Hepatology* **50**(4): 62. [PDF Full-Text](#) (Scroll down to abstract #62)

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Gastroenterology

Kwo, P. Y., E. Lawitz, J. McCone, E. R. Schiff, J. M. Vierling, D. Pound, M. Davis, J. S. Galati, S. C. Gordon, N. Ravendhran, L. Rossaro, F. H. Anderson, I. M. Jacobson, R. Rubin, K. Koury, N. Boparai, E. I. Chaudhri, C. A. Brass and J. K. Albrecht (2009). "Response-Guided Therapy (Rgt) for Boceprevir (Boc) Combination Treatment? - Results from Hcv Sprint-1." *Hepatology* **50**(4): 1582. [PDF Full-Text](#) (Scroll down to abstract #1582)

[Kwo, Paul Y.] Indiana Univ, Sch Med, Div Gastroenterol Hepatol, Indianapolis, IN USA. [Lawitz, Eric] Alamo Med Res, San Antonio, TX USA. [McCone, Jonathan] Mt Vernon Endoscopy Ctr, Alexandria, VA USA. [Schiff, Eugene R.] Univ Miami, Ctr Liver Dis, Miami, FL USA. [Vierling, John M.] Baylor Coll Med, Houston, TX 77030 USA. [Pound, David] Indianapolis Gastroenterol Res Fdn, Indianapolis, IN USA. [Davis, Mitchell] S Florida Ctr Gastroenterol, Wellington, FL USA. [Galati, Joseph S.] Liver Specialists Texas, Houston, TX USA. [Gordon, Stuart C.] Henry Ford Hosp, Detroit, MI 48202 USA. [Ravendhran, Natarajan] Digest Dis Associates, Baltimore, MD USA. [Rossaro, Lorenzo] Univ Calif Davis, Sacramento, CA 95817 USA. [Anderson, Frank H.] Liver & Intestinal Res Ctr, Galveston, TX USA. [Jacobson, Ira M.] Cornell Univ, Weill Med Coll, New York, NY 10021 USA. [Rubin, Raymond] Digest Healthcare Georgia, Atlanta, GA USA. [Koury, Kenneth; Boparai, Navdeep; Chaudhri, Eirum I.; Brass, Clifford A.; Albrecht, Janice K.] Schering Plough Res Inst, Kenilworth, NJ USA.

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Gastroenterology

Layden, J. E., K. A. Brown, M. R. Lucey, H. S. Te, S. L. Eswaran, K. Richie, C. J. Fimmel, J. Gangar, T. J. Layden, S. J. Cotler and N. M. Clark (2009). "Hepatitis C Virus (Hcv) Progresses More Rapidly after Orthotopic Liver Transplantation (Olt) in African Americans (Aa) Compared to Whites (W)." Hepatology **50**(4): 190. [PDF Full-Text](#) (Scroll down to abstract 190)

[Layden, Jennifer E.; Gangar, Jinal; Layden, Thomas J.; Cotler, Scott J.; Clark, Nina M.] Univ Illinois, Chicago, IL USA. [Brown, Kimberly Ann] Henry Ford, Med, Detroit, MI USA. [Lucey, Michael R.; Richie, Kelly] Univ Wisconsin, Madison, WI USA. [Te, Helen S.] Univ Chicago, Chicago, IL USA. [Eswaran, Sheila L.; Fimmel, Claus J.] Loyola Univ, Maywood, IL 60153 USA.

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Gastroenterology

Melia, M., A. Muir, J. McCone, M. L. Shiffman, J. W. King, S. K. Herrine, G. W. Galler, J. R. Bloomer, F. Nunes, K. A. Brown, K. D. Mullen, N. Ravendhran, W. M. Cassidy, R. H. Ghalib, N. Boparai, R. Y. Jiang, S. Noviello, C. A. Brass, J. K. Albrecht, J. G. McHutchison and M. S. Sulkowski (2009). "Analysis of Reasons for Treatment Ineligibility in the Ideal Study: African Americans (Aa) Vs Non-African Americans (Non-Aa)." Hepatology **50**(4): 848. [PDF Full-Text](#) (Scroll down to abstract 848)

[Melia, Michael; Sulkowski, Mark S.] Johns Hopkins Univ, Sch Med, Baltimore, MD USA. [Muir, Andrew; McHutchison, John G.] Duke Clin Res Inst, Durham, NC USA. [McCone, Jonathan] Mt Vernon Endoscopy Ctr, Alexandria, VA USA. [Shiffman, Mitchell L.] Virginia Commonwealth Univ, Med Ctr, Richmond, VA USA. [King, John W.] Louisiana State Univ, Hlth Sci Ctr, Shreveport, LA 71105 USA. [Herrine, Steven K.] Thomas Jefferson Univ, Philadelphia, PA 19107 USA. [Galler, Greg Wayne] Kelsey Res Fdn, Houston, TX USA. [Bloomer, Joseph R.] Univ Alabama, Birmingham Liver Ctr, Birmingham, AL USA. [Nunes, Frederick] Penn Hosp, Philadelphia, PA 19107 USA. [Brown, Kimberly Ann] Henry Ford Hosp, Detroit, MI 48202 USA. [Mullen, Kevin D.] Metro Hlth Med Ctr, Cleveland, OH USA. [Ravendhran, Natarajan] Digest Dis Associates, Baltimore, MD USA. [Cassidy, William M.] Louisiana State Univ, Hlth Sci Ctr, Baton Rouge, LA 70803 USA. [Ghalib, Reem H.] Liver Inst Methodist Dallas, Dallas, TX USA. [Boparai, Navdeep; Jiang, Ruiyun; Noviello, Stephanie; Brass, Clifford A.; Albrecht, Janice K.] Schering Plough Corp, Res Inst, Kenilworth, NJ 07033 USA.

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Gastroenterology

Moeller, M. J., G. Divine and K. A. Brown (2009). "Impact of Length of Therapy and Predictive Value Models on Svr in Hcv Patients Post Olt." Hepatology **50**(4): 187. [PDF Full-Text](#) (Scroll down to abstract #187)

[Moeller, Matthew J.; Divine, George; Brown, Kimberly Ann] Henry Ford Hosp, Detroit, MI 48202 USA.

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Gastroenterology

Moonka, D. K., D. Kim, A. Kapke, K. A. Brown and A. Yoshida (2009). "The Influence of Induction Therapy on Graft and Patient Survival in Patients with and without Hepatitis C after Liver Transplantation." Am J Transplant. Epub Ahead of Print. [PDF Full-Text](#)

The Division of Gastroenterology, Henry Ford Health System, Detroit, MI.

We used the United Network for Organ Sharing Database to determine the influence of antibody-based induction therapy on patient and graft survival in orthotopic liver transplant (OLT) recipients with and without hepatitis C (HCV). We identified all initial OLT patients with HCV serology. Patients were divided into four groups: HCV positive without induction (17 362), HCV positive with induction (3479), HCV negative without induction (20 417) and HCV negative with induction (4357). Both HCV positive and negative patients who received induction did better than those who did not. For HCV positive patients, 5-year patient survival was 70.8% versus 68.7% ($p = 0.004$) and graft survival was 65.2% versus 62.1% ($p < 0.001$). For HCV negative patients, 5-year patient survival was 78.8% versus 76.7% ($p < 0.001$) and graft survival was 74.0% versus 70.8% ($p < 0.001$). On multivariate analysis, induction was associated with improved patient (HR = 0.91: $p = 0.024$) and graft (HR = 0.88: $p < 0.001$) survival in HCV positive patients and improved patient (HR = 0.87: $p = 0.003$) and graft survival (HR = 0.87: $p < 0.001$) in HCV negative patients. The benefit of induction occurred early and largely dissipated when patients with death within a year were censored. The benefit of induction therapy appeared most pronounced in patients with renal insufficiency or on organ-perfusion support at transplant.

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Gastroenterology

Rustgi, V. K., W. M. Lee, E. Lawitz, S. C. Gordon, N. Afdhal, F. Poordad, H. L. Bonkovsky, L. Bengtsson, G. Chandorkar, M. Harding, L. McNair, M. Aalyson, J. Alam, R. Kauffman, S. Gharakhanian and J. G. McHutchison (2009). "Merimepodib, Pegylated Interferon, and Ribavirin in Genotype 1 Chronic Hepatitis C Pegylated Interferon and Ribavirin Nonresponders." Hepatology **50**(6): 1719-1726. [PDF Full-Text](#)

[McHutchison, John G.] Duke Univ, Med Ctr, Duke Clin Res Inst, Div Gastroenterol, Durham, NC 27707 USA. [Rustgi, Vinod K.] Georgetown Univ, Med Ctr, Fairfax, VA USA. [Lee, William M.] Univ Texas SW Med Ctr Dallas, Dept Internal Med, Dallas, TX 75390 USA. [Lawitz, Eric] Alamo Med Res, San Antonio, TX USA. [Gordon, Stuart C.] Henry Ford Hlth Syst, Div Gastroenterol & Hepatol, Detroit, MI USA. [Afdhal, Nezam] Beth Israel Deaconess Med Ctr, Boston, MA 02215 USA. [Poordad, Fred] Cedars Sinai Med Ctr, Los Angeles, CA 90048 USA. [Bonkovsky, Herbert L.] Univ Connecticut, Ctr Hlth, Farmington, CT USA. [Bengtsson, Leif; Chandorkar, Gurudatt; Harding, Matthew; McNair, Lindsay; Aalyson, Molly; Alam, John; Kauffman, Robert; Gharakhanian, Shahin] Vertex Pharmaceut Inc, Cambridge, MA USA. McHutchison, JG, Duke Univ, Med Ctr, Duke Clin Res Inst, Div Gastroenterol, 2400 Pratt St, Room 0311, Terrace Level, Durham, NC 27707 USA. mchut001@mc.duke.edu

