

Henry Ford Health System Publication List - May 2010

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Allergy & Immunology

Sikka, N., G. Wegienka, S. Havstad, J. Genaw, A. M. Carlin and E. Zoratti (2010). "Respiratory medication prescriptions before and after bariatric surgery." Ann Allergy Asthma Immunol **104**(4): 326-30. [Article Request Form](#)

Division of Allergy and Immunology, Department of Internal Medicine, Henry Ford Hospital, Detroit, Michigan, USA. naveen_sikka@yahoo.com

BACKGROUND: Increased body mass index is associated with asthma and frequent respiratory complaints. Bariatric surgery often results in rapid weight loss associated with an improved respiratory status. **OBJECTIVE:** To assess whether patients undergoing bariatric surgery would have fewer respiratory symptoms after surgery as evidenced by decreases in respiratory prescription drug claims. **METHODS:** A retrospective cohort of 320 patients continuously enrolled in a large, southeast Michigan health maintenance organization were studied for 1 year before and 1 year after bariatric surgery. The health maintenance organization claims database was used to compare respiratory prescriptions filled before and after surgery. Respiratory medications included bronchodilator inhalers, inhaled corticosteroids, oral corticosteroids, theophylline, and leukotriene antagonists. **RESULTS:** Of 320 surgical patients, 64 (20%) filled at least 1 respiratory medication prescription for a total of 468 prescriptions during the 2-year observation period. Of the prescriptions filled, 35% were beta-agonists, 38% inhaled corticosteroids, 12% oral corticosteroids, 15% leukotriene antagonists, and less than 1% theophylline. Total respiratory medication prescription fills decreased by 49% (from 314 to 154 prescriptions) in the postsurgical year, with only 43.1% of patients filling prescriptions in the year before surgery also filling a prescription in the postsurgical surveillance period. Analyses restricted to 40 patients with physician-diagnosed asthma revealed mean (SD) presurgical prescription fills of 7.0 (6.9) per year, decreasing to 3.8 (6.1) per year in the postsurgical year ($P = .002$). **CONCLUSION:** Respiratory medication use decreases significantly after bariatric surgery. A secondary benefit of bariatric surgery may include a decrease in respiratory symptoms and concomitant medication use.

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Anesthesiology

Nagaraja, T. N., K. A. Keenan, P. A. Whitton, K. Karki, J. D. Fenstermacher and R. A. Knight (2010). "Imaging Brain Microvascular Pathology in Stroke by Fluorescence Laser Scanning Confocal Microscopy: A New Method for Fluorescence Quantification." Stroke **41**(4): E284-E284. [Article Request Form](#)

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8:30am-5:00pm F

[Nagaraja, Tavarekere N.; Keenan, Kelly A.; Whitton, Polly A.; Karki, Kishor; Fenstermacher, Joseph D.; Knight, Robert A.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Behavioral Services

Lajiness-O'Neill, R., L. Erdodi and E. D. Bigler (2010). "Memory and Learning in Pediatric Traumatic Brain Injury: A Review and Examination of Moderators of Outcome." Applied Neuropsychology **17**(2): 83-92. [Article Request Form](#)

[Lajiness-O'Neill, Renee; Erdodi, Laszlo] Eastern Michigan Univ, Dept Psychol, Ypsilanti, MI 48197 USA. [Lajiness-O'Neill, Renee] Henry Ford Hlth Syst, Dept Behav Serv, Div Neuropsychol, Detroit, MI USA. [Bigler, Erin D.] Brigham Young Univ, Dept Psychol, Provo, UT 84602 USA. [Bigler, Erin D.] Brigham Young Univ, Dept Neurosci, Provo, UT 84602 USA. [Bigler, Erin D.] Univ Utah, Dept Psychiat, Salt Lake City, UT USA. Lajiness-O'Neill, R., Eastern Michigan Univ, Dept Psychol, 537 F Mark Jefferson, Ypsilanti, MI 48197 USA. rlajines@emich.edu

This article reviews empirically supported assessment methods to examine impairments in memory and learning following pediatric traumatic brain injury (TBI). Critical factors affecting outcome are explored with an emphasis on an examination of age at injury. The article closes with discussion of current evidence-based interventions for deficits in memory and learning following pediatric TBI.

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Biostatistics & Research Epidemiology

Laiyemo, A. O., C. Doubeni, P. F. Pinsky, V. P. Doria-Rose, R. Bresalier, L. E. Lamerato, E. D. Crawford, P. Kvale, M. Fouad, T. Hickey, T. Riley, J. Weissfeld, R. E. Schoen, P. M. Marcus, P. C. Prorok and C. D. Berg (2010). "Race and Colorectal Cancer Disparities: Health-Care Utilization vs Different Cancer Susceptibilities." Journal of the National Cancer Institute **102**(8): 538-546. [PDF Full-Text](#)

[Laiyemo, Adeyinka O.] Howard Univ, Coll Med, Div Gastroenterol, Dept Med,Canc Ctr, Washington, DC 20060 USA. [Laiyemo, Adeyinka O.; Doria-Rose, V. Paul; Marcus, Pamela M.; Prorok, Philip C.] NCI, Biometry Res Grp, Canc Prevent Div, NIH, Bethesda, MD 20892 USA. [Doubeni, Chyke] Univ Massachusetts, Dept Family Med, Worcester, MA 01605 USA. [Pinsky, Paul F.; Berg, Christine D.] NCI, Early Detect Res Grp, Canc Prevent Div, NIH, Bethesda, MD 20892 USA. [Bresalier, Robert] Univ Texas MD Anderson Canc Ctr, Dept Gastroenterol Hepatol & Nutr, Houston, TX 77030 USA. [Lamerato, Lois E.] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Crawford, E. David] Univ Colorado, Hlth Sci Ctr, Dept Surg, Denver, CO 80262 USA. [Kvale, Paul] Henry Ford Hosp, Dept Med, Detroit, MI 48202 USA. [Fouad, Mona] Univ Alabama, Dept Med, Div Prevent Med, Birmingham, AL 35294 USA. [Hickey, Thomas; Riley, Thomas] Informat Management Serv Inc, Rockville, MD USA. [Weissfeld, Joel; Schoen, Robert E.] Univ Pittsburgh, Dept Med & Epidemiol, Pittsburgh, PA USA.

Laiyemo, AO, Howard Univ, Coll Med, Div Gastroenterol, Dept Med,Canc Ctr, Rm 329,2041 Georgia Ave NW, Washington, DC 20060 USA. adeyinka.laiyemo@howard.edu

Background It is unclear whether the disproportionately higher incidence and mortality from colorectal cancer among blacks compared with whites reflect differences in health-care utilization or colorectal cancer susceptibility. **Methods** A total of 60 572 non-Hispanic white and black participants in the ongoing Prostate, Lung, Colorectal, and Ovarian (PLCO) Cancer Screening Trial underwent trial-sponsored screening flexible sigmoidoscopy (FSG) without biopsy at baseline in 10 geographically dispersed centers from November 1993 to July 2001. Subjects with polyps or mass lesions detected by FSG were referred to their physicians for diagnostic workup, the cost of which was not covered by PLCO. The records of follow-up evaluations were collected and reviewed. We used log binomial modeling with adjustment for age, education, sex, body mass index, smoking, family history of colorectal cancer, colon examination within previous 3 years, personal history of polyps, and screening center to examine whether utilization of diagnostic colonoscopy and yield of neoplasia differed by race. **Results** Among 57 561 whites and 3011 blacks who underwent FSG, 13 743 (23.9%) and 767 (25.5%) had abnormal examinations, respectively. A total of 9944 (72.4%) whites and 480 (62.6%) blacks had diagnostic colonoscopy within 1 year following the abnormal FSG screening. When compared with whites, blacks were less likely to undergo diagnostic evaluation (adjusted risk ratio = 0.88, 95% confidence interval = 0.83 to 0.93). Overall, among subjects with diagnostic colonoscopy (n = 10 424), there was no statistically significant difference by race in the prevalence of adenoma, advanced adenoma, advanced

pathology in small adenomas (high-grade dysplasia or villous histology in adenomas < 10 mm), or colorectal cancer. Conclusions We observed a lower follow-up for screen-detected abnormalities among blacks when compared with whites but little difference in the yield of colorectal neoplasia. Health-care utilization may be playing more of a role in colorectal cancer racial disparity than biology. *J Natl Cancer Inst* 2010; 102: 538-546

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Biostatistics & Research Epidemiology

Ownby, D. R., E. L. Peterson, L. K. Williams, E. M. Zoratti, G. R. Wegienka, K. J. Woodcroft, C. L. M. Joseph and C. C. Johnson (2010). "Variation of dust endotoxin concentrations by location and time within homes of young children." *Pediatric Allergy and Immunology* **21**(3): 533-540. [PDF Full-Text](#)

[Ownby, Dennis R.] Med Coll Georgia, Dept Allergy & Immunol, Augusta, GA 30912 USA. [Peterson, Edward L.; Williams, L. Keoki; Zoratti, Edward M.; Wegienka, Ganesa R.; Woodcroft, Kimberley J.; Joseph, Christine L. M.; Johnson, Christine C.] Henry Ford Hlth Syst, Dept Biostat & Res Epidemiol, Detroit, MI USA. Ownby, DR, Med Coll Georgia, Dept Allergy & Immunol, 1120 15th St, BG 1019, Augusta, GA 30912 USA. downby@mcg.edu

Endotoxin may affect the development of allergic disease in childhood but little is known about endotoxin variation within homes. We sought to determine endotoxin concentration agreement within homes when five locations were each sampled twice 5 months apart. Endotoxin was measured using the recombinant Limulus factor C assay in dust samples from 585 homes of children enrolled in a prospective study and again in 335 homes 5 months later. The five locations sampled in each home were the child's bedroom floor, child's bed, mother's bedroom floor, mother's bed and living room floor. Concentrations of 4 allergens (Can f 1, Fel d 1, Der f 1 and Bla g 2) were also measured from the child's bedroom floor. In pair-wise comparisons, endotoxin concentrations in all locations within each home were significantly different from all other locations ($p < 0.001$) except for the child's and mother's bedroom floors ($p = 0.272$). Spearman correlations between endotoxin concentrations from the different locations were all statistically significant ($p < 0.05$) but of modest magnitude ($r = 0.24-0.54$). Similarly, correlations at each site over the 5 month observation interval were statistically significant but modest ($r = 0.17-0.44$). Pets and season of the year did not affect correlations, although correlations were lower if the floor was not carpeted. Endotoxin concentrations at all locations were minimally correlated with allergen concentrations in both negative and positive directions ($r = -0.12$ to 0.12). We conclude that a single measurement of endotoxin from a home dust sample provides an imprecise estimate of dust endotoxin concentrations in other locations within the home and over a relatively short observation interval.

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Bone & Joint Center

Deneweth, J. M., M. J. Bey, S. G. McLean, T. R. Lock, P. A. Kolowich and S. Tashman (2010). "Tibiofemoral Joint Kinematics of the Anterior Cruciate Ligament-Reconstructed Knee During a Single-Legged Hop Landing." *Am J Sports Med* **Epub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Hospital.

BACKGROUND: Abnormal 3-dimensional tibiofemoral joint kinematics have been identified in anterior cruciate ligament-reconstructed knees during functional gait tasks, which is suggested to directly affect risk of knee osteoarthritis. However, the extent to which similar high-risk abnormalities are present during more demanding maneuvers, such as single-legged hopping, is largely unknown. **HYPOTHESIS:** When performing a single-legged forward hop landing, the reconstructed knee will demonstrate altered sagittal, frontal, and transverse plane kinematics compared with the contralateral limb. **STUDY DESIGN:** Controlled laboratory study. **METHODS:** High-speed biplane radiography was used to quantify bilateral 3-dimensional tibiofemoral joint kinematics in 9 subjects with unilaterally reconstructed anterior cruciate ligaments (mean time after surgery, 4 months) during 3 single-legged, forward hop landing trials. Mean subject-based initial foot contact and maximum stance (0-250 ms) values were calculated for each kinematic variable. Two-tailed paired t tests were subsequently applied to examine for the main effect of limb (reconstructed vs contralateral). **RESULTS:** The reconstructed knees exhibited significantly greater extension ($P = .04$), external tibial rotation ($P = .006$), and medial tibial translation ($P = .02$) than the contralateral knees at initial contact. Reconstructed knees underwent significantly greater maximum flexion ($P = .05$), maximum external tibial rotation ($P = .01$), and maximum anterior tibial translation ($P = .02$). No significant differences existed between limbs for initial contact ($P = .65$)

or maximum adduction-abduction ($P = .55$). CONCLUSION: Tibiofemoral joint kinematics of the anterior cruciate ligament-reconstructed knee are significantly different from those of the uninjured contralateral limb during a single-legged hop landing. This altered kinematic profile, in conjunction with the large impact loads associated with hopping, may further contribute to the risk of posttraumatic knee osteoarthritis. CLINICAL RELEVANCE: Returning to sports involving dynamic single-legged landings at 4 months after anterior cruciate ligament reconstruction surgery may contribute to accelerated knee joint degeneration.

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Bone & Joint Center

Shen, J. B., M. Z. Yang, D. H. Ju, H. Jiang, J. P. Zheng, Z. H. Xu and L. Li (2010). "Disruption of SM22 Promotes Inflammation After Artery Injury via Nuclear Factor kappa B Activation." Circulation Research **106**(8): 1351-1362. [PDF Full-Text](#)

[Shen, Jianbin; Yang, Maozhou; Ju, Donghong; Jiang, Hong; Zheng, Jian-Pu; Xu, Zhonghui; Li, Li] Wayne State Univ, Dept Internal Med, Detroit, MI 48202 USA. [Shen, Jianbin; Xu, Zhonghui; Li, Li] Wayne State Univ, Ctr Mol Med & Genet, Detroit, MI 48202 USA. [Li, Li] Wayne State Univ, Cardiovasc Res Inst, Detroit, MI 48202 USA. [Yang, Maozhou] Henry Ford Hosp, Ctr Bone & Joint, Detroit, MI 48202 USA. Li, L, 421 E Canfield Ave, Room 1107, Detroit, MI 48201 USA. lili@med.wayne.edu

Rationale: SM22 (or transgelin), an actin-binding protein abundant in vascular smooth muscle cells (VSMCs), is downregulated in atherosclerosis, aneurysm and various cancers. Abolishing SM22 in apolipoprotein E knockout mice accelerates atherogenesis. However, it is unclear whether SM22 disruption independently promotes arterial inflammation. Objective: To investigate whether SM22 disruption directly promotes inflammation on arterial injury and to characterize the underlying mechanisms. Methods and Results: Using carotid denudation as an artery injury model, we showed that Sm22 knockout (Sm22^{-/-}) mice developed enhanced inflammatory responses with higher induction of proinflammatory genes, including Vcam1, Icam1, Cx3cl1, Ccl2, and Ptgs2. Higher expression of these genes was confirmed in primary Sm22^{-/-} VSMCs and in PAC1 cells after Sm22 knockdown, whereas SM22 recapitulation in primary Sm22^{-/-} VSMCs decreased their expression. NF- κ B2 was prominently activated in both injured carotids of Sm22^{-/-} mice and in PAC1 cells after Sm22 knockdown and may mediate upregulation of these proinflammatory genes. As a NF- κ B activator, reactive oxygen species (ROS) increased in primary Sm22^{-/-} VSMCs and in PAC1 cells after Sm22 knockdown. ROS scavengers blocked NF- κ B activation and induction of proinflammatory genes. Furthermore, Sm22 knockdown increased Sod2 expression and activated p47phox, reflecting contributions of mitochondria and NADPH oxidase to the augmented ROS production; this may result from actin and microtubule cytoskeletal remodeling. Conclusions: Our findings show that SM22 downregulation can induce proinflammatory VSMCs through activation of ROS-mediated NF- κ B pathways. This study provides initial evidence linking VSMC cytoskeleton remodeling with arterial inflammation. (Circ Res. 2010;106:1351-1362.)

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Bone & Joint Center

Wallace, J. M., B. Erickson, C. M. Les, B. G. Orr and M. M. B. Holl (2010). "Distribution of type I collagen morphologies in bone: Relation to estrogen depletion." Bone **46**(5): 1349-1354. [PDF Full-Text](#)

[Wallace, Joseph M.; Holl, Mark M. Banaszak] Univ Michigan, Dept Chem, Ann Arbor, MI 48109 USA. [Wallace, Joseph M.; Erickson, Blake; Orr, Bradford G.; Holl, Mark M. Banaszak] Univ Michigan, Michigan Nanotechnol Inst Med & Biol Sci, Ann Arbor, MI 48109 USA. [Erickson, Blake; Holl, Mark M. Banaszak] Univ Michigan, Program Biophys, Ann Arbor, MI 48109 USA. [Les, Clifford M.] Henry Ford Hosp, Ctr Bone & Joint, Detroit, MI 48202 USA. [Orr, Bradford G.; Holl, Mark M. Banaszak] Univ Michigan, Program Appl Phys, Ann Arbor, MI 48109 USA. [Orr, Bradford G.] Univ Michigan, Dept Phys, Ann Arbor, MI 48109 USA. [Holl, Mark M. Banaszak] Univ Michigan, Program Macromol Sci & Engr, Ann Arbor, MI 48109 USA. Wallace, JM, Univ Michigan, Dept Chem, 930 N Univ Ave, Ann Arbor, MI 48109 USA. jmwallac@umich.edu berick@umich.edu cles1@hfh.org orr@umich.edu mbanasza@umich.edu

Bone is an amazing material evolved by nature to elegantly balance structural and metabolic needs in the body. Bone health is an integral part of overall health, but our lack of understanding of the ultrastructure of healthy bone precludes us from knowing how disease may impact nanoscale properties in this biological material. Here, we show that quantitative assessments of a distribution of Type I collagen fibril morphologies can be made using atomic force microscopy (AFM). We demonstrate that normal bone contains a distribution

of collagen fibril morphologies and that changes in this distribution can be directly related to disease state. Specifically, by monitoring changes in the collagen fibril distribution of sham-operated and estrogen-depleted sheep, we have shown the ability to detect estrogen-deficiency-induced changes in Type I collagen in bone. This discovery provides new insight into the ultrastructure of bone as a tissue and the role of material structure in bone disease. The observation offers the possibility of a much-needed in vitro procedure to complement the current methods used to diagnose osteoporosis and other bone disease. (C) 2009 Elsevier Inc. All rights reserved.

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Cardiology

Hammoud, Z. T., Y. Mechref, A. Hussein, S. Bekesova, M. Zhang, K. A. Kesler and M. V. Novotny (2010). "Comparative glycomic profiling in esophageal adenocarcinoma." J Thorac Cardiovasc Surg **139**(5): 1216-23. [PDF Full-Text](#)

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OBJECTIVE: Aberrant glycosylation has been implicated in various types of cancers. Cancerous cells with altered glycosylation of their surface proteins shed such proteins into the circulating fluids. Glycomic profiling of such fluids shows the altered glycosylation. We performed glycomic profiling of serum from patients with no known disease, Barrett's without dysplasia, with high-grade dysplasia, and with esophageal adenocarcinoma in an attempt to delineate distinct differences in glycosylation among these groups. METHODS: Serum samples from patients with Barrett's metaplasia (N = 5), high-grade dysplasia (N = 11), and esophageal adenocarcinoma (N = 50) were collected; samples from 18 healthy volunteers were used as control. Serum N-glycans were enzymatically released and then applied to both C18 Sep-Pak (Waters, Milford, MA) cartridges and activated charcoal cartridges. N-glycans were permethylated and then spotted directly onto a matrix-assisted laser desorption ionization plate. Mass spectra were acquired using the Applied Biosystems 4800 MALDI TOF/TOF Analyzer (Applied Biosystems Inc, Framingham, Mass). The obtained matrix-assisted laser desorption ionization-mass spectrometry data were processed using DataExplorer files (Applied Biosystems Inc) listing m/z values and intensities. RESULTS: The intensities of 98 glycans were significantly different among the 3 groups; 26 of these corresponded to known glycan structures. Pairwise comparisons showed that 8 glycans were significantly different in all 3 pairwise comparisons. CONCLUSION: We demonstrated that comparative glycomic profiling of esophageal adenocarcinoma reveals a subset of glycans that can be selected as candidate biomarkers. These markers can differentiate normal from high-grade dysplasia, normal from esophageal adenocarcinoma, and high-grade dysplasia from esophageal adenocarcinoma. Further validation will be necessary to determine the clinical utility of these glycan biomarkers.