Merimepodib (MMPD) is an orally administered, inosine monophosphate dehydrogenase inhibitor that has shown antiviral activity in nonresponders with chronic hepatitis C (CHC) when combined with pegylated interferon alfa 2a (Peg-IFN-alfa-2a) and ribavirin (RBV). We conducted a randomized, double-blind, multicenter, phase 2b study to evaluate the antiviral activity, safety, and tolerability of MMPD in combination with Peg-IFN-alfa-2a and RBV in patients with genotype 1 CHC who were nonresponders to prior therapy with Peg-IFN and RBV. Patients received 50 mg MMPD, 100 mg MMPD, or placebo every 12 hours, in addition to Peg-IFN-alfa-2a and RBV, for 24 weeks. Patients with a 2-log or more decrease from baseline or undetectable hepatitis C virus (HCV) RNA levels at week 24 were then eligible to continue Peg-IFN-alfa-2a and RBV for a further 24 weeks, followed by 24 weeks of follow-up. The primary efficacy endpoint was sustained virological response (SVR) rate at week 72 in all randomized patients who received at least one dose of study drug and had a history of nonresponse to standard therapy. A total of 354 patients were randomized to treatment (117 to placebo; 119 to 50 mg MMPD; 118 to 100 mg MMPD), and 286 completed the core study. The proportion of patients who achieved SVR was similar among the treatment groups: 6% (6/107) for 50 mg MMPD, 4% (5/112) for 100 mg MMPD, and 5% (5/104) for placebo ($P = 0.8431$). Adverse-event profiles for the MMPD combination groups were similar to that for Peg-IFN-alfa and RBV alone. Nausea, arthralgia, cough, dyspnea, neutropenia, and anemia were more common in patients taking MMPD. Conclusion: The addition of MMPD to Peg-IFN-alfa-2a and RBV combination therapy did not increase the proportion of nonresponder patients with genotype 1 CHC achieving an SVR. (HFPATOLOGY 2009;50:1719-1726.)

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Gastroenterology

Tang, J., L. Lamerato, M. J. Sheehan, R. Krajenta and S. C. Gordon (2009). "Is Previous Exposure to Hepatitis B a Risk Factor for Pancreatic Cancer?" Hepatology **50**(4): 1486. [PDF Full-Text](#) (Scroll down to abstract #1486)

[Tang, Jeffrey; Lamerato, Lois; Sheehan, Michael J.; Krajenta, Richard; Gordon, Stuart C.] Henry Ford Hlth Syst, Detroit, MI USA.

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Gastroenterology

Vierling, J. M., F. Poordad, E. Lawitz, R. H. Ghalib, W. M. Lee, N. Ravendhran, J. S. Galati, B. R. Bacon, S. L. Flamm, L. A. Balart, B. Freilich, E. R. Schiff, I. M. Jacobson, P. Y. Kwo, S. C. Gordon, M. S. Sulkowski, N. Boparai, E. I. Chaudhri, C. Brass, E. A. Hughes and J. K. Albrecht (2009). "ONCE DAILY NARLAPREVIR (SCH 900518) IN COMBINATION WITH PEGINTRON (TM) (PEGINTERFERON ALFA-2B)/RIBAVIRIN FOR TREATMENT-NAIVE SUBJECTS WITH GENOTYPE-1 CHC: INTERIM RESULTS FROM NEXT-1, A PHASE 2A STUDY." Hepatology **50**(6): LB4. [Article Request Form](#)

[Vierling, John M.] Baylor Coll Med, Houston, TX 77030 USA. [Poordad, Fred] Cedars Sinai Med Ctr, Los Angeles, CA 90048 USA. [Lawitz, Eric] Alamo Med Res, San Antonio, TX USA. [Ghalib, Reem H.] Liver Inst Methodist Dallas, Dallas, TX USA. [Lee, William M.] Univ Texas SW Med Ctr Dallas, Dallas, TX 75390 USA. [Ravendhran, Natarajan] Digest Dis Associates, Baltimore, MD USA. [Galati, Joseph S.] Liver Specialists Texas, Houston, TX USA. [Bacon, Bruce R.] St Louis Univ, Sch Med, St Louis, MO USA. [Flamm, Steven L.] NW Mem Hosp, Chicago, IL 60611 USA. [Balart, Luis A.] Tulane Univ, Hlth Sci Ctr, New Orleans, LA 70118 USA. [Freilich, Bradley] Kansas City Gastroenterol & Hepatol, Kansas City, MO USA. [Schiff, Eugene R.] Univ Miami, Ctr Liver Dis, Miami, FL USA. [Jacobson, Ira M.] Cornell Univ, Weill Med Coll, New York, NY 10021 USA. [Kwo, Paul Y.] Indiana Univ, Sch Med, Indianapolis, IN USA. [Gordon, Stuart C.] Henry Ford Hosp, Detroit, MI 48202 USA. [Sulkowski, Mark S.] Johns Hopkins Rockland Phys Practice & Res Grp, Greenspring Stn, MD USA. [Boparai, Navdeep; Chaudhri, Eirum I.; Brass, Clifford; Hughes, Eric A.; Albrecht, Janice K.] Schering Plough Res Inst, Kenilworth, NJ USA.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Morse, M., R. Chapman, J. Powderly, D. Wang, T. Keler, L. Z. He, V. Ramikrishna, L. Vitale, T. Clay, J. Green and T. Davis (2009). "A Clinical Study Combining Multiple Immune Modulators and an Antigen-Presenting Cell-targeted hCG beta Vaccine (CDX-1307)." Journal of Immunotherapy **32**(9): 1006-1006. [Article Request Form](#)

[Morse, Michael; Clay, Timothy] Duke Univ, Med Ctr, Durham, NC 27706 USA. Carolina BioOncol Inst, Huntersville, NC USA. Henry Ford Hlth Syst, Detroit, MI USA. [Keler, Tibot; He, Lizhen; Ramikrishna, Venky; Vitale, Laura; Green, Jennifer; Davis, Thomas] Celldex Therapeut Inc, Needham, MA USA.

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Hypertension & Vascular Research

Ardanaz, N., X. P. Yang, M. E. Cifuentes, M. J. Haurani, K. W. Jackson, T. D. Liao, O. A. Carretero and P. J. Pagano (2010). "Lack of Glutathione Peroxidase 1 Accelerates Cardiac-Specific Hypertrophy and Dysfunction in Angiotensin II Hypertension." Hypertension **55**(1): 116-U208. [Article Request Form](#)

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Pagano, PJ, Univ Pittsburgh, Sch Med, Dept Pharmacol & Chem Biol, Room 10043, BST-3, 3501 5th Ave, Pittsburgh, PA 15261 USA. pagano@pitt.edu

Glutathione peroxidase 1 (Gpx1) plays an important role in cellular defense by converting hydrogen peroxide and organic hydroperoxides to nonreactive products, and Gpx1(-/-) mice, which are characterized by reduced tissue glutathione peroxidase activity, are known to exhibit enhanced oxidative stress. Peroxides participate in tissue injury, as well as the hypertrophy of cultured cells, yet the role of Gpx1 to prevent end organ damage in cardiovascular tissue is not clear. We postulated that Gpx1 deletion would potentiate both aortic and cardiac hypertrophy, as well as mean arterial blood pressure, in response to angiotensin II (AngII). Our results show that short-term AngII markedly increased left ventricular mass, myocyte cross-sectional area, and interventricular septum thickness and decreased shortening fraction in Gpx1(-/-) mice as compared with wild-type animals. On the other hand, AngII resulted in a similar increase in mean arterial blood pressure in wild-type and Gpx1(-/-) mice. Collagen deposition increased in response to AngII, but no differences were found between strains. Vascular hypertrophy increased to the same extent in Gpx1(-/-) and wild-type mice. Collectively, our results indicate that Gpx1 deficiency accelerates cardiac hypertrophy and dysfunction but has no effect on vascular hypertrophy and mean arterial blood pressure and suggest a major role for Gpx1 in cardiac dysfunction in AngII-dependent hypertension. (Hypertension. 2010;55:116-123.)

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Hypertension & Vascular Research

Harding, P., X. P. Yang, J. J. Yang, E. G. Shesely, Q. He and M. C. Lapointe (2009). "Gene Expression Profiling of Dilated Cardiomyopathy in Aged Male EP4 Knockout Mice." Am J Physiol Heart Circ Physiol. EPub Ahead of Print. [PDF Full-Text](#)

Henry Ford Health System.

Using a line of mice with cardiac-specific knockout (KO) of the EP4 receptor gene, experiments were designed to determine if a cardiac phenotype developed with age. Cardiac function was assessed by echocardiography in 23-33-week-old male and female KO and littermate controls (Cont or WT) mice. After echocardiography, hearts were removed to assess weight and then some were further processed for histology [myocyte cross-sectional area (MCSA), interstitial collagen fraction (ICF) and macrophage infiltration] and some for extraction of total RNA and protein. Aged male KO mice had reduced ejection fraction (EF) coupled with left ventricular dilatation. MCSA and infiltrating macrophages were not different between groups, but ICF increased by 39% in KO mice. In contrast to male KO mice, 30-32-week-old female KO mice only had a slight reduction in EF. To understand gene expression differences between male WT and KO mice, whole genome gene expression profiling (Illumina BeadChips) on hearts of 30-32 week old mice was done. Data indicated that 156 genes were overexpressed in the KO hearts more than 2-fold, including genes involved in remodeling, inflammation, and oxidative stress. Overexpressed chemokines/cytokines were further examined in hearts of 10-12-week old male KO mice, and it was found that growth-differentiation factor-15 (GDF-15) expression was higher in KO vs. WT hearts. In conclusion, EP4 knockdown in cardiac myocytes in aged male KO mice is in part associated with increased fibrosis, reduced EF and dilated cardiomyopathy. Early overexpression of GDF-15 in hearts of male KO mice may contribute to or be a marker of the disease phenotype. The absence of serious cardiac dysfunction in aged female mice suggests a sexual dimorphism in the phenotype. Key words: heart, gene array, EP4, remodeling.