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Cardiology

Myers, J., R. L. Goldsmith, S. J. Keteyian, C. A. Brawner, D. A. Brazil, H. Aldred, J. K. Ehrman and D. Burkhoff (2010). "The Ventilatory Anaerobic Threshold in Heart Failure: A Multicenter Evaluation of Reliability." Journal of Cardiac Failure **16**(1): 76-83. [PDF Full-Text](#)

[Myers, Jonathan] Stanford Univ, VA Palo Alto Hlth Care Syst, Palo Alto, CA 94304 USA. [Goldsmith, Rochelle L.; Brazil, Deirdre A.; Burkhoff, Daniel] Columbia Univ, New York Presbyterian Med Ctr, New York, NY USA. [Keteyian, Steven J.; Brawner, Clinton A.; Aldred, Heather; Ehrman, Jonathan K.] Henry Ford Hosp, Detroit, MI 48202 USA.

Myers, J, Stanford Univ, VA Palo Alto Hlth Care Syst, Cardiol 111C,3801 Miranda Ave, Palo Alto, CA 94304 USA. drj993@aol.com

Background: The ventilatory threshold (VT) is usually determined by visual assessment of the point where the rate of elimination of carbon dioxide (VCO₂) increases nonlinearly with respect to oxygen uptake (VO₂) (the V-Slope method). We quantified the reliability of VT determination using data from a multicenter study in patients with heart failure. Methods and Results: The Fix-Heart Failure-5 study of cardiac contractility modulation enrolled 428 patients from 50 centers in the United States. Cardiopulmonary exercise tests were performed at baseline and 12, 24, and 50 weeks after randomization, which provided 1679 tests. The VT was determined from each test in a core laboratory by 2 independent readers. VT could not be determined for 276 tests (16.4% indeterminate). Inter-observer variability (quantified by the 95% limits of agreement, LoA, expressed as a percent of the mean value) was 20.2% between the 2 readers, with a coefficient of variation (CV) of 7.3%.

Intra-observer variability was assessed by resubmitting (blinded) 179 tests to the same readers; the LoA was 24.7% for reader 1 and 16.9% for reader 2, with CVs of 6.1 and 8.9%, respectively. Ninety-one tests were submitted to 2 additional readers at a second core lab. Inter-observer variability in the second lab was 26.7% with a CV of 9.6%. Inter-laboratory variability was 21.4%, with a CV of 7.7%. Conclusions: Inter-observer, intra-observer, and inter-site variation in determining the VT should be considered when using the VT as an end point in clinical trials of heart failure. (I Cardiac Fail 2010;16:76-83)

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Dermatology

Gold, L. S. (2010). "Fixed-combination products in the management of acne vulgaris." Cutis **85**(3): 160-7. [PDF Full-Text](#) (ID=sladenjournals@hfhs.org / PW=frank)

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Acne vulgaris is the most common dermatologic disorder in the United States. Although its cause is unknown, various factors are implicated in its pathogenesis. No single topical antiacne medication acts on all the major pathophysiologic events. Combined use of agents with different modes of action provides better patient outcomes than monotherapy. Topical fixed-combination therapies include antibiotics with benzoyl peroxide (BPO) or retinoids, and retinoids with BPO. With increased efficacy can come increased irritation from the combination or formulation excipients. Surfactants, preservatives, and high levels of organic solvents including alcohols found in some products are potential irritants. This review considers data on topical fixed-combination acne medications and developments focused on newer lower concentration, optimized formulations aimed at reducing dryness and irritation without compromising efficacy. In the absence of direct comparative clinical trials, this review provides timely guidance for clinicians on the use of these agents.

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Dermatology

Lim, H. W. and R. J. Sage (2010). "Photoprotection and vitamin D." Dermatol Ther **23**(1): 1. [PDF Full-Text](#)

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Dermatology

Mahmoud, B. H., D. Srivastava, J. J. Janiga, J. J. Yang, H. W. Lim and D. M. Ozog (2010). "Safety and Efficacy of Erbium-Doped Yttrium Aluminum Garnet Fractionated Laser for Treatment of Acne Scars in Type IV to VI Skin." Dermatologic Surgery **36**(5): 602-609. [PDF Full-Text](#)

[Mahmoud, Bassel H.; Srivastava, Divya; Janiga, Jennifer J.; Lim, Henry W.; Ozog, David M.] Henry Ford Hosp, Dept Dermatol, Multicultural Dermatol Ctr, Detroit, MI 48202 USA. [Yang, James J.] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. Ozog, DM, Henry Ford Hosp, Dept Dermatol, Multicultural Dermatol Ctr, 3031 W Grand Blvd, Suite 800, Detroit, MI 48202 USA. dozog1@hfhs.org

BACKGROUND Ablative resurfacing lasers are effective for treatment of acne scars, but they have a high risk of complications. Fractional lasers have less severe side effects but more moderate efficacy than ablative devices. Studies were performed in individuals with Fitzpatrick skin type I to VI. **OBJECTIVE** To determine the efficacy and safety of an erbium 1,550-nm fractional laser in the treatment of facial acne scars in Fitzpatrick skin types IV to VI. **METHODS** We conducted a prospective, single-blind, randomized trial in patients with acne scars (n=15), skin type IV to VI, with a 1,550-nm erbium fractionated laser. Patients were divided into two groups; one was treated with 10 mJ and the other with 40 mJ. Five monthly laser sessions were performed. A patient questionnaire was distributed. **RESULTS** There was a significant improvement in the acne scarring and overall appearance (p <.001). No significant difference was found between 10 and 40 mJ. Patients were highly satisfied with their results. Significant postinflammatory hyperpigmentation was seen; pain was significantly higher in darker skin. **CONCLUSIONS** Fractional photothermolysis is effective for the treatment of acne scars, but practitioners should be aware of the higher incidence of pain and postinflammatory hyperpigmentation in individuals with skin types IV to VI. The study was funded by Reliant Technologies, Inc., which participated in

the study design. Galderma (Ft. Worth, TX) provided Tri-luma cream and GlaxoSmithKline (Research Triangle Park, NC) provided valacyclovir (Valtrex).

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Dermatology

Rondina, A. and A. C. Watson (2010). "Bullous Sweet's syndrome and pseudolymphoma precipitated by IL-2 therapy." *Cutis* **85**(4): 206-13. [PDF Full-Text](#) (ID=sladenjournals@hfhs.org / PW=frank)

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IL-2 is a key cytokine in cell-mediated immunity and currently is used in clinical trials as immunologic therapy in human immunodeficiency virus (HIV)-positive patients. Although cutaneous reactions to IL-2 therapy are common, bullous reactions are rare. We report a case of an HIV-positive patient who received multiple cycles of IL-2 therapy and developed a bullous eruption soon after each cycle was initiated. Pathology results from 2 separate outbreaks revealed a diffuse dermal neutrophilic infiltrate with leukocytoclasia. Epidermal spongiosis and focal intraepidermal vesiculation also were present. The patient discontinued IL-2 therapy but restarted 5 years later, at which time he presented with a pseudolymphomatous reaction that resolved after discontinuation of therapy. This patient is an unusual case of 2 different eruptions--Sweet's syndrome and pseudolymphoma-precipitated by IL-2 therapy in the same patient. Cutaneous eruptions to IL-2 therapy also are reviewed.

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Dermatology

Ross, I. and T. Shwayder (2010). "Tubular Apocrine Adenoma: Presentation in the Vaginal Introitus of an Eight-Year-Old." *Pediatric Dermatology* **27**(2): 200-201. [PDF Full-Text](#)

[Ross, Ishai] Wayne State Univ, Dept Urol, Univ Hlth Ctr, Detroit, MI 48201 USA. [Shwayder, Tor] Henry Ford Hosp, Detroit, MI 48202 USA.

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Tubular apocrine adenoma is a very rare hamartomatous lesion that to our knowledge has never been described in the anogenital region in the pediatric population. A brief report of a tubular apocrine adenoma in the vaginal introitus of an 8-year-old.

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Dermatology

Sage, R. J., R. L. Moy and D. J. Kouba (2010). "The Filleted Ellipse Technique Is Useful for Taking Initial Mohs Layers on Linear Excisions with Positive Margins." *Dermatol Surg* **Epub Ahead of Print**. [PDF Full-Text](#)

Division of Mohs Micrographic Surgery, Department of Dermatology, Henry Ford Health System, Detroit, Michigan.

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Dermatology

Tierney, E. P. and I. Hamzavi (2010). "Progressive Macular Hypomelanosis Arising in a Young African American Woman in Association With Pregnancy and a Toxic Nodular Goiter." *Journal of Drugs in Dermatology* **9**(4): 393-397. [PDF Full-Text](#)

[Tierney, Emily P.] Boston Univ, Sch Med, Dept Dermatol, Boston, MA 02118 USA. [Tierney, Emily P.; Hamzavi, Iltefat] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.

Tierney, EP, Boston Univ, Sch Med, Dept Dermatol, 609 Albany St, Boston, MA 02118 USA. emily.tierney@stanfordalumni.org

The authors present the case of a 23-year-old woman of French-Caribbean descent who presented with progression of hypopigmented, scaly ovoid macules on her neck, chest, abdomen and back. She was two months pregnant at the time of the onset of the pigmentary change was also simultaneously diagnosed with a toxic nodular goiter of her thyroid gland. Initial fungal culture, KOH and biopsy were positive for fungal hyphae, and she was treated with four weeks of oral ketoconazole and topical selenium sulfide shampoo. As she had continued progression of her hypopigmented lesions after treatment for pityriasis versicolor, a thorough physical examination (under room light and Wood's lamp) and repeat biopsy were performed. On examination, she demonstrated persistence of the ovoid hypopigmented macules on her neck, chest and abdomen with interval improvement of the superficial scaling. Under Wood's lamp examination, hypopigmented lesions demonstrated a characteristic follicular pink fluorescence associated with porphyrin production by *Propionibacterium acnes* (*P. acnes*) described previously in the lesions of progressive macular hypomelanosis (PMH). PMH was confirmed histologically by the findings in the second biopsy of a decrease in epidermal melanin pigment and the persistence of pityriasis versicolor was ruled out by an absence of fungal hyphae. Based upon the literature suggesting improvement of PMH with antibiotic therapy to decrease *P. acnes* colonization, she was treated with 10% benzoyl peroxide wash, clindamycin 1% solution and oral, twice-daily tetracycline 500 mg. During six months of this treatment, she experienced re-pigmentation of many of her existing skin lesions and cessation of the development of new hypopigmented macules.

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Dermatology

Tierney, E. P., R. J. Sage and T. Shwayder (2010). "Kwashiorkor from a severe dietary restriction in an 8-month infant in suburban Detroit, Michigan: case report and review of the literature." International Journal of Dermatology **49**(5): 500-506. [PDF Full-Text](#)

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Kwashiorkor is a type of protein-calorie malnutrition often seen in children of impoverished countries and famine. The condition occurs in the setting of insufficient protein intake in the presence of sufficient caloric intake. We report a case of a 8-month-old male infant in the suburban Detroit, MI, USA who presented with diffuse edema, erythroderma and desquamation, a "bull-dog" face, diarrhea, and irritability, consistent with kwashiorkor as a result of severe dietary restriction. The mother had placed the child on a severely restrictive diet, consisting only of RICE DREAM (R) milk, sweet potatoes and bananas, with the assumption that it would help his rash. Nineteen prior cases of kwashiorkor induced in infants by dietary restriction of "well intending" parents have been reported in the US literature. Malnutrition is often under diagnosed or misdiagnosed in developed countries such as the United States. The results, if unrecognized or untreated, may be devastating. This makes it imperative that physicians consider this diagnosis, recognize potential risk factors and be prepared to accurately assess overall nutritional status of patients.

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Dermatology

Wei, Q. Q., K. Bhatt, H. Z. He, Q. S. Mi, V. H. Haase and Z. Dong (2010). "Targeted Deletion of Dicer from Proximal Tubules Protects against Renal Ischemia-Reperfusion Injury." Journal of the American Society of Nephrology **21**(5): 756-761. [PDF Full-Text](#)

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MicroRNAs are endogenous, noncoding, small RNAs that regulate expression and function of genes, but little is known about regulation of microRNA in the kidneys under normal or pathologic states. Here, we generated a mouse model in which the proximal tubular cells lack Dicer, a key enzyme for microRNA production. These mice had normal renal function and histology under control conditions despite a global downregulation of

microRNAs in the renal cortex; however, these animals were remarkably resistant to renal ischemia-reperfusion injury (IRI), showing significantly better renal function, less tissue damage, lower tubular apoptosis, and improved survival compared with their wild-type littermates. Microarray analysis showed altered expression of specific microRNAs during renal IRI. Taken together, these results demonstrate evidence for a pathogenic role of Dicer and associated microRNAs in renal IRI.

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Emergency Medicine

Khalid, I., P. Doshi and B. DiGiovine (2010). "Early Enteral Nutrition and Outcomes of Critically Ill Patients Treated with Vasopressors and Mechanical Ventilation." [American Journal of Critical Care](#) **19**(3): 261-268. [PDF Full-Text](#)

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Objective To determine the effect of early enteral feeding on the outcome of critically ill medical patients whose hemodynamic condition is unstable. **Methods** Prospectively collected data in a multi-institutional medical intensive care unit database were analyzed retrospectively. A total of 1174 patients were identified who required mechanical ventilation for more than 2 days and were treated with vasopressor agents to support blood pressure. The patients were divided into 2 groups: those who received enteral nutrition (n = 707) within 48 hours of the start of mechanical ventilation, termed the early enteral nutrition group, and those who did not (n = 467), termed the late enteral nutrition group. The primary end points were overall intensive care unit and hospital mortality. Subgroup analyses were used to evaluate potential confounding variables. The data were also analyzed after adjustments for confounding by matching for propensity score. **Results** Intensive care unit and hospital mortality were lower in the early enteral nutrition group than in the late enteral group: 22.5% vs 28.3%; P = .03; and 34.0% vs 44.0%; P < .001, respectively. The beneficial effect of early feeding was more evident in the sickest patients, that is, those treated with multiple vasopressors (odds ratio, 0.36; 95% confidence interval, 0.15-0.85) and those without early improvement (odds ratio, 0.59; 95% confidence interval, 0.39-0.90). When adjustments were made for confounding by matching for propensity score, early feeding was associated with decreased hospital mortality. **Conclusion** Early enteral nutrition may be associated with reduced intensive care unit and hospital mortality in patients whose hemodynamic condition is unstable. (American Journal of Critical Care. 2010;19:261-268)

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Emergency Medicine

Maisel, A., C. Mueller, R. Nowak, W. F. Peacock, J. W. Landsberg, P. Ponikowski, M. Mockel, C. Hogan, A. H. B. Wu, M. Richards, P. Clopton, G. S. Filippatos, S. Di Somma, I. Anand, L. Ng, L. B. Daniels, S. X. Neath, R. Christenson, M. Potocki, J. McCord, G. Terracciano, D. Kremastinos, O. Hartmann, S. von Haehling, A. Bergmann, N. G. Morgenthaler and S. D. Anker (2010). "Mid-Region Pro-Hormone Markers for Diagnosis and Prognosis in Acute Dyspnea Results From the BACH (Biomarkers in Acute Heart Failure) Trial." [Journal of the American College of Cardiology](#) **55**(19): 2062-2076. [PDF Full-Text](#)

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Objectives Our purpose was to assess the diagnostic utility of mid-regional pro-atrial natriuretic peptide (MR-proANP) for the diagnosis of acute heart failure (AHF) and the prognostic value of mid-regional pro-adrenomedullin (MR-proADM) in patients with AHF. **Background** There are some caveats and limitations to natriuretic peptide testing in the acute dyspneic patient. **Methods** The BACH (Biomarkers in Acute Heart Failure) trial was a prospective, 15-center, international study of 1,641 patients presenting to the emergency department with dyspnea. A noninferiority test of MR-proANP versus B-type natriuretic peptide (BNP) for diagnosis of AHF and a superiority test of MR-proADM versus BNP for 90-day survival were conducted. Other end points were exploratory. **Results** MR-proANP (>120 pmol/l) proved noninferior to BNP (>100 pg/ml) for the diagnosis of AHF (accuracy difference 0.9%). In tests of secondary diagnostic objectives, MR-proANP levels added to the utility of BNP levels in patients with intermediate BNP values and with obesity but not in renal insufficiency, the elderly, or patients with edema. Using cut-off values from receiver-operating characteristic analysis, the accuracy to predict 90-day survival of heart failure patients was 73% (95% confidence interval: 70% to 77%) for MR-proADM and 62% (95% confidence interval: 58% to 66%) for BNP (difference $p < 0.001$). In adjusted multivariable Cox regression, MR-proADM, but not BNP, carried independent prognostic value ($p < 0.001$). Results were consistent using NT-proBNP instead of BNP ($p < 0.001$). None of the biomarkers was able to predict rehospitalization or visits to the emergency department with clinical relevance. **Conclusions** MR-proANP is as useful as BNP for AHF diagnosis in dyspneic patients and may provide additional clinical utility when BNP is difficult to interpret. MR-proADM identifies patients with high 90-day mortality risk and adds prognostic value to BNP. (Biomarkers in Acute Heart Failure [BACH]; NCT00537628) (J Am Coll Cardiol 2010;55:2062-76) (C) 2010 by the American College of Cardiology Foundation

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Emergency Medicine

Miller, J. B., G. Khalsa and T. Vohra (2010). "Spontaneous spinal epidural hematoma presenting as flank pain and constipation." Am J Emerg Med **28**(4): 536 e3-5. [PDF Full-Text](#)

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Gastroenterology

Gordon, F. D., R. S. Brown, P. Kwo, R. J. Ghalib, J. Crippin, H. Vargas, K. Brown, T. Schiano, X. Yu, E. Chaudhri and L. Pedicone (2010). "Peginterferon Alfa-2b and Ribavirin for Hepatitis C Recurrence Post Orthotopic Liver Transplantation (OLT): Final Results from the Protect Study." Journal of Hepatology **52**: S10-S11. [PDF Full-Text](#)

[Gordon, F. D.] Lahey Clin Fdn, Med Ctr, Burlington, MA 01805 USA. [Brown, R. S., Jr.] Columbia Univ, Coll Phys & Surg, New York Presbyterian Hosp, New York, NY USA. [Kwo, P.] Indiana Univ, Indianapolis, IN 46204 USA. [Ghalib, R. J.] Liver Inst Methodist Dallas Med Ctr, Dallas, TX USA. [Crippin, J.] Washington Univ, St Louis, MO USA. [Vargas, H.] Mayo Clin, Div Transplantat Med, Scottsdale, AZ USA. [Brown, K.] Henry Ford Hosp, Detroit, MI 48202 USA. [Schiano, T.] Mt Sinai Med Ctr, New York, NY 10029 USA. [Yu, X.; Chaudhri, E.; Pedicone, L.] Schering Plough Res Inst, Kenilworth, NJ USA. fredric_d_gorclon@lahey.org

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Gastroenterology

Lleo, A., M. R. Martin, L. Zammataro, M. J. Mayo, N. Bach, S. Shimodas, S. Gordon, M. Folci, P. Invernizzi, M. Podda, M. E. Gershwin, J. M. Lasalle and C. Selmi (2010). "Consistent DNA Methylation Differences in 46 Genome-Wide Loci in Monozygotic Twins Discordant for Primary Biliary Cirrhosis." Journal of Hepatology **52**: S29-S29. [PDF Full-Text](#)

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Gastroenterology

McHutchison, J. G., A. J. Thompson, I. M. Jacobson, T. D. Boyer, E. R. Schiff, G. T. Everson, J. M. Vierling, M. L. Shiffman, R. S. Brown, A. M. Di Bisceglie, S. C. Gordon, W. M. Lee, Z. Guo, T. H. King, B. Armstrong, T. C. Rodell and D. Apelian (2010).