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Hypertension & Vascular Research

Liao, T. D., X. P. Yang, M. D'Ambrosio, Y. Zhang, N. E. Rhaleb and O. A. Carretero (2009). "N-Acetyl-Seryl-Aspartyl-Lysyl-Proline Attenuates Renal Injury and Dysfunction in Hypertensive Rats With Reduced Renal Mass. Council for High Blood Pressure Research." Hypertension. EPub Ahead of Print. [Article Request Form](#)

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

N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) is a naturally occurring peptide of which the plasma concentration is increased 4- to 5-fold by angiotensin-converting enzyme inhibitors. We reported previously

that, in models of both hypertension and postmyocardial infarction, Ac-SDKP reduces cardiac inflammation and fibrosis. However, it is unknown whether Ac-SDKP can prevent or reverse renal injury and dysfunction in hypertension. In the present study, we tested the hypothesis that, in rats with 5/6 nephrectomy (5/6Nx)-induced hypertension, Ac-SDKP reduces renal damage, albuminuria, and dysfunction by decreasing inflammatory cell infiltration and renal fibrosis and by increasing nephrin protein. Ac-SDKP (800 µg/kg per day, SC via osmotic minipump) or vehicle was either started 7 days before 5/6Nx (prevention) and continued for 3 weeks or started 3 weeks after 5/6Nx (reversal) and continued for another 3 weeks. Rats with 5/6Nx developed high blood pressure, left ventricular hypertrophy, albuminuria, decreased glomerular filtration rate, and increased macrophage infiltration (inflammation) and renal collagen content (fibrosis). Ac-SDKP did not affect blood pressure or left ventricular hypertrophy in either group; however, it significantly reduced albuminuria, renal inflammation, and fibrosis and improved glomerular filtration rate in both prevention and reversal groups. Moreover, slit diaphragm nephrin protein expression in the glomerular filtration barrier was significantly decreased in hypertensive rats. This effect was partially prevented or reversed by Ac-SDKP. We concluded that Ac-SDKP greatly attenuates albuminuria and renal fibrosis and improves renal function in rats with 5/6Nx. These effects may be related to decreased inflammation (macrophages) and increased nephrin protein.

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Hypertension & Vascular Research

Ortiz-Capisano, M. C., T. D. Liao, P. A. Ortiz and W. H. Beierwaltes (2009). "Calcium-dependent phosphodiesterase 1C inhibits renin release from isolated juxtaglomerular cells." *Am J Physiol Regul Integr Comp Physiol* **297**(5): R1469-76. PMC2777770. [PDF Full-Text](#)

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

Renin release from the juxtaglomerular (JG) cell is stimulated by the second messenger cAMP and inhibited by calcium. We previously showed JG cells contain a calcium sensing receptor (CaSR), which, when stimulated, decreases cAMP formation and inhibits renin release. We hypothesize CaSR activation decreases cAMP and renin release, in part, by stimulating a calcium calmodulin-activated phosphodiesterase 1 (PDE1). We incubated our primary culture of JG cells with two selective PDE1 inhibitors [8-methoxymethyl-IBMX (8-MM-IBMX; 20 µM) and vinpocetine (40 µM)] and the calmodulin inhibitor W-7 (10 µM) and measured cAMP and renin release. Stimulation of the JG cell CaSR with the calcimimetic cinacalcet (1 µM) resulted in decreased cAMP from a basal of 1.13 ± 0.14 to 0.69 ± 0.08 pM/mg protein (P < 0.001) and in renin release from 0.89 ± 0.16 to 0.38 ± 0.08 µg ANG I/mlxh(-1)xmg protein(-1) (P < 0.001). However, the addition of 8-MM-IBMX with cinacalcet returned both cAMP (1.10 ± 0.19 pM/mg protein) and renin (0.57 ± 0.16 µg ANG I/mlxh(-1)xmg protein(-1)) to basal levels. Similar results were obtained with vinpocetine, and also with W-7. Combining 8-MM-IBMX and W-7 had no additive effect. To determine which PDE1 isoform is involved, we performed Western blot analysis for PDE1A, B, and C. Only Western blot analysis for PDE1C showed a characteristic band apparent at 80 kDa. Immunofluorescence showed cytoplasmic distribution of PDE1C and renin in the JG cells. In conclusion, PDE1C is expressed in isolated JG cells, and contributes to calcium's inhibitory modulation of renin release from JG cells.

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Hypertension & Vascular Research

Rabindranath, K. S., T. Bansal, J. Adams, R. Das, R. Shail, A. M. MacLeod, C. Moore and A. Besarab (2009). "Systematic review of antimicrobials for the prevention of haemodialysis catheter-related infections." *Nephrology Dialysis Transplantation* **24**(12): 3763-3774. [PDF Full-Text](#)

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Background. Almost 30% of chronic haemodialysis (HD) patients are dependent on central venous catheters (CVCs) for their vascular access, and catheter-related bacteraemia (CRB) is the major reason for catheter loss

and has been associated with substantial morbidity, including meta-static infections. This systematic review evaluates the benefits and harms of antimicrobial interventions for the prevention of catheter-related infections (CRIs). Methods. MEDLINE (1950-May 2009), EMBASE (1980-May 2009) CENTRAL(up to May 2009) and bibliographies of retrieved articles were searched for relevant RCTs. Analysis was by a random effects model and results expressed as rate ratio, relative risk (RR) and weighted mean difference (WMD) with 95% confidence intervals (CI). Results. A total of 29 trials with 2886 patients and 3005 catheters were included. Antimicrobial catheter locks (AMLs) significantly reduced the rates of CRBs (rate ratio, 0.33, 95% CI 0.24-0.45) and exit-site infections (ESIs) (rate ratio 0.67, 95% CI 0.47-0.96). Exit-site antimicrobial application also significantly reduced the rates of CRBs (rate ratio 0.21, 95% CI 0.12-0.36) and ESIs (rate ratio 0.22, 95% CI 0.10-0.47). Antimicrobial coating of HD catheters and the use of peri-operative antimicrobials did not result in significant reduction in rates of CRBs and ESIs. Conclusion. The use of AMLs and exit-site antimicrobials are useful measures in the reduction of CRIs, whereas antimicrobial impregnated catheters and peri-operative systemic antimicrobial administration have not been found to be beneficial. Further head-to-head trials of various AMLs and exit-site antimicrobials are needed to know about their comparative clinical efficacy.

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Infectious Diseases

Reyes, K., R. Malik, C. Moore, S. Donabedian, M. Perri, L. Johnson and M. Zervos (2009). "Evaluation of Risk Factors for Co-Infection or Co-Colonization with Vancomycin-Resistant Enterococcus and Methicillin-Resistant Staphylococcus aureus." J Clin Microbiol. Epub Ahead of Print. [Article Request Form](#)

Division of Infectious Diseases, Henry Ford Health System, Detroit, Michigan; Wayne State University, School of Medicine, Detroit, Michigan; and St. Joseph's Mercy Oakland Hospital, Pontiac, Michigan.

We retrospectively evaluated 410 patients with co-infection or co-colonization due to vancomycin-resistant Enterococcus (VRE) and methicillin-resistant Staphylococcus aureus (MRSA). The prevalence rate was 19.8%. Risk factors included isolation of VRE faecalis, use of linezolid and of clindamycin. Inc18-like vanA plasmids occurred in 7% of VRE faecalis, none in VRE faecium.

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Internal Medicine

Novak, J. E. and L. A. Szczech (2009). "Management of HIV-infected patients with ESRD." Adv Chronic Kidney Dis **17**(1): 102-10. [PDF Full-Text](#)

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Patients infected with human immunodeficiency virus (HIV) often progress to ESRD. In the era of highly active antiretroviral therapy, the care of these patients has become increasingly complex as survival has improved. Patients infected with HIV who also have ESRD are at risk for critical interactions between medication regimens to treat both of these conditions. Within this population, hemo- and peritoneal dialysis as well as kidney transplantation are life sustaining but present a host of obstacles related to HIV monitoring and risk of transmission, access thrombosis, infection, and rejection. Knowledge of antiretroviral regimens, drug interactions, and HIV resistance as well as the management of ESRD in the presence of HIV infection will improve the care of these unique patients.

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Medical Genetics

Barker, S. D., S. Bale, J. Booker, A. Buller, S. Das, K. Friedman, A. K. Godwin, W. W. Grody, E. Highsmith, J. A. Kant, E. Lyon, R. Mao, K. G. Monaghan, D. A. Payne, V. M. Pratt, I. Schrijver, A. E. Shrimpton, E. Spector, M. Telatar, L. Toji, K. Weck, B. Zehnbauser and L. V. Kalman (2009). "Development and Characterization of Reference Materials for MTHFR, SERPINA1, RET, BRCA1, and BRCA2 Genetic Testing." Journal of Molecular Diagnostics **11**(6): 553-561. [PDF Full-Text](#)

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Well-characterized reference materials (RMs) are integral in maintaining clinical laboratory quality assurance for genetic testing. These RMs can be used for quality control, monitoring of test performance, test validation, and proficiency testing of DNA-based genetic tests. To address the need for such materials, the Centers for Disease Control and Prevention established the Genetic Testing Reference Material Coordination Program (GeT-RM), which works with the genetics community to improve public availability of characterized RMs for genetic testing. To date, the GeT-RM program has coordinated the characterization of publicly available genomic DNA RMs for a number of disorders, including cystic fibrosis, Huntington disease, fragile X, and several genetic conditions with relatively high prevalence in the Ashkenazi Jewish population. Genotypic information about a number of other cell lines has been collected and is also available. The present study includes the development and commutability/genotype characterization of 10 DNA samples for clinically relevant mutations or sequence variants in the following genes: MTHFR; SERPINA1; RET; BRCA1; and BRCA2. DNA samples were analyzed by 19 clinical genetic laboratories using a variety of assays and technology platforms. Concordance was 100% for all samples, with no differences observed between laboratories using different methods. All DNA samples are available from Coriell Cell Repositories and characterization information can be found on the GeT-RM website. (J Mol Diagn 2009, 11:553-561; DOI: 10.2353/jmoldx.2009.090078)

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Neurology

Ascherio, A., P. A. LeWitt, K. Xu, S. Eberly, A. Watts, W. R. Matson, C. Marras, K. Kiebertz, A. Rudolph, M. B. Bogdanov, S. R. Schwid, M. Tennis, C. M. Tanner, M. F. Beal, A. E. Lang, D. Oakes, S. Fahn, I. Shoulson and M. A. Schwarzschild (2009). "Urate as a Predictor of the Rate of Clinical Decline in Parkinson Disease." Archives of Neurology **66**(12): 1460-1468.