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Gastroenterology

Pockros, P. J., S. C. Gordon, A. McCullough, M. Charlton, N. Bzowej, J. Vierling, M. Bansal, B. Yoffe, G. Everson, M. Huyghe, A. Fox, S. Mento, O. Bohm, B. Plouffe, R. Cross and M. Shiffman (2010). "Randomized, Placebo-Controlled, Double-Blind, Dose Response (Rpdcbdr) Trial of Cts-1027, an Inhibitor of Matrix Metalloproteases (Mmps) in Patients with HCV Who Had Failed Prior Therapies." Journal of Hepatology **52**: S297-S298. [PDF Full-Text](#)

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Gastroenterology

Vierling, J. M., R. Ralston, E. J. Lawitz, J. McCone, S. Gordon, D. Pound, M. Davis, J. Galati, I. Jacobson, L. Rossaro, F. H. Anderson, J. King, W. Cassidy, M. Bourliere, R. Esteban-Mur, N. Ravendhran, G. Galler, P. Mendez, C. A. Brass and J. K. Albrecht (2010). "Long-Term Outcomes Following Combination Treatment with Boceprevir Plus Peg-Intron/Ribavirin (P/R) in Patients with Chronic Hepatitis C, Genotype 1 (HCV-G1)." Journal of Hepatology **52**: S470-S471. [PDF Full-Text](#)

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Allen, K. N. and E. Kachalsky (2010). "Aging with Hemophilia: Implications for Social Work Practice." *Social Work in Health Care* **49**(4): 327-344. [Article Request Form](#)

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Individuals with hemophilia and other congenital bleeding disorders are surviving beyond any life expectancy previously predicted and now face conditions associated with "normal" aging. Hemophilia along with co-morbid conditions of HIV and Hepatitis C complicate treatment for heart disease, cancer, kidney disease, and other age-related diseases. Lack of understanding of the condition, its treatment, and its costs hampers care, particularly when patients are treated outside of specialty clinics. This article provides an overview of bleeding disorders with a special focus on aging considerations. The role of social work in specialized hemophilia treatment centers is described and suggestions made to other social workers who may encounter this population in their practice. Finally, the need for policy and advocacy strategies is also addressed.

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Rustin, G. J., G. Shreeves, P. D. Nathan, A. Gaya, T. S. Ganesan, D. Wang, J. Boxall, L. Poupard, D. J. Chaplin, M. R. L. Stratford, J. Balkissoon and M. Zweifel (2010). "A Phase Ib trial of CA4P (combretastatin A-4 phosphate), carboplatin, and paclitaxel in patients with advanced cancer." *British Journal of Cancer* **102**(9): 1355-1360. [PDF Full-Text](#)

[Rustin, G. J.; Shreeves, G.; Nathan, P. D.; Gaya, A.; Boxall, J.; Poupard, L.; Zweifel, M.] Mt Vernon Canc Ctr, Dept Med Oncol, Northwood, Middx, England. [Ganesan, T. S.] Churchill Hosp, Oxford OX3 7LJ, England. [Wang, D.] Henry Ford Hlth Syst, Josephine Ford Canc Ctr, Detroit, MI USA. [Chaplin, D. J.; Balkissoon, J.] OXiGENE Inc, San Francisco, CA USA. [Stratford, M. R. L.] Univ Oxford, Gray Inst Radiat Oncol & Biol, Oxford, England.

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BACKGROUND: The vascular disrupting agent combretastatin A4 phosphate (CA4P) causes major regression of animal tumours when given as combination therapy. **METHODS:** Patients with advanced cancer refractory to standard therapy were treated with CA4P as a 10-min infusion, 20 h before carboplatin, paclitaxel, or paclitaxel, followed by carboplatin. **RESULTS:** Combretastatin A4 phosphate was escalated from 36 to 54 mg m⁻² with the carboplatin area under the concentration curve (AUC) 4-5, from 27 to 54 mg m⁻² with paclitaxel 135-175 mg m⁻², and from 54 to 72 mg m⁻² with carboplatin AUC 5 and paclitaxel 175 mg m⁻². Grade 3 or 4 neutropenia was seen in 17%, and thrombocytopenia only in 4% of 46 patients. Grade 1-3 hypertension (26% of patients) and grade 1-3 tumour pain (65% of patients) were the most typical non-haematological toxicities. Dose-limiting toxicity of grade 3 hypertension or grade 3 ataxia was seen in two patients at 72 mg m⁻². Responses were seen in 10 of 46 (22%) patients with ovarian, oesophageal, small-cell lung cancer, and melanoma. **CONCLUSION:** The combination of CA4P with carboplatin and paclitaxel was well tolerated in the majority of patients with adequate premedication and had antitumour activity in patients who were heavily pretreated. *British Journal of Cancer* (2010) 102, 1355-1360. doi:10.1038/sj.bjc.6605650 www.bjcancer.com Published online 13 April 2010 (C) 2010 Cancer Research UK

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Hypertension & Vascular Research

Herrera, M. and J. L. Garvin (2010). "Angiotensin II Stimulates Thick Ascending Limb NO Production via AT(2) Receptors and Akt1-dependent Nitric-oxide Synthase 3 (NOS3) Activation." Journal of Biological Chemistry **285**(20): 14932-14940. [PDF Full-Text](#)

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Angiotensin II (Ang II) acutely stimulates thick ascending limb (TAL) NO via an unknown mechanism. In endothelial cells, activation of Ang II type 2 receptor (AT(2)) stimulates NO. Akt1 activates NOS3 by direct phosphorylation. We hypothesized that Ang II stimulates TAL NO production via AT(2)-mediated Akt1 activation, which phosphorylates NOS3 at serine 1177. We measured NO production by fluorescence microscopy. In isolated TALs, Ang II (100 nM) increased NO production by 1.1 +/- 0.2 fluorescence units/min ($p < 0.01$). Ang II increased cGMP accumulation by 4.9 +/- 1.3 fmol/ μ g ($p < 0.01$). Upon adding the AT(2) antagonist PD123319 (1 μ M), Ang II failed to stimulate NO (0.1 +/- 0.1 fluorescence units/min; $p < 0.001$ versus Ang II); adding the AT(1) antagonist losartan (1 μ M) resulted in Ang II stimulating NO by 0.9 +/- 0.1 fluorescence units/min. Akt inhibitor (5 μ M) blocked Ang II-stimulated NO (-0.1 +/- 0.2 fluorescence units/min versus inhibitor alone). Phospho-Akt1 increased by 72% after 5 min ($p < 0.006$), returning to basal after 10 min. Phospho-Akt2 did not change after 5 min but increased by 115 and 163% after 10 and 15 min ($p < 0.02$). Phospho-Akt3 did not change. An AT(2) agonist increased pAkt1 by 78% ($p < 0.02$), PI3K inhibition blocked this effect. In TALs transduced with dominant negative Akt1, Ang II failed to stimulate NO (0.1 +/- 0.2 fluorescence units/min versus 1.2 +/- 0.2 for controls; $p < 0.001$). Ang II increased phospho-NOS3 at serine 1177 by 130% ($p < 0.01$) and 150% after 5 and 10 min ($p < 0.02$). Ang II increased phospho-NOS3 at serine 633 by 50% after 5 min ($p < 0.01$). Akt inhibition prevented NOS3 phosphorylation. We concluded that Ang II enhances TAL NO production via activation of AT(2) and Akt1-dependent phosphorylation of NOS3 at serines 1177 and 633.

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Hypertension & Vascular Research

Peng, H. M., O. A. Carretero, E. L. Peterson and N. E. Rhaleb (2010). "Ac-SDKP inhibits transforming growth factor-beta 1-induced differentiation of human cardiac fibroblasts into myofibroblasts." American Journal of Physiology-Heart and Circulatory Physiology **298**(5): H1357-H1364. [PDF Full-Text](#)

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Peng H, Carretero OA, Peterson EL, Rhaleb N. Ac-SDKP inhibits transforming growth factor-beta 1-induced differentiation of human cardiac fibroblasts into myofibroblasts. *Am J Physiol Heart Circ Physiol* 298: H1357-H1364, 2010. First published February 12, 2010; doi:10.1152/ajpheart.00464.2009. N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) inhibits collagen production and cell proliferation in cultured rat cardiac fibroblasts, but its effect on differentiation of fibroblasts into myofibroblasts is not known. High amounts of transforming growth factor-beta 1 (TGF-beta 1) have been found in fibrotic cardiac tissue. TGF-beta 1 converts fibroblasts into myofibroblasts, which produce more extracellular matrix proteins than fibroblasts. We hypothesized that 1) Ac-SDKP inhibits TGF-beta 1-induced differentiation of fibroblasts into myofibroblasts; and 2) this effect is mediated in part by blocking phosphorylation of small-mothers-against-decapentaplegic (Smad) 2 and extracellular signal-regulated kinase (ERK) 1/2. For this study, we used human fetal cardiac fibroblasts (HCFs), which do not spontaneously become myofibroblasts when cultured at low passages. We investigated the effect of Ac-SDKP on TGF-beta 1-induced HCF transformation into myofibroblasts, Smad2 and ERK1/2 phosphorylation, Smad7 expression, cell proliferation, and collagen production. We also investigated TGF-beta 1 production by HCFs stimulated with endothelin-1 (ET-1). As expected, HCFs treated with TGF-beta 1 transformed into myofibroblasts as indicated by increased expression of alpha-smooth muscle actin and a higher proportion of the embryonic isoform of smooth muscle myosin compared with untreated cells. TGF-beta 1 also increased Smad2 and ERK1/2 phosphorylation but did not affect Smad7 expression. In addition, TGF-beta 1 stimulated HCF proliferation as indicated by an increase in mitochondrial dehydrogenase activity and

collagen production (hydroxyproline assay). AcSDKP significantly inhibited all of the effects of TGF-beta 1. It also inhibited ET-1-stimulated TGF-beta 1 production. We concluded that Ac-SDKP markedly suppresses differentiation of human cardiac fibroblasts into myofibroblasts, probably by inhibiting the TGF-beta/Smad/ERK1/2 signaling pathway, and thus mediating its anti-fibrotic effects.