[PDF Full-Text](#)

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Background: The risk of Parkinson disease (PD) and its rate of progression may decline with increasing concentration of blood urate, a major antioxidant. Objective: To determine whether serum and cerebrospinal

fluid concentrations of urate predict clinical progression in patients with PD. Design, Setting, and Participants: Eight hundred subjects with early PD enrolled in the Deprenyl and Tocopherol Antioxidative Therapy of Parkinsonism (DATATOP) trial. The pretreatment urate concentration was measured in serum for 774 subjects and in cerebrospinal fluid for 713 subjects. Main Outcome Measures: Treatment-, age-, and sex-adjusted hazard ratios (HRs) for clinical disability requiring levodopa therapy, the prespecified primary end point of the original DATATOP trial. Results: The HR of progressing to the primary end point decreased with increasing serum urate concentrations (HR for highest vs lowest quintile=0.64; 95% confidence interval [CI], 0.44-0.94; HR for a 1-SD increase=0.82; 95% CI, 0.73-0.93). In analyses stratified by alpha-tocopherol treatment (2000 IU/d), a decrease in the HR for the primary end point was seen only among subjects not treated with alpha-tocopherol (HR for a 1-SD increase=0.75; 95% CI, 0.62-0.89; vs HR for those treated=0.90; 95% CI, 0.75-1.08). Results were similar for the rate of change in the Unified Parkinson's Disease Rating Scale score. Cerebrospinal fluid urate concentration was also inversely related to both the primary end point (HR for highest vs lowest quintile=0.65; 95% CI, 0.44-0.96; HR for a 1-SD increase=0.89; 95% CI, 0.79-1.02) and the rate of change in the Unified Parkinson's Disease Rating Scale score. As with serum urate concentration, these associations were present only among subjects not treated with alpha-tocopherol. Conclusions: Higher serum and cerebrospinal fluid urate concentrations at baseline were associated with slower rates of clinical decline. The findings strengthen the link between urate concentration and PD and the rationale for considering central nervous system urate concentration elevation as a potential strategy to slow PD progression.

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Neurology

Cerghet, M., R. P. Skoff, M. Swamydas and D. Bessert (2009). "Sexual dimorphism in the white matter of rodents." J Neurol Sci **286**(1-2): 76-80. PMC2760672. [PDF Full-Text](#)

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Sexual dimorphism of astrocytes and neurons is well documented in many brain and spinal cord structures. Sexual dimorphism of oligodendrocytes (Olg) and myelin has received less attention. We recently showed that density of Olg in corpus callosum, fornix, and spinal cord of wild-type male rodents is more densely packed than in females; myelin proteins and myelin gene expression are likewise greater in males than in female rodents. However, glial cell proliferation and cell death were two times greater in female corpus callosum. Endogenous sex hormones, specifically lack of androgens, produce an Olg female phenotype in castrated male mouse. In vitro studies using Olg culture also showed differences between males and females Olg survival and signaling pathways in response to sexual hormones. Sexual dimorphism of white matter tracts and glia in rodents indicates the necessity for controlling gender in the experimental studies of neurodegenerative disorders. Most importantly, our studies suggest that hormones may contribute to sexual dimorphism observed in certain human diseases including multiple sclerosis.

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Neurology

Cui, X., M. Chopp, A. Zacharek, C. Roberts, M. Lu, S. Savant-Bhonsale and J. Chen (2009). "Chemokine, vascular and therapeutic effects of combination Simvastatin and BMSC treatment of stroke." Neurobiol Dis **36**(1): 35-41. PMC2748847. [Article Request Form](#)

Department of Neurology, E&R Bldg., Room 3091, Henry Ford Hospital, 2799 W Grand Blvd, Detroit, MI 48202, USA.

We investigated the additive therapeutic effect of the combination treatment of stroke with sub-therapeutic doses of Simvastatin, a HMG-CoA reductase inhibitor, and bone marrow stromal cells (BMSCs). Rats were administered Simvastatin (0.5 mg/kg), BMSCs (1x10⁶) or combination of Simvastatin and BMSCs starting at 24 h after stroke. Combination treatment significantly improved neurological outcome, enhanced angiogenesis and arteriogenesis, and increased the number of engrafted-BMSCs in the ischemic brain. The number of engrafted-BMSCs and arteriogenesis was significantly correlated with functional outcome. Simvastatin significantly increased stromal cell-derived factor-1 (SDF1) expression in the ischemic brain and chemokine (CXC motif) receptor-4 (CXCR4) in BMSCs, and increased BMSC migration to RBMECs and astrocytes. Combination treatment of stroke upregulates the SDF1/CXCR4 axis and enhances BMSC migration into the ischemic brain, amplifies arteriogenesis and angiogenesis, and improves functional outcome after stroke.

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Neurology

Jiang, Q., Z. G. Zhang and M. Chopp (2009). "MRI of Stroke Recovery." Stroke. [Article Request Form](#)

From the Department of Neurology, Henry Ford Health System, Detroit, Mich.

MRI is a vital tool for the measurement of acute stroke and has been used to visualize changes in activation patterns during stroke recovery. There is emerging interest on using MRI to monitor the structural substrates of spontaneous recovery and neurorestorative treatment of stroke. In this review, we describe the use of MRI and its associated challenges to measure vascular and neuronal remodeling in response to spontaneous and therapy-induced stroke recovery. We demonstrate that MRI methodologies may be used in real-time monitoring of recovery from stroke.

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Neurology

Mikkelsen, T., N. A. Paleologos, P. D. Robinson, M. Ammirati, D. W. Andrews, A. L. Asher, S. H. Burri, C. S. Cobbs, L. E. Gaspar, D. Kondziolka, M. E. Linskey, J. S. Loeffler, M. McDermott, M. P. Mehta, J. J. Olson, R. A. Patchell, T. C. Ryken and S. N. Kalkanis (2009). "The role of prophylactic anticonvulsants in the management of brain metastases: a systematic review and evidence-based clinical practice guideline." J Neurooncol. EPub Ahead of Print. [PDF Full-Text](#)

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

QUESTION : Do prophylactic anticonvulsants decrease the risk of seizure in patients with metastatic brain tumors compared with no treatment? Target population These recommendations apply to adults with solid brain metastases who have not experienced a seizure due to their metastatic brain disease. Recommendation Level 3 For adults with brain metastases who have not experienced a seizure due to their metastatic brain disease, routine prophylactic use of anticonvulsants is not recommended. Only a single underpowered randomized controlled trial (RCT), which did not detect a difference in seizure occurrence, provides evidence for decision-making purposes.

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Neurology

Silver, B., S. McCarthy, M. Lu, P. Mitsias, A. N. Russman, A. Katramados, D. C. Morris, C. A. Lewandowski and M. Chopp (2009). "Sildenafil treatment of subacute ischemic stroke: a safety study at 25-mg daily for 2 weeks." J Stroke Cerebrovasc Dis **18**(5): 381-3. [Article Request Form](#)

Department of Neurology, Henry Ford Hospital, Detroit, Michigan 48202, USA. bsilver1@hfhs.org

BACKGROUND: In several animal studies of young and aged rats with ischemic stroke, treatment with sildenafil improved functional outcomes compared with placebo. We conducted a safety study of sildenafil (25 mg daily for 2 weeks) shortly after ischemic stroke onset. METHODS: We recruited patients aged 18 to 80 years with ischemic stroke, National Institutes of Health stroke scale (NIHSS) score 2 to 21, between days 2 and 9 after symptom onset. Patients were treated with sildenafil for 2 weeks (25 mg daily). The primary outcome measure was the adverse occurrence of any of the following during the treatment period: stroke worsening, new stroke, myocardial infarction, vision loss, hearing loss, or death from any cause. Secondary outcome measures were NIHSS score, Barthel indices, and modified Rankin score at 90 days. RESULTS: Twelve patients were recruited. Mean age was 57 years, 5 were female, and median NIHSS score at entry was 9.5 (range 2-20). The primary outcome measure occurred in one patient (sudden death). Another patient committed suicide 2 months after study entry (and 6 weeks after treatment with sildenafil had been completed). Among the 10 survivors, at 90 days, median NIHSS score was 2 (range 0-12), median Barthel index was 95 (range 15-100), and median modified Rankin score was 1.5 (range 0-5). CONCLUSIONS: Sildenafil (25 mg daily for 2 weeks) appeared to be safe in this group of patients with mild to moderately severe stroke. Further studies of higher doses will be tested.

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Neurology

Smith, B. J., E. K. St Louis, J. M. Stern, C. Green and T. Bramley (2009). "Concerns with AED Conversion: Comparison of Patient and Physician Perspectives." Curr Neuropharmacol **7**(2): 120-4. PMC2730003. [Article Request Form](#)

Henry Ford Hospital, Detroit, Michigan, USA.

When discussing AED conversion in the clinic, both the patient and physician perspectives on the goals and risks of this change are important to consider. To identify patient-reported and clinician-perceived concerns, a panel of epilepsy specialists was questioned about the topics discussed with patients and the clinician's perspective of patient concerns. Findings of a literature review of articles that report patient-expressed concerns regarding their epilepsy and treatment were also reviewed. Results showed that the specialist panel appropriately identified patient-reported concerns of driving ability, medication cost, seizure control, and medication side effects. Additionally, patient-reported concerns of independence, employment issues, social stigma, medication dependence, and undesirable cognitive effects are important to address when considering and initiating AED conversion.

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Neurology

Zhang, J., Z. G. Zhang, D. Morris, Y. Li, C. Roberts, S. B. Elias and M. Chopp (2009). "Neurological Functional Recovery after Thymosin Beta4 Treatment in Mice with Experimental Auto Encephalomyelitis." Neuroscience **164**(4): 1887-1893. [PDF Full-Text](#)

[Zhang, J.; Zhang, Z. G.; Li, Y.; Roberts, C.; Elias, S. B.; Chopp, M.] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Morris, D.] Henry Ford Hlth Syst, Dept Emergency Med, Detroit, MI 48202 USA. [Chopp, M.] Oakland Univ, Dept Phys, Rochester, MI 48309 USA. Chopp, M, Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. chopp@neuro.hfh.edu

In the present study, we hypothesized that thymosin beta 4 (Tbeta4) is a potential therapy of multiple sclerosis (MS). To test this hypothesis, SJL/J mice (n=21) were subjected to experimental autoimmune encephalomyelitis (EAE), an animal model of MS. EAE mice were treated with saline or Tbeta4 (6 mg/kg, n=10) every 3 days starting on the day of myelin proteolipid protein (PLP) immunization for total five doses. Neurological function, inflammatory infiltration, oligodendrocyte progenitor cells (OPCs) and mature oligodendrocytes were measured in the brain of EAE mice. Double immunohistochemical staining was used to detect proliferation and differentiation of OPCs. Tbeta4 was used to treat N20.1 cells (premature oligodendrocyte cell line) in vitro, and proliferation of N20.1 cells was measured by bromodeoxyuridine (BrdU) immunostaining. Tbeta4 treatment improved functional recovery after EAE. Inflammatory infiltrates were significantly reduced in the Tbeta4 treatment group compared to the saline groups (3.6±0.3/slide vs 5±0.5/slide, P<0.05). NG2(+) OPCs (447.7±41.9 vs 195.2±31/mm²) in subventricular zone (SVZ), 75.1±4.7 vs 41.7±0.2/mm²) in white matter), CNPase(+) mature oligodendrocytes (267.5±10.3 vs 141.4±22.9/mm²), BrdU(+) with NG2(+) OPCs (32.9±3.7 vs 17.9±3.6/mm²), BrdU(+) with CNPase+ mature oligodendrocytes (18.2±1.7 vs 10.7±2.2/mm²) were significantly increased in the Tbeta4 treated mice compared to those of saline controls (P<0.05). These data indicate that Tbeta4 treatment improved functional recovery after EAE, possibly, via reducing inflammatory infiltrates, and stimulating oligodendrogenesis. (C) 2009 IBRO. Published by Elsevier Ltd. All rights reserved.

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Neurology

Zhang, L., M. Chopp, L. Jia, Y. Cui, M. Lu and Z. G. Zhang (2009). "Atorvastatin extends the therapeutic window for tPA to 6 h after the onset of embolic stroke in rats." J Cereb Blood Flow Metab **29**(11): 1816-24. [Article Request Form](#)

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

We investigated the neuroprotective effect of atorvastatin in combination with delayed thrombolytic therapy in a rat model of embolic stroke. Rats subjected to embolic middle cerebral artery (MCA) occlusion were treated with atorvastatin at 4 h, followed by tissue plasminogen activator (tPA) at 6 or 8 h after stroke. The combination of atorvastatin at 4 h and tPA at 6 h significantly decreased the size of the embolus at the origin of the MCA, improved microvascular patency, and reduced infarct volume, but did not increase the incidence of hemorrhagic transformation compared with vehicle-treated control animals. However, monotherapy with tPA at 6 h increased the incidence of hemorrhagic transformation and failed to reduce infarct volume compared with the control group. In addition, adjuvant treatment with atorvastatin at 4 h and with tPA at 6 h reduced tPA-induced upregulation of protease-activated receptor-1, intercellular adhesion molecule-1, and matrix metalloproteinase-9, and concomitantly reduced cerebral microvascular platelet, neutrophil, and fibrin deposition compared with rats treated with tPA alone at 6 h. In conclusion, a combination of atorvastatin and tPA extended the therapeutic window for stroke to 6 h without increasing the incidence of hemorrhagic transformation. Atorvastatin blocked delayed tPA-potentiated adverse cerebral vascular events, which likely contributes to the neuroprotective effect of the combination therapy.

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Neurosurgery

Kalkanis, S. N., D. Kondziolka, L. E. Gaspar, S. H. Burri, A. L. Asher, C. S. Cobbs, M. Ammirati, P. D. Robinson, D. W. Andrews, J. S. Loeffler, M. McDermott, M. P. Mehta, T. Mikkelsen, J. J. Olson, N. A. Paleologos, R. A. Patchell, T. C. Ryken and M. E. Linskey (2009). "The role of surgical resection in the management of newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline." J Neurooncol. Epub Ahead of Print. [Article Request Form](#)

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QUESTION : Should patients with newly-diagnosed metastatic brain tumors undergo open surgical resection versus whole brain radiation therapy (WBRT) and/or other treatment modalities such as radiosurgery, and in what clinical settings? Target population These recommendations apply to adults with a newly diagnosed single brain metastasis amenable to surgical resection. Recommendations Surgical resection plus WBRT versus surgical resection alone Level 1 Surgical resection followed by WBRT represents a superior treatment modality, in terms of improving tumor control at the original site of the metastasis and in the brain overall, when compared to surgical resection alone. Surgical resection plus WBRT versus SRS +/- WBRT Level 2 Surgical resection plus WBRT, versus stereotactic radiosurgery (SRS) plus WBRT, both represent effective treatment strategies, resulting in relatively equal survival rates. SRS has not been assessed from an evidence-based standpoint for larger lesions (>3 cm) or for those causing significant mass effect (>1 cm midline shift). Level 3 Underpowered class I evidence along with the preponderance of conflicting class II evidence suggests that SRS alone may provide equivalent functional and survival outcomes compared with resection + WBRT for patients with single brain metastases, so long as ready detection of distant site failure and salvage SRS are possible. Note The following question is fully addressed in the WBRT guideline paper within this series by Gaspar et al. Given that the recommendation resulting from the systematic review of the literature on this topic is also highly relevant to the discussion of the role of surgical resection in the management of brain metastases, this recommendation has been included below. Question Does surgical resection in addition to WBRT improve outcomes when compared with WBRT alone? Target population This recommendation applies to adults with a newly diagnosed single brain metastasis amenable to surgical resection; however, the recommendation does not apply to relatively radiosensitive tumors histologies (i.e., small cell lung cancer, leukemia, lymphoma, germ cell tumors and multiple myeloma). Recommendation Surgical resection plus WBRT versus WBRT alone Level 1 Class I evidence supports the use of surgical resection plus post-operative WBRT, as compared to WBRT alone, in patients with good performance status (functionally independent and spending less than 50% of time in bed) and limited extra-cranial disease. There is insufficient evidence to make a recommendation for patients with poor performance scores, advanced systemic disease, or multiple brain metastases.

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Neurosurgery

Kalkanis, S. N. and M. E. Linskey (2009). "Evidence-based clinical practice parameter guidelines for the treatment of patients with metastatic brain tumors: introduction." J Neurooncol. Epub of Ahead of Print. [PDF Full-Text](#)

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Otolaryngology

Worsham, M., J. Stephen, M. Lu, A. Kapke and M. Benninger (2009). "Modeling survival outcome of primary HNSCC in an ethnically diverse primary care cohort." *Oral Oncology*: 77-78. [Article Request Form](#)

[Worsham, M.; Stephen, J.; Lu, M.; Kapke, A.] Henry Ford Hlth Syst, Detroit, MI 48202 USA. [Benninger, M.] Cleveland Clin, Cleveland, OH 44106 USA.

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Pathology

Mei, K. Y., A. J. Liu, R. W. Allan, P. Wang, Z. L. Lane, T. W. Abel, L. X. Wei, H. Cheng, S. P. Guo, Y. Peng, D. Rakheja, M. Wang, J. Ma, M. M. Rodriguez, J. P. Li and D. F. Cao (2009). "Diagnostic utility of SALL4 in primary germ cell tumors of the central nervous system: a study of 77 cases." *Modern Pathology* **22**(12): 1628-1636. [PDF Full-Text](#)

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Primary germ cell tumors of the central nervous system (CNS) sometimes pose diagnostic difficulty. In this study we analyzed the diagnostic utility of a novel marker, SALL4, in 77 such tumors (59 pure and 18 mixed) consisting of the following tumors/tumor components: 49 germinomas, 7 embryonal carcinomas, 27 yolk sac tumors, 3 choriocarcinomas, and 14 teratomas. We also stained SALL4 in 99 primary non-germ cell tumors to test SALL4 specificity. We compared SALL4 with OCT4 in all germ cell tumors and compared SALL4 with a-fetoprotein and glypican-3 in all yolk sac tumors. The staining was semiquantitatively scored as 0 (no staining), 1+ (<= 30%), 2+ (31-60%), 3+ (61-90%), and 4+ (>90%). Strong SALL4 staining was observed in all 49 germinomas (4+ in 48, 3+ in 1), 7 embryonal carcinomas (all 4+), and 27 yolk sac tumors (1+ in 1, 2+ in 2, 3+ in 7, 4+ in 17). SALL4 staining, 1+ weak to focally strong, was observed in 2 of 3 choriocarcinomas (in mononucleated trophoblasts) and in 9 of 14 teratomas (in primitive neuroepithelium and teratomatous glands). All germinomas and embryonal carcinomas showed strong OCT4 staining (4+ in all except 1 germinoma with 3+), whereas other germ cell tumors were negative. Out of 27 yolk sac tumors, 26 showed positive a-fetoprotein staining (1+ in 9, 2+ in 7, 3+ in 5, and 4+ in 5). All yolk sac tumors showed positive glypican-3 staining (1+ in 6, 2+ in 6, 3+ in 7, and 4+ in 8). The mean percentage of yolk sac tumor cells stained was 84% with SALL4, 45% with a-fetoprotein, and 63% with glypican-3 (P<0.01). No non-germ cell tumors showed SALL4 staining. Our results indicate that SALL4 is a novel sensitive diagnostic marker for primary germ cell tumors of the CNS with high specificity. SALL4 is a more sensitive marker than a-fetoprotein and glypican-3 for yolk sac tumors. *Modern Pathology* (2009) 22, 1628-1636; doi:10.1038/modpathol.2009.148; published online 9 October 2009

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Pathology

Pimentel, J. D., F. A. Meier and L. P. Samuel (2009). "Chorioamnionitis and Neonatal Sepsis from Community-associated MRSA." Emerging Infectious Diseases **15**(12): 2069-2071. [Article Request Form](#)

[Pimentel, Jason D.] Henry Ford Hosp, Dept Pathol & Lab Med, Detroit, MI 48202 USA.