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Hypertension and Vascular Research

Ohishi, M., G. J. Dusting, P. A. Fennessy, F. A. O. Mendelsohn, X. C. Li and J. L. Zhuo (2010). "Increased expression and co-localization of ACE, angiotensin II AT1 receptors and inducible nitric oxide synthase in atherosclerotic human coronary arteries." Int J Physiol Pathophysiol Pharmacol **2**(2): 111-24. [Article Request Form](#)

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

Using immunohistochemistry and quantitative in vitro autoradiography, the present study was undertaken to examine whether co-expression of pro-atherosclerotic factors, ACE, the AT1 receptor, and iNOS, increased in early and advanced atherosclerotic lesions of human coronary arteries. In normal coronary arteries, ACE and eNOS were strongly co-expressed in endothelial cells (ECs), whereas the AT1 receptor was expressed in medial smooth muscle cells (SMCs). By contrast, iNOS was not expressed in ECs and SMCs. In early atherosclerotic lesions and atheromatous plaques, ACE, the AT1 receptor and iNOS immunostaining were primarily co-localized in infiltrated macrophages and SMCs adjacent to macrophages. eNOS expression was lower in ECs than in normal arteries, and absent in accumulated macrophages and SMCs. In fibrosclerotic plaques, ACE, the AT1 receptor, and iNOS immunostaining were still positive in macrophages as well as new microvessels within the plaques. Interestingly, SMCs in vasa vasorum of the adventitia in atheromatous and fibrosclerotic plaques were also strongly positive for AT1 receptor and iNOS, while ECs of the vasa vasorum were positive for ACE and eNOS. The present study demonstrates that multiple proatherosclerotic factors ACE, AT1 receptor and iNOS are co-localized almost exclusively in infiltrated macrophages and SMCs that have accumulated in or adjacent to early and advanced atherosclerotic plaques, while the anti-atherosclerotic enzyme eNOS is reduced in ECs. These data therefore suggest that increased formation of Ang II and iNOS in infiltrated macrophages and medial SMCs might well play important roles in the development and progression of human coronary atherosclerosis.

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Internal Medicine

Gonzalez, H. C. and V. Velanovich (2010). "Enterra Therapy: gastric neurostimulator for gastroparesis." Expert Rev Med Devices **7**(3): 319-32. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, MI 48202, USA.

Gastroparesis is a chronic disorder of gastric motility characterized by delayed gastric emptying in the absence of mechanical obstruction, which can lead to symptoms of nausea, vomiting, bloating, abdominal pain, postprandial fullness and weight loss. Although there are many etiologies, the primary causes are diabetes or are idiopathic. The mainstay of treatment is dietary and drug therapies. However, many patients will continue to suffer intractable symptoms despite these treatments. Gastric neurostimulation with the Enterra Therapy system has been approved for use under the Humanitarian Device Exemption by the US FDA. The device produces pulses of electrical stimulation that are delivered to the stomach continuously. One randomized clinical trial and multiple nonrandomized unblinded clinical trials and case series have documented improvement of symptoms in intractable diabetic and idiopathic gastroparesis. The purpose of this article is to introduce the Enterra Therapy gastric neurostimulator. Gastroparesis and its pathophysiology will be discussed in this clinical context to enhance the understanding of the device and its development. We will analyze the device in detail, its placement and the results of studies evaluating its efficacy.

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Internal Medicine

Keteyian, S. J. (2010). "Exercise in the management of patients with chronic heart failure." Curr Heart Fail Rep **7**(1): 35-41. [PDF Full-Text](#)

Department of Medicine, Henry Ford Hospital, 6525 Second Avenue, Detroit, MI, 48202, USA.
sketeyi1@hfhs.org

Despite the establishment of feasibility and physiologic benefits, questions remained about the safety and clinical effectiveness of physical exercise in patients with heart failure. In 2002, however, the Heart Failure: A Controlled Trial Investigating Outcomes of Exercise Training trial showed that physical exercise is safe, improves health status, increases cardiorespiratory capacity, and yields a modest reduction in clinical events among patients with HF. The magnitude of these benefits may relate to the volume of exercise completed.

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Internal Medicine

Undrovinas, N. A., V. A. Maltsev, L. Belardinelli, H. N. Sabbah and A. Undrovinas (2010). "Late sodium current contributes to diastolic cell Ca(2+) accumulation in chronic heart failure." J Physiol Sci **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Internal Medicine, Henry Ford Hospital, Detroit, MI, USA.

We elucidate the role of late Na(+) current (I(NaL)) for diastolic intracellular Ca(2+) (DCa) accumulation in chronic heart failure (HF). HF was induced in 19 dogs by multiple coronary artery microembolizations; 6 normal dogs served as control. Ca(2+) transients were recorded in field-paced (0.25 or 1.5 Hz) fluo-4-loaded ventricular myocytes (VM). I(NaL) and action potentials were recorded by patch-clamp. Failing VM, but not normal VM, exhibited (1) prolonged action potentials and Ca(2+) transients at 0.25 Hz, (2) substantial DCa accumulation at 1.5 Hz, and (3) spontaneous Ca(2+) releases, which occurred after 1.5 Hz stimulation trains in ~31% cases. Selective I(NaL) blocker ranolazine (10 μM) or the prototypical Na(+) channel blocker tetrodotoxin (2 μM) reversibly improved function of failing VM. The DCa accumulation and the beneficial effect of I(NaL) blockade were reproduced in silico using an excitation-contraction coupling model. We conclude that I(NaL) contributes to diastolic Ca(2+) accumulation and spontaneous Ca(2+) release in HF.

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Medical Education

Buckley, J. D., B. Joyce, A. J. Garcia, J. Jordan and E. Scher (2010). "Linking residency training effectiveness to clinical outcomes: a quality improvement approach." Jt Comm J Qual Patient Saf **36**(5): 203-8. [PDF Full-Text](#)

Department of Medicine, Indiana University, Indianapolis, USA. johnbuck@iupui.edu

BACKGROUND: The Accreditation Council for Graduate Medical Education (ACGME)'s Outcome Project requires training programs to use external measures such as quality of care indicators to assess their effectiveness. A practical, quality improvement (QI) process was implemented at Henry Ford Hospital to enhance the training program's educational effectiveness and clinical outcomes. **METHODS:** A QI process consisting of a modified Plan-Do-Study-Act (PDSA) cycle was applied to residency and fellowship curricula in a medical intensive care unit (MICU). The PDSA activities focused on improving clinical outcomes but also outlined educational goals for residents and fellows, defined teaching methods, and determined assessment methods for the ACGME curricula. The improvement process linked clinical outcomes to specific competency-based educational objectives. Residents and fellows received instruction on QI and applied the new curricula to their clinical training in the MICU. **RESULTS:** Two of seven MICU clinical outcomes demonstrated initial performance below national benchmarks: iatrogenic pneumothorax rate and sepsis-specific mortality. During the QI process, clinical outcomes in both areas improved. Training program directors used the MICU clinical outcomes as indicators of their programs' educational effectiveness. They also assessed individual trainee performance in QI initiatives through direct observation and review of their written summaries of these projects. **CONCLUSIONS:** Training programs can use hospital-tracked clinical outcomes to analyze their educational strengths and weaknesses and accordingly to enhance their educational curricula. Linking competency-based learning objectives for trainees to the clinical outcomes of their patients can improve physician education and patient care.

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Neurology

Bagher-Ebadian, H., R. Paudyal, T. N. Nagaraja, R. L. Croxen, J. D. Fenstermacher and J. R. Ewing (2010). "MRI Estimation of Gadolinium and Albumin Effects on Water-Proton." *Neuroimage Epub Ahead of Print*. [Article Request Form](#)

Department of Neurology, Henry Ford Hospital; Department of Physics, Oakland University.

The longitudinal relaxivity on the protons of water of a Gd-chelate-albumin compound was measured at 7T as a function of the macromolecular content of a cross-linked matrix. In agreement with previous works, the results demonstrate that the effect of Gadolinium on water proton relaxivity is not constant, rising moderately with increase in the concentration of bovine serum albumin (BSA). About 35% variation in relaxivity was observed over a 0 to 25% range of BSA concentrations ($R=3.893+0.0502 \times \text{BSA} [\%]$, Standard Errors and p-values for slope and intercept are: SE=0.0119, and 0.1740, $t=4.215$, and 22.383, $p<0.014$, and 0.001).

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Neurology

Cui, X., M. Chopp, A. Zacharek, C. Roberts and J. L. Chen (2010). "Niacin Treatment of Stroke Increases Neuronal Migration and Axonal Regeneration in Rats." *Stroke* **41**(4): E298-E298. [Article Request Form](#)

[Cui, Xu; Chopp, Michael; Zacharek, Alex; Roberts, Cynthia; Chen, Jieli] Henry Ford Hlth Syst, Detroit, MI USA.

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Neurology

Gumenyuk, V., T. Roth, O. Korzyukov, C. Jefferson, A. Kick, L. Spear, N. Tepley and C. L. Drake (2010). "Shift work sleep disorder is associated with an attenuated brain response of sensory memory and an increased brain response to novelty: an ERP study." *Sleep* **33**(5): 703-13. 2864886. [PDF Full-Text](#)

Henry Ford Hospital, Department of Neurology/Sleep Center, CFP3, 2799 West Grand Boulevard, Detroit, MI 48202, USA. vgumenyu@neurnis.neuro.hfh.edu

STUDY OBJECTIVE: To study the neurophysiological changes in attention and memory functions in shift work sleep disorder (SWSD), using event-related brain potentials (ERPs). **PARTICIPANTS:** 9 healthy night workers (NW) (mean age = 40 y; SD +/- 8.9 y); 8 night workers meeting diagnostic criteria for SWSD (mean age = 37 y +/- 9.4 y) and 9 healthy day workers (DW) (mean age = 35 y +/- 7.3 y). **METHODS AND PROCEDURE:** Using standard PSG the sleep related measures (TIB, TST, SOL, SE, and sleep stage distribution) were obtained prior to EEG/ERP study. Measures of habitual sleep were obtained from 2 week sleep logs and sleepiness was assessed with standardized measures. Using 32-EEG leads the ERPs to 3 types of sounds (novel, duration deviant, and simple tone) were obtained. The mismatch negativity (MMN) reflecting memory processing and P3a-reflecting the shift of involuntary attention were obtained. **STATISTICAL ANALYSIS:** The statistical comparisons of ERPs and sleep related parameters were performed using repeated measured ANOVAs and t-tests where appropriate. **RESULTS:** Patients with SWSD had reduced TST and increased WASO relative to healthy workers. ERP results demonstrated significant attenuation of MMN amplitude over frontal regions in SWSD patients relative to NW and DW. In the SWSD patients, the P3a was increased to novelty across frontocentral brain regions with respect to the same locations in healthy controls. **CONCLUSION:** The ERP evidence of sensory memory reduction and attentional hyper-reaction to novel sound in conjunction with disturbed sleep suggests the need for more neurophysiological studies in SWSD workers.