Pimentel, JD, Henry Ford Hosp, Dept Pathol & Lab Med, 2799 W Grand Blvd, Detroit, MI 48202 USA.

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Pharmacy

Adams, J., N. Patel, N. Mankaryous, M. Tadros and C. D. Miller (2009). "Nonnucleoside Reverse Transcriptase Inhibitor Resistance and the Role of the Second-Generation Agents (January)." Ann Pharmacother. Epub Ahead of Print. [Article Request Form](#)

Henry Ford Hospital, Detroit, MI.

OBJECTIVE: To review the current state of nonnucleoside reverse transcriptase inhibitor (NNRTI) resistance, discuss the promising role of second-generation NNRTIs, and provide insight into their clinical utility. **DATA SOURCES:** Articles were identified through searches of MEDLINE (May 2000-August 2009) and International Pharmaceutical Abstracts (May 1998- August 2009), using the key words etravirine, rilpivirine, TMC125, TMC278, diarylpyrimidine, NNRTI, and resistance. **STUDY SELECTION AND DATA EXTRACTION:** Clinical trials, resistance studies, and pharmacokinetic data were selected for review. **DATA SYNTHESIS:** NNRTIs are an integral class of antiretroviral agents utilized for the treatment of HIV-1 infection. These agents have become preferred therapy options for treatment-naive individuals per treatment guideline recommendations and have gained increased popularity over protease inhibitor-based antiretroviral therapy. However, available NNRTIs possess inherent characteristics, such as low genetic barrier to resistance and high degree of cross-resistance, that limit their use in HIV therapy. Due to the growing utilization of this highly efficacious antiretroviral class and the increased capability for resistance development, many HIV-infected patients have experienced treatment failure of an NNRTI. Cross-resistance makes other first-generation NNRTI agents unavailable for future use. Etravirine and rilpivirine are second-generation NNRTIs that are not significantly hampered by cross-resistance and possess potent antiretroviral activity against current NNRTI-resistant viral strains. These agents provide new and important therapy options for many HIV-infected patients. **CONCLUSIONS:** NNRTI resistance is an increasing problem that may impair the chances for therapeutic success in HIV-infected patients. Novel agents such as etravirine and rilpivirine provide new, sensitive options for patients and significantly improve the rate of virologic suppression when appropriately applied.

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Radiation Oncology

Fragoso, M., I. Kawrakow, B. A. Faddegon, T. D. Solberg and I. J. Chetty (2009). "Fast, accurate photon beam accelerator modeling using BEAMnrc: A systematic investigation of efficiency enhancing methods and cross-section data." Medical Physics **36**(12): 5451-5466. [Article Request Form](#)

[Fragoso, Margarida; Chetty, Indrin J.] Henry Ford Hlth Syst, Detroit, MI 48202 USA. [Kawrakow, Iwan] Natl Res Council Canada, Ottawa, ON K1A 0R6, Canada. [Faddegon, Bruce A.] Univ Calif San Francisco, San Francisco, CA 94143 USA. [Solberg, Timothy D.] Univ Texas SW Med Ctr Dallas, Dallas, TX 75390 USA. Fragoso, M, Univ Cape Verde, Praia, Cape Verde.

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In this work, an investigation of efficiency enhancing methods and cross-section data in the BEAMnrc Monte Carlo (MC) code system is presented. Additionally, BEAMnrc was compared with VMC++, another special-purpose MC code system that has recently been enhanced for the simulation of the entire treatment head. BEAMnrc and VMC++ were used to simulate a 6 MV photon beam from a Siemens Primus linear accelerator (linac) and phase space (PHSP) files were generated at 100 cm source-to-surface distance for the 10 x 10 and 40 x 40 cm(2) field sizes. The BEAMnrc parameters/techniques under investigation were grouped by (i) photon and bremsstrahlung cross sections, (ii) approximate efficiency improving techniques (AEITs), (iii) variance reduction techniques (VRTs), and (iv) a VRT (bremsstrahlung photon splitting) in combination with an AEIT (charged particle range rejection). The BEAMnrc PHSP file obtained without the efficiency enhancing

techniques under study or, when not possible, with their default values (e.g., EXACT algorithm for the boundary crossing algorithm) and with the default cross-section data (PEGS4 and Bethe-Heitler) was used as the "base line" for accuracy verification of the PHSP files generated from the different groups described previously. Subsequently, a selection of the PHSP files was used as input for DOSXYZnrc-based water phantom dose calculations, which were verified against measurements. The performance of the different VRTs and AEITs available in BEAMnrc and of VMC++ was specified by the relative efficiency, i. e., by the efficiency of the MC simulation relative to that of the BEAMnrc base-line calculation. The highest relative efficiencies were similar to 935 (similar to 111 min on a single 2.6 GHz processor) and similar to 200 (similar to 45 min on a single processor) for the 10 x 10 field size with 50 million histories and 40 x 40 cm(2) field size with 100 million histories, respectively, using the VRT directional bremsstrahlung splitting (DBS) with no electron splitting. When DBS was used with electron splitting and combined with augmented charged particle range rejection, a technique recently introduced in BEAMnrc, relative efficiencies were similar to 420 (similar to 253 min on a single processor) and similar to 175 (similar to 58 min on a single processor) for the 10 x 10 and 40 x 40 cm(2) field sizes, respectively. Calculations of the Siemens Primus treatment head with VMC++ produced relative efficiencies of similar to 1400 (similar to 6 min on a single processor) and similar to 60 (similar to 4 min on a single processor) for the 10 x 10 and 40 x 40 cm(2) field sizes, respectively. BEAMnrc PHSP calculations with DBS alone or DBS in combination with charged particle range rejection were more efficient than the other efficiency enhancing techniques used. Using VMC++, accurate simulations of the entire linac treatment head were performed within minutes on a single processor. Noteworthy differences (+1% -3%) in the mean energy, planar fluence, and angular and spectral distributions were observed with the NIST bremsstrahlung cross sections compared with those of Bethe-Heitler (BEAMnrc default bremsstrahlung cross section). However, MC calculated dose distributions in water phantoms (using combinations of VRTs/AEITs and cross-section data) agreed within 2% of measurements. Furthermore, MC calculated dose distributions in a simulated water/air/water phantom, using NIST cross sections, were within 2% agreement with the BEAMnrc Bethe-Heitler default case. (C) 2009 American Association of Physicists in Medicine. [DOI: 10.1118/1.3253300]

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Radiation Oncology

Shin, D. A., R. Huh, S. S. Chung, J. Rock and S. Ryu (2009). "Stereotactic spine radiosurgery for intradural and intramedullary metastasis." Neurosurgical Focus **27**(6). [PDF Full-Text](#)

[Shin, Dong Ah; Huh, Ryoong; Chung, Sang Sup] CHA Univ, Dept Neurosurg, Pochon, South Korea. [Ryu, Samuel] Henry Ford Hosp, Dept Radiat Oncol, Detroit, MI 48202 USA. [Rock, Jack; Ryu, Samuel] Henry Ford Hosp, Dept Neurosurg, Detroit, MI 48202 USA.
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Object. Stereotactic radiosurgery (SRS) has become an important treatment alternative to surgery for a variety of spinal lesions. However, the use of SRS in the management of intradural intramedullary (IDIM) metastasis remains controversial. The aim of this study was to determine the clinical efficacy and safety of SRS for treatment of IDIM metastasis. Methods. Nine patients with 11 IDIM metastases treated with SRS at Henry Ford Hospital were retrospectively reviewed. The mean age at presentation was 50 years, with a range of 14-71 years. There were 4 intradural extramedullary and 7 intramedullary lesions. The radiosurgery procedure used techniques of image-guided and intensity-modulated radiation. The mean treatment dose was 13.8 Gy, with a range of 10-16 Gy. All patients had clinical follow-up (except in 1 lesion), with an emphasis on initial symptoms and ambulatory status, and 8 patients (9 lesions) had imaging studies. The median follow-up duration was 10 months. Results. The presenting symptoms were improved in 8 (80%) of 10 evaluable lesions, unchanged in 1 case, and worsened in 1 case. Radiographic responses were seen as follows: complete response in 2 (22%) of 9; partial response in 3 (33%) of 9; stable disease in 3 (33%) of 9; and progressive disease in 1 (11%) of 9. After radiosurgery, 7 patients (78%) remained ambulatory until the last follow-up visit. The overall median survival time after SRS was 8 months, with a range of 2-19 months. No radiation toxicity was detected clinically during the follow-up period. Conclusions. Despite the fact that this was a small series of patients with IDIM metastasis who had limited treatment options, SRS appears to be an effective and safe method of treating patients with these lesions. (DOI: 10.3171/2009.9.FOCUS09194)

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Sleep Medicine

Roth, T. (2009). "Sleep duration, insomnia and longevity." Sleep Medicine **10**(10): 1071-1072. [PDF Full-Text](#)

Henry Ford Hosp, Sleep Disorders & Res Ctr, Detroit, MI 48202 USA.
Roth, T, Henry Ford Hosp, Sleep Disorders & Res Ctr, 2799 W Grand Blvd, CFP-3, Detroit, MI 48202 USA.
troth1@hfhs.org

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Sleep Medicine

Schwartz, J. R., T. Roth, M. Hirshkowitz and K. P. Wright (2009). "Recognition and management of excessive sleepiness in the primary care setting." Prim Care Companion J Clin Psychiatry **11**(5): 197-204. PMC2781030. [Article Request Form](#)

INTEGRIS Sleep Disorders Centers, University of Oklahoma Health Science Center, Oklahoma City ; Henry Ford Sleep Disorder Center, Detroit, Michigan ; Michael E. DeBakey VA Medical Center, VAMC Sleep Center, and Baylor College of Medicine, Houston, Texas ; and Department of Integrative Physiology, Sleep and Chronobiology Laboratory, University of Colorado at Boulder.

BACKGROUND: Excessive sleepiness often goes unrecognized in the primary care setting despite its high prevalence and deleterious effects on both individual and public safety. Patients with neurologic and psychiatric illnesses, as well as those with acute and chronic medical conditions, plus those with sleep disorders, often have symptoms of excessive sleepiness, tiredness, and fatigue. Recognition and prompt treatment of these symptoms are important, even though their etiology may not be immediately understood. This review focuses on the underlying causes, consequences, identification, and treatment of excessive sleepiness. **DATA SOURCES:** A search of the literature to 2007 was performed using the PubMed search engine. English-language articles were identified using the following search terms: excessive sleepiness, fatigue, circadian rhythm, obstructive sleep apnea, shift work disorder, narcolepsy, drowsy driving, and wakefulness. Additional references were identified through bibliography reviews of relevant articles. **DATA SYNTHESIS:** Current assessments of the prevalence, consequences, and etiologies of excessive sleepiness, with leading treatment strategies, were extracted, reviewed, and summarized to meet the objectives of this article. **CONCLUSIONS:** Excessive sleepiness is associated with a wide range of medical, neurologic, and psychiatric disorders frequently seen in primary care practice. Excessive sleepiness is a serious, debilitating, potentially life-threatening condition, yet also treatable, and it is important to initiate appropriate intervention as early as possible. Physicians should place increasing emphasis on the substantial benefits that accompany improvements in wakefulness.

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Surgery

Benninger, M. S., K. McFarlin, D. R. Hamilton, I. Rubinfeld, A. E. Sargsyan, S. M. Melton, M. Mohyi and S. A. Dulchavsky (2009). "Ultrasound evaluation of sinus fluid levels in swine during microgravity conditions." Aviat Space Environ Med **80**(12): 1063-5. [Article Request Form](#)

Department of Surgery, CFP-1, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202, USA.

BACKGROUND: Acute rhinosinusitis is a common problem that could occur in space secondary to absence of gravity-dependent drainage or odontogenic or external sources of infection. The purpose of this study was to determine the efficacy of ultrasound to determine sinus fluid distribution levels in swine and to assess the accuracy of ultrasound in the animal during normal and microgravity conditions. **METHODS:** Anesthetized swine had a catheter placed through a frontal bone window to allow aliquots of a viscous solution to be injected at 1 G (N = 4) or during brief microgravity parabolic flights (N = 4). Ultrasound examinations were performed with a high frequency probe during baseline and fluid-induced conditions. **RESULTS:** There was a consistent air-fluid level interface seen on ultrasound examination with the injection of 1 ml of fluid during 1-G conditions. Microgravity conditions caused the rapid (< 10 s) dissolution of the air-fluid level associated with dispersion of the fluid to the walls of the sinus cavity in a uniform fashion. The air-fluid interface was recreated with return to 1 G. **CONCLUSIONS:** Ultrasound is a reliable diagnostic test for assessing fluid levels; these experiments demonstrate the technique can be used during microgravity conditions with attention to altered fluid behavior in the absence of gravity.

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Surgery

Cheaito, A., A. Yoshida, D. Y. Kim, D. Moonka, K. A. Brown and M. S. Abouljoud (2009). "Impact of Pre-Operative Tumor Volume and Staging of Hcc on Transplant Outcomes: A Single Center Experience." Hepatology **50**(4): 556. [PDF Full-Text](#) (Scroll down to abstract #556)

[Cheaito, Ali; Yoshida, Atsushi; Kim, Dean Y.; Moonka, Dilip; Brown, Kimberly Ann; Abouljoud, Marwan S.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Cheaito, A., A. Yoshida, D. Y. Kim, D. Moonka, K. A. Brown and M. S. Abouljoud (2009). "Effect of Rfa and Tace on Recurrence of Hepatocellular Carcinoma after Liver Transplantation: 8 Year Experience with 145 Patients." Hepatology **50**(4): 627. [PDF Full-Text](#) (Scroll down to abstract #627)

[Cheaito, Ali; Yoshida, Atushi; Kim, Dean Y.; Abouljoud, Marwan S.] Henry Ford Hosp, Inst Transplantat, Detroit, MI 48202 USA.

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Surgery

Deeb, D., X. Gao, H. Jiang, B. Janic, A. S. Arbab, Y. Rojanasakul, S. A. Dulchavsky and S. C. Gautam (2010). "Oleanane triterpenoid CDDO-Me inhibits growth and induces apoptosis in prostate cancer cells through a ROS-dependent mechanism." Biochem Pharmacol **79**(3): 350-60. [Article Request Form](#)

Department of Surgery, Henry Ford Health System, Detroit, MI 48202, USA.

CDDO-Me, a synthetic triterpenoid derived from oleanolic acid, is a promising anticancer agent that has shown strong activity against a wide variety of cancer types in vitro and in vivo. We have previously shown that CDDO-Me induces apoptosis in prostate cancer cells irrespective of their hormonal status. To further understand the proapoptotic mechanism of CDDO-Me, we investigated the role of reactive oxygen species (ROS) in mediating the apoptosis inducing activity of CDDO-Me in LNCaP and PC-3 prostate cancer cell lines. Here, we show that CDDO-Me induces ROS generation from both nonmitochondrial and mitochondrial sources, which is associated with the induction of apoptosis as characterized by increased annexin V-binding, cleavage of PARP-1 and procaspases-3, -8, -9, loss of mitochondrial membrane potential and release of cytochrome c. In addition, CDDO-Me inhibited cell survival Akt, NF-kappaB and mTOR signaling proteins. The inhibition of ROS generation by N-acetylcysteine (NAC) or by overexpression of antioxidant enzymes glutathione peroxidase (GPx) and superoxide dismutase-1 (SOD-1) prevented CDDO-Me-induced apoptosis. Pretreatment with NAC blocked annexin V-binding, cleavage of PARP-1 and procaspases-3, -8, -9, loss of mitochondrial membrane potential and release of cytochrome c by CDDO-Me. NAC also prevented the inhibition of constitutively active Akt, NF-kappaB and mTOR by CDDO-Me. Together, these data indicate that ROS plays an essential role in the induction of apoptosis by CDDO-Me in prostate cancer cells.

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Surgery

Kakkos, S. K., J. C. Lin, J. Sparks, M. Telly, M. McPharlin and D. J. Reddy (2009). "Prospective comparison of the pneumatic cuff and manual compression methods in diagnosing lower extremity venous reflux." Vasc Endovascular Surg **43**(5): 480-4. [Article Request Form](#)

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

AIM: To compare pneumatic cuff with manual compression in diagnosing reflux in patients with chronic venous insufficiency (CVI). Patients and METHODS: Eighteen patients (Clinical Etiologic Anatomic Pathophysiologic [CEAP 2-5], median Venous Clinical Severity Score [VCSS 6.5]) were studied. The VenaPulse device (ACI Medical, San Marcos, California) was used for cuff inflation. The hemodynamic performance of the 2 methods was tested in the first 9 patients, while their diagnostic value was tested in the last 9 patients. RESULTS: Both

methods induced equal compression with median peak velocity of the antegrade flow (PVA) being 86 cm/s ($P = .65$). Coefficient of variation (CV) for PVA in the superficial veins was significantly higher with the manual method (16.8%) compared to the VenaPulse method (9.5%, $P < .001$), while sensitivity and specificity were 85% and 100%, and 78% ($\kappa = .68$, $P < .001$) and 100%, respectively. **CONCLUSIONS:** Pneumatic cuff and manual compression were shown to be equally effective in diagnosing venous reflux. Cost-effectiveness and ease-of-use studies comparing these methods are justified.

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Surgery

Koestner, A., M. R. Walters, C. Mattice, P. Manion and C. Seguin (2009). "Senior lifestyles and injury prevention: Evaluating the effectiveness of an injury prevention program for older adults." *J Trauma Nur* **16**(2): 87-92. [PDF Full-Text](#)

Borgess Medical Center, Kalamazoo, Michigan 48048; amyjoestner@borgess.com

The purpose of this multicenter, before-and-after observational study was to determine whether a short educational intervention was associated with improvement in self-reported safety behavior in older adults. We developed 4 original injury prevention presentations with companion testing materials: Motor Vehicle Safety, Fall Prevention, Pedestrian Safety, and Home Safety. Participants also completed pre-post Short Form Health Survey Instrument (SF-12) quality-of-life surveys. Of 414 participants, 226 completed follow-up testing and SF-12 surveys, for a 54.6% response rate. Those who completed either Pedestrian or Home Safety program showed no significant changes ($P > .05$) in either test scores or SF-12, and they comprised 61.9% of the final sample. Participants in the Motor Vehicle Safety and Fall Prevention programs accounted for 38.1% of the final sample and did show significant improvements between pre-post test scores. Only Fall Prevention participants showed significant differences in pre-post SF-12 scores. In the Fall Prevention group, numerous SF-12 subscores from the initial survey were significantly inversely correlated with pretest scores, and improvements in some SF-12 subscores correlated with improvements in test scores. Findings from the Fall Prevention group suggest that seniors with quality-of-life limitations may be aware of their increased risk and more willing to make changes to enhance safety. Further study is needed because many questions regarding optimal approaches to injury prevention in the aging demographic remain unanswered.