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Neurology

Liu, X. S., M. Chopp, R. L. Zhang, L. F. Jia, H. Teng, C. Chen and Z. G. Zhang (2010). "Genomic Profiling of microRNAs in the Subventricular Zone After Cerebral Ischemia: miR-124 is Associated With Neurogenesis Induced by Stroke." *Stroke* **41**(4): E231-E231. [Article Request Form](#)

[Liu, Xian Shuang; Chopp, Michael; Zhang, Rui Lan; Jia, Long Fei; Teng, Hua; Chen, Charles; Zhang, Zheng Gang] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA.

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Neurology

Liu, X. S., Y. Li, X. L. Wang, H. Q. Xin, L. H. Shen, Z. G. Zhang and M. Chopp (2010). "tPA Expression in Single Astrocytes Captured With Laser Microdissection is Increased After Treatment of Stroke in Mice With Bone Marrow Stromal Cells." Stroke **41**(4): E349-E349.

[Article Request Form](#)

[Liu, Xian Shuang; Li, Yi; Wang, Xin Li; Xin, Hong Qi; Shen, Li Hong; Zhang, Zheng Gang; Chopp, Michael] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI USA.

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Neurology

Mikkelsen, T., J. Anderson, T. J. Doyle, D. Croteau, R. Avedissian, S. Ryu and L. Schultz (2010). "Phase I/II dose escalation trial of concurrent temozolomide and whole brain radiation therapy for multiple brain metastasis." J Neurooncol **Epub Ahead of Print**.

[PDF Full-Text](#)

Hermelin Brain Tumor Center, Henry Ford Health System, 2799 W Grand Blvd, Detroit, MI, 48202, USA, nstom@neuro.hfh.edu.

This study sought to establish the recommended phase II dose and efficacy of temozolomide (TMZ) with concurrent radiotherapy in patients with brain metastases. Patients were stratified by prior systemic therapy (≤ 1 vs. >math>\geq 2</math>) and enrolled in cohorts of escalating doses of daily TMZ for 14 days (group A: 75, 95, 115, 135, or 150 mg/m², group B: 75, 90, 105, 120, or 135 mg/m²). Endpoints included safety and clinical activity. For group A (≤ 1 prior chemotherapy) no dose limiting toxicity was seen at 75 and 95 mg/m². Five of eight patients experienced dose limiting toxicities at 115 mg/m², thus the recommended phase II dose was 95 mg/m². Arm B (>math>\geq 2</math> prior chemotherapy regimens) was closed due to poor enrollment. In the phase II portion, 17 patients in group A were treated. There were 0 patients with complete radiographic response, three with a partial response, ten remained stable, and four demonstrated early progression. The 3 and 6 month progression-free survival (PFS) rates were 41 and 18% with a median PFS time of 2.4 months. Overall survival at 3 and 6 months was 53 and 41%, respectively, with a median survival time of 4.1 months. The maximum tolerated dose of daily TMZ with concurrent WBRT was 95 mg/m². Despite dose escalation, outcomes did not appear to be improved in the sample treated.

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Neurology

Mitsias, P., Q. Jiang, A. Katramados, Q. M. Zhao, B. Silver, L. Li, L. Schultz and M. Chopp (2010). "Multiparametric Magnetic Resonance Imaging Characteristics of Stroke Recovery." Stroke **41**(4): E234-E234. [Article Request Form](#)

[Mitsias, Panayiotis; Jiang, Quan; Katramados, Angelos; Zhao, Qingming; Silver, Brian; Li, Lian; Schultz, Lonni; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Mitsias, P., M. Lu, H. Bagher-Ebadian, J. R. Ewing, H. Soltanian-Zadeh, A. Kapke and M. Chopp (2010). "Multiparametric MRI ISODATA Analysis in the Assessment of Acute Ischemic Stroke." Stroke **41**(4): E343-E343. [Article Request Form](#)

[Mitsias, Panayiotis; Lu, Mei; Bagher-Ebadian, Hassan; Ewing, James R.; Soltanian-Zadeh, Hamid; Kapke, Alissa; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Morris, D. C., M. Chopp, L. Zhang, M. Lu and Z. G. Zhang (2010). "Treatment of Acute Stroke With Thymosin beta 4." Stroke **41**(4): E209-E209. [Article Request Form](#)

[Morris, Daniel C.; Chopp, Michael; Zhang, Li; Lu, Mei; Zhang, Zheng G.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Ray, A. and S. M. Bowyer (2010). "Clinical applications of magnetoencephalography in epilepsy." Ann Indian Acad Neurol **13**(1): 14-22. 2859582. [PDF Full-Text](#)

Comprehensive Epilepsy Program, Henry Ford Hospital, Detroit MI.

Magnetoencephalography (MEG) is being used with increased frequency in the pre-surgical evaluation of patients with epilepsy. One of the major advantages of this technique over the EEG is the lack of distortion of MEG signals by the skull and intervening soft tissue. In addition, the MEG preferentially records activity from tangential sources thus recording activity predominantly from sulci, which is not contaminated by activity from apical gyral (radial) sources. While the MEG is probably more sensitive than the EEG in detecting interictal spikes, especially in the some locations such as the superficial frontal cortex and the lateral temporal neocortex, both techniques are usually complementary to each other. The diagnostic accuracy of MEG source localization is usually better as compared to scalp EEG localization. Functional localization of eloquent cortex is another major application of the MEG. The combination of high spatial and temporal resolution of this technique makes it an extremely helpful tool for accurate localization of visual, somatosensory and auditory cortices as well as complex cognitive functions like language. Potential future applications include lateralization of memory function.

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Neurology

Rogers, L. R., J. Gutierrez, L. Scarpace, L. Schultz, S. Ryu, B. Lord, B. Movsas, J. Honsowetz and R. Jain (2010). "Morphologic magnetic resonance imaging features of therapy-induced cerebral necrosis." J Neurooncol **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA, Lisa.Rogers1@UHhospitals.org .

To describe the morphologic magnetic resonance imaging (MRI) findings in histologically proven therapy-induced cerebral necrosis. We retrospectively reviewed the morphologic MRI findings in patients with therapy-induced cerebral necrosis. Images were reviewed for size, location, and characteristics of signal intensity abnormalities and T1-contrast enhancement. Images were also assessed for mass effect, necrosis, cyst, atrophy, cortical thinning, and leukoencephalopathy. The individual imaging characteristics were correlated with clinical and treatment variables. There were 44 patients. Seventy percent had a glioma, all patients had received radiation, and 57% had received chemotherapy in close proximity to radiation. All images demonstrated contrast enhancement, predominantly in the white matter. Enhancement was present in the periventricular/subependymal region in 50% of cases and the corpus callosum in 27%. The most common pattern of lesion peripheral enhancement was "spreading wavefront" and of interior enhancement was "Swiss cheese/soap bubble." The enhancing lesion was single in 60% of cases. Mass effect was present in 93% of patients. Location and patterns of enhancement were significantly associated with the interval from brain radiation to the diagnosis of therapy-induced cerebral necrosis, tumor histology, patient age, type of radiation, and administration of systemic chemotherapy. This is the largest study of the morphologic conventional MRI findings in pathologically confirmed therapy-induced cerebral necrosis. We characterized the imaging findings in a variety of tumor types following a variety of radiation treatments and other antineoplastic therapy. These findings may be of value in identifying therapy-induced cerebral necrosis in patients treated for a brain tumor.

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Neurology

Shehadah, A., J. Chen, X. Cui, C. Roberts, M. Lu and M. Chopp (2010). "Combination treatment of experimental stroke with Niaspan and Simvastatin, reduces axonal damage and improves functional outcome." J Neurol Sci **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Neurology, Henry Ford Health Sciences Center, Detroit, MI, 48202, United States.

In this study we examined the effect of combination treatment of experimental stroke with Niaspan, a prolonged-release formulation of Niacin (vitamin B3), and Simvastatin, a cholesterol-lowering drug, on functional outcome, axonal damage, axonal density and the of Iba-1 immunoreactive microglia expression in the ischemic brain of rats. Adult male rats were subjected to 2h middle cerebral artery occlusion (MCAo) and treated with or without Niaspan alone, Simvastatin alone and combination Niaspan and Simvastatin starting 24h after MCAo and daily for 14days. Neurological functional tests were performed. Axonal damage and density were evaluated by Amyloid Precursor Protein (APP) and Bielschowsky silver, respectively. Nogo66 Receptor (NgR) expression and immunoreactive microglia (Iba-1) were also measured in the ischemic brain. Niaspan and Simvastatin monotherapy and combination treatment significantly promote functional outcome after stroke ($p < 0.05$) compared to MCAo control animals. Combination treatment with Niaspan and Simvastatin induces additive but not synergetic effects when compared to Niaspan or Simvastatin monotherapy groups. Combination treatment significantly decreased APP expression and increased Bielschowsky silver expression. NGR and Iba-1 expression were significantly decreased in the ischemic brain. These data suggest that treatment of experimental stroke with combination of Niaspan and Simvastatin significantly improves functional outcome, reduces axonal damage and increases axonal density. Decreased expression of the NGR and reduced activated microglia may contribute to functional recovery after stroke.

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Neurology

Shehadah, A., J. L. Chen, X. Cui, C. Roberts, M. Lu and M. Chopp (2010). "Combination Treatment With Niaspan and Simvastatin of Experimental Stroke, Induces Axonal Regeneration and Improves Functional Outcome." *Stroke* **41**(4): E300-E300. [Article Request Form](#)

[Shehadah, Amjad; Chen, Jieli; Cui, Xu; Roberts, Cynthia; Lu, Mei; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Shehadah, A., J. L. Chen, A. Zacharek, X. Cui, C. Roberts, M. Lu and M. Chopp (2010). "Comparison of Bone Marrow Stromal Cells Derived From Stroke Rats and Normal Rats for the Treatment of Stroke." *Stroke* **41**(4): E350-E350. [Article Request Form](#)

[Shehadah, Amjad; Chen, Jieli; Zacharek, Alex; Cui, Xu; Roberts, Cynthia; Lu, Mei; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Shen, L. H., Y. Li and M. Chopp (2010). "Astrocytic endogenous glial cell derived neurotrophic factor production is enhanced by bone marrow stromal cell transplantation in the ischemic boundary zone after stroke in adult rats." *Glia* **58**(9): 1074-81. [PDF Full-Text](#)

Department of Neurology, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan 48202, USA.