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Surgery

Vanderlan, W. B., B. E. Tew, C. Y. Seguin, M. M. Mata, J. J. Yang, H. M. Horst, F. N. Obeid and N. E. McSwain (2009). "Neurologic sequelae of penetrating cervical trauma." *Spine* **34**(24): 2646-53. [PDF Full-Text](#)

Department of Surgery, Tulane University, New Orleans, LA; blakevanderlan@yahoo.com

STUDY DESIGN: Multicenter, retrospective chart analysis was performed using data housed in the trauma registries of 2 independent American College of Surgeons verified, Level I Trauma centers. The trauma registries were queried for all cases of penetrating cervical trauma. Abstracted data included age, sex, race, mechanism of injury, Glasgow Coma Scale (GCS) level on arrival, neurologic findings on arrival, zone of injury, associated injuries, imaging studies and results, operations performed, neurologic sequelae, disposition from the hospital and the presence or absence of neurologic injury, cervical spine fracture, and cervical spine immobilization. **OBJECTIVE:** The purpose of this study was to determine the relationship between cervical spine immobilization and neurologic sequelae in penetrating cervical trauma. **SUMMARY OF BACKGROUND DATA:** Current recommendations for cervical spine immobilization in penetrating cervical trauma developed by empiric extension of blunt trauma protocols without evidentiary support. No evidence exists to support cervical spine immobilization as a means of preventing neurologic injury progression in cases of penetrating cervical injury. **METHODS:** Abstracted data were organized, entered into a database, and compared statistically. Significance was accepted for $P < 0.05$. **RESULTS:** A total of 196 patient charts formed the study cohort. Neurologic injuries either improved or remained static. No patient could be determined to have benefited from cervical spine immobilization in this study as the only 2 patients presenting with unstable cervical spine fractures were completely neurologically devastated at the time of injury. Prehospital cervical spine immobilization may have negatively affected patients with vascular and airway injuries. Decreased cervical spine immobilization rates at one institution did not affect neurologic outcome. **CONCLUSION:** Cervical spine immobilization does not appear to prevent progression of neurologic injury in cases of penetrating cervical trauma. Comorbid penetrating injuries may be negatively impacted by prehospital cervical spine immobilization.

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Urology

Krane, L. S., S. A. Kaul, H. J. Stricker, J. O. Peabody, M. Menon and P. K. Agarwal (2010). "Men Presenting for Radical Prostatectomy on Preoperative Statin Therapy Have Reduced Serum Prostate Specific Antigen." Journal of Urology **183**(1): 118-123. [PDF Full-Text](#)

[Krane, L. Spencer] Henry Ford Hlth Syst, Vattikuti Urol Inst, Detroit, MI 48202 USA. [Krane, L. Spencer] Wake Forest Univ, Dept Urol, Winston Salem, NC 27109 USA.

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Purpose: Studies have suggested that statin (3-hydroxy-3-methyl-glutaryl-coenzyme A reductase inhibitors) medication use may decrease prostate specific antigen in healthy men. We determined the effect of preoperative statin use on total preoperative prostate specific antigen and the risk of biochemical recurrence in patients with prostate cancer presenting for radical prostatectomy. Materials and Methods: A retrospective review of 3,828 patients undergoing radical prostatectomy from January 2001 to July 2008 at our institution identified 1,031 on statin medications. We compared these 1,031 patients to the remaining 2,797 not on statins preoperatively. We evaluated differences in prostate specific antigen overall, and when patients were stratified by age specific groups, body mass index and Gleason grades on final pathology. We also investigated differences in biochemical recurrence rates. Results: Overall median serum prostate specific antigen was lower in patients on preoperative statins (5.0 vs 5.2 ng/ml, $p = 0.002$). Median prostate specific antigen was lower in men on statins with Gleason grades 7 or 8/9 disease ($p < 0.05$). Using a multivariate logistic regression model statin therapy was associated with a 4.7% decrease in prostate specific antigen ($p < 0.001$). Statin therapy was not associated with an overall decreased risk of biochemical recurrence ($p = 0.73$) at a mean followup of 26 months. Conclusions: In this cohort of men presenting for radical prostatectomy serum prostate specific antigen is significantly lower in patients with prostate cancer on preoperative statins compared to those not taking these medications. Prospective studies are required to evaluate if this decrease in prostate specific antigen leads to later detection of prostate cancer or variations in oncological outcomes.

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Urology

Krane, L. S., C. Wambi, A. Bhandari and H. J. Stricker (2009). "Posterior support for urethrovesical anastomosis in robotic radical prostatectomy: single surgeon analysis." Can J Urol **16**(5): 4836-40. [Article Request Form](#)

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

INTRODUCTION: Posterior urethrovesical anastomotic support has been reported to improve early return of urinary continence following radical prostatectomy. We adapted this technique to evaluate enhancement of early urinary control in patients undergoing robotic radical prostatectomy. MATERIALS AND METHODS: Forty-two consecutive men undergoing radical prostatectomy by a single surgeon between September and December 2007 received a posterior urethrovesical supporting stitch prior to the standard urethrovesical anastomosis (group 1). Operative data, postoperative complications, and follow up data were compared with those of the 42 consecutive men who underwent robotic radical prostatectomy by the same surgeon between March and August 2007 with a standard urethrovesical anastomosis (group 2). Continence was assessed at routine follow up visit 6 to 8 weeks following catheter removal. Continence was defined as zero pads or small security liner for infrequent urinary leakage in 24 hours. RESULTS: Thirty-four (81%) and 37 (88%) men in groups 1 and 2 respectively had follow up available between 45 and 75 days following prostatectomy. Preoperative demographics were similar between the two groups. At a mean follow up of 60 and 53 days following surgery, 29/34 (85%) of men in group 1 and 32/37 (86%) of men in group 2 were continent. On multivariate logistic regression analysis, no factors were associated with improved continence between the two groups. CONCLUSIONS: Posterior urethrovesical anastomotic support did not result in improved early urinary control following radical prostatectomy. Excellent urinary control can be achieved in the patients undergoing robotic radical prostatectomy without posterior urethrovesical anastomotic support.

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Urology

Patel, M. N., M. Bhandari, M. Menon and C. G. Rogers (2009). "Robotic-assisted partial nephrectomy: Has it come of age?" Indian J Urol **25**(4): 523-8. [PDF Full-Text](#)

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI, USA.

Surgical resection is the gold standard for the treatment of renal cell carcinoma, and partial nephrectomy (PN) is the treatment of choice for tumors smaller than 4 cm in size. A laparoscopic PN is a viable alternative to a traditional open PN, demonstrating good oncologic and functional outcomes. A laparoscopic PN is a challenging procedure, particularly performing intracorporeal suturing under the time constraints of warm ischemia. The introduction of the da Vinci surgical system (Intuitive Surgical Inc., Sunnyvale, CA) with wristed instruments and magnified, 3-dimensional vision may facilitate the technical challenges of a minimally invasive PN. The technique of robotic partial nephrectomy (RPN) is still evolving and a number of institutions have recently reported their results. In this article, we present a review of the literature and our technique for robotic PN using a transperitoneal approach.

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Urology

Patel, M. N., L. S. Krane, A. Bhandari, R. G. Laungani, A. Shrivastava, S. A. Siddiqui, M. Menon and C. G. Rogers (2009). "Robotic Partial Nephrectomy for Renal Tumors Larger Than 4cm." Eur Urol. EPub Ahead of Print. [PDF Full-Text](#)

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

BACKGROUND: Minimally invasive partial nephrectomy (PN) is most commonly performed for renal tumors ≤ 4 cm in size. Robotic PN (RPN) for tumors >4 cm has not been assessed. **OBJECTIVE:** To evaluate the safety and feasibility of RPN for tumors >4 cm in the context of patients undergoing RPN for tumors ≤ 4 cm. **DESIGN, SETTING, AND PARTICIPANTS:** We reviewed data for 71 consecutive patients who underwent transperitoneal RPN at a tertiary care center between August 2007 and September 2009 by a single surgeon. Patients were stratified into two groups: 15 with tumors >4 cm on preoperative imaging (group 1) and 56 patients with tumors ≤ 4 cm (group 2). **INTERVENTION:** All patients underwent transperitoneal RPN by a single surgeon. **MEASUREMENTS:** Preoperative, perioperative, pathologic, and functional outcomes data were analyzed and compared between groups. We used chi(2) and student t tests for categorical and continuous variables, respectively. A p value <0.05 was considered statistically significant. **RESULTS AND LIMITATIONS:** Mean radiographic tumor size was 5.0cm (4.1-7.9) for group 1 and 2.1cm (0.7-3.8) for group 2. No significant differences were found between groups for estimated blood loss, total operative time, hospital stay, complication rates, and change in estimated glomerular filtration rate. Patients with larger tumors had longer median warm ischemia times (25 vs 20min; $p=0.011$). Limitations of our study include the retrospective nature the analysis, small sample size, and single-surgeon experience. **CONCLUSIONS:** In our initial experience, RPN for tumors >4 cm is safe and feasible, showing comparable outcomes to RPN for smaller tumors, although with longer warm ischemia times. Future studies with extended follow-up are necessary to determine the viability of RPN for large tumors as an effective form of treatment.

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Urology

Rogers, C. G. and J. J. Patard (2009). "Open to debate. The motion: Robotic partial nephrectomy is better than open partial nephrectomy." Eur Urol **56**(3): 568-70. [PDF Full-Text](#)

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