Bone marrow stromal cells (BMSCs) facilitate functional recovery in rats after focal ischemic attack. Growing evidence suggests that the secretion of various bioactive factors underlies BMSCs' beneficial effects. This study investigates the expression of glial cell derived neurotrophic factor (GDNF) in the ischemic hemisphere with or without BMSC administration. Adult male Wistar rats were subjected to 2 h of middle cerebral artery occlusion followed by an injection of 3×10^6 BMSCs ($n = 11$) or phosphate-buffered saline ($n = 10$) into the tail vein 24 h later. Animals were sacrificed seven days later. Single and double immunohistochemical staining was performed to measure GDNF, Ki67, doublecortin, and glial fibrillary acidic protein expression as well as the number of apoptotic cells along the ischemic boundary zone (IBZ) and/or in the subventricular zone (SVZ). BMSC treatment significantly increased GDNF expression and decreased the number of apoptotic cells in the IBZ ($P < 0.05$). GDNF expression was colocalized with GFAP. Meanwhile, BMSCs increased the number of Ki-67 positive cells and the density of DCX positive migrating neuroblasts ($P < 0.05$). GDNF expression was

significantly increased in single astrocytes collected from animals treated with BMSCs, and in astrocytes cocultured with BMSCs after OGD ($P < 0.05$). Our data suggest that BMSCs increase GDNF levels in the ischemic hemisphere; the major source of GDNF protein is reactive astrocytes. We propose that the increase of GDNF in response to BMSC administration creates a hospitable environment for local cellular repair as well as for migrating neuroblasts from the SVZ, and thus contributes to the functional improvement.

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Neurology

Shen, L. S., H. Q. Xin, Y. Li, Y. S. Cui, L. Zhang and M. Chopp (2010). "Endogenous Tissue Plasminogen Activator is Essential for the Functional Benefit of Bone Marrow Stromal Cell Treatment of Stroke in Mice." Stroke **41**(4): E386-E386. [Article Request Form](#)

[Shen, Lihong; Xin, Hongqi; Li, Yi; Cui, Yisheng; Zhang, Li; Chopp, Michael] Henry Ford Hlth Syst, Detroit, MI USA.

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Neurology

Smith, B. J. and A. J. Cole (2010). "Management of epilepsy in drug-resistant patients." CNS Spectr **15**(1 Suppl 2): 1, 3-7; quiz 7-8. [Article Request Form](#)

Henry Ford Hospital, Detroit, Michigan, USA.

Epilepsy affects > 2 million people in the United States, making it one of the most common neurobiological conditions. Typically, epilepsy is treated with one of several available antiepileptic drugs and patients are able to experience freedom from seizures with minimal side effects. However, there are some patients who do not respond to treatment and require the use of multiple drug combinations or surgical intervention. Although there are few studies supporting its use, multi-drug regimens have been known to be helpful for patients, although clinicians should monitor patients for adverse side effects. Vagus nerve stimulation is the only US Food and Drug Administration-approved surgical neurostimulation therapy for epilepsy, and patients' conditions often progress for many years before epilepsy surgery options are considered. Lastly, due to the chronic nature of epilepsy, clinicians should be aware of the presence of comorbid psychiatric conditions as well. This supplement is Part One in the "Case in Point: Evidence-Based Insights for Epilepsy Management" series. In this Expert Review Supplement, Andrew J. Cole, MD, FRCPC, outlines a case of a patient with drug resistant epilepsy, and Brien J. Smith, MD, outlines the best practices for the case patient including discussion on defining drug resistance in patients as well as the benefits and risks of available and emerging drug and surgical treatments.

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Neurology

Teng, H., M. Chopp, A. Hozeska-Solgot, L. H. Shen, B. J. Qiu, R. J. Liu and Z. G. Zhang (2010). "Sonic Hedgehog Mediates Cerebral Angiogenesis Through Activation of Tissue Plasminogen Activator." Stroke **41**(4): E347-E348. [Article Request Form](#)

[Teng, Hua; Chopp, Michael; Hozeska-Solgot, Ann; Shen, Lihong; Qiu, Bingjie; Liu, Renjay; Zhang, Zheng Gang] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. [Chopp, Michael] Oakland Univ, Dept Phys, Detroit, MI USA. [Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI USA.

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Neurology

Varelas, P. N., T. Abdelhak, J. Wellwood, D. Benczarski, S. B. Elias and M. Rosenblum (2010). "The Appointment of Neurointensivists Is Financially Beneficial to the Employer." Neurocrit Care **Epub Ahead of Print**. [PDF Full-Text](#)

Department of Neurology, K-11, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI, 48202, USA, varelas@neuro.hfh.edu

BACKGROUND: Although the impact of a neurointensivist (NI) on patient outcomes has been examined in the past, the financial impact has not been estimated before. **METHODS:** We extracted the financial data from the Neuro-Intensive Care Unit (NICU) at Henry Ford Hospital during two 3-year periods, one before and one after the appointment of a NI. Net revenue (NR), total direct expenses (TDE), and contribution margin (CM) were compared between these two periods both for Henry Ford Hospital and the Henry Ford Medical Group. **RESULTS:** The average number of admissions increased by 24% during the period when the NI was present, the number of patient-days by 25% and the average length of stay by 2%. In the second period, when the NI was billing for critical care time spent in the NICU, as well as for procedures he performed, the mean yearly NR was \$402,000, the TDE \$317,000 and the NR/TDE 1.24 (>1.0 represents profitability). The combined mean NR (Henry Ford Hospital + Medical Group) increased by 54.6%, the combined TDE by 42.2% and the combined CM by 91.2% in the period when the NI was present. This is reflected in the combined mean CM per admission, which also increased by 56.4% in the after period. **CONCLUSION:** This study shows a significant financial benefit for the Henry Ford Health System during the period when a NI was present in the NICU.

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Neurology

Wang, L., M. Chopp, H. Teng, M. Bolz, X. L. Wang, R. L. Zhang, L. Zhang and Z. G. Zhang (2010). "Tumor Necrosis Factor Alpha Primes Cerebral Endothelial Cells for Erythropoietin-induced Angiogenesis." *Stroke* **41**(4): E347-E347. [Article Request Form](#)

[Wang, Lei; Chopp, Michael; Teng, Hua; Bolz, Marianne; Wang, Xin Li; Zhang, Rui Lan; Zhang, Lucille; Zhang, Zheng Gang] Henry Ford Hlth Syst, Detroit, MI USA.

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Neurology

Xin, H. Q., Y. Li, L. H. Shen, X. L. Wang, J. Zhang, Z. G. Zhang and M. Chopp (2010). "BMSCs Increase tPA Activity in Astrocytes Which Facilitates Neurite Outgrowth After Stroke." *Stroke* **41**(4): E373-E373. [Article Request Form](#)

[Xin, Hongqi; Li, Yi; Shen, Li Hong; Wang, Xinli; Zhang, Jing; Zhang, Zheng Gang; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Xin, H. Q., L. H. Shen, Y. Li, Z. G. Zhang and M. Chopp (2010). "Shh and Tgf-beta Signaling Pathways Activated by BMSCs Increase tPA Activity After Stroke in Mice." *Stroke* **41**(4): E300-E300. [Article Request Form](#)

[Xin, Hongqi; Shen, Li Hong; Li, Yi; Zhang, Zheng Gang; Chopp, Michael] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Zhang, C. L., M. Chopp, Y. S. Cui, M. Lu, A. Kapke, J. R. Barber, S. C. Ng and Z. G. Zhang (2010). "Delayed Treatment With Arimoclomol, a Co-inducer of Heat Shock Proteins, Improves Neurological Outcome After Embolic Stroke in the Rat." *Stroke* **41**(4): E349-E349. [Article Request Form](#)

[Zhang, Chunling; Chopp, Michael; Cui, Yisheng; Lu, Mei; Kapke, Alissa; Zhang, Zheng Gang] Henry Ford Hosp, Detroit, MI 48202 USA. [Chopp, Michael] Oakland Univ, Rochester, MI 48063 USA. [Barber, Jack R.; Ng, Shi Chung] CytRx Corp, San Diego, CA USA.

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Neurology

Zhang, L., M. Chopp, Y. Ueno, Y. S. Cui, M. Wei and Z. G. Zhang (2010). "Combination Therapy of VELCADE and Low Dose tPA at 2h Provides Potent Neuroprotection in Aged Rats After Focal Cerebral Ischemia." Stroke **41**(4): E392-E392. [Article Request Form](#)

[Zhang, Li; Chopp, Michael; Ueno, Yuji; Cui, Yisheng; Wei, Min; Zhang, Zheng Gang] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurology

Zhang, L., Z. G. Zhang, B. Buller, J. Jiang, Y. T. Jiang, D. P. Zhao, X. S. Liu, D. Morris and M. Chopp (2010). "Combination Treatment With VELCADE and Low-Dose Tissue Plasminogen Activator Provides Potent Neuroprotection in Aged Rats After Embolic Focal Ischemia." Stroke **41**(5): 1001-1007. [PDF Full-Text](#)

[Zhang, Li; Zhang, Zheng Gang; Buller, Ben; Jiang, James; Jiang, Yanting; Zhao, Danping; Liu, Xianshuang; Chopp, Michael] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Morris, Dan] Henry Ford Hlth Syst, Dept Emergency Med, Detroit, MI 48202 USA. [Buller, Ben; Chopp, Michael] Oakland Univ, Dept Phys, Rochester, MI USA.

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Background and Purpose-Treatment with a selective proteasome inhibitor, VELCADE, in combination with tissue plasminogen activator (tPA) extended the therapeutic window to 6 hours in young rats after stroke. However, stroke is a major cause of death and disability in the elderly. The present study investigated the effect of VELCADE in combination with a low-dose tPA on aged rats after embolic stroke. Methods-Male Wistar rats at the age of 18 to 20 months were treated with VELCADE (0.2 mg/kg) alone, a low-dose tPA (5 mg/kg) alone, combination of VELCADE and tPA, or saline 2 hours after embolic middle cerebral artery occlusion. To test the contribution of endothelial nitric oxide synthase to VELCADE-mediated neuroprotection, endothelial nitric oxide synthase knockout and wild-type mice were treated with VELCADE (0.5 mg/kg) 2 hours after embolic stroke. Results-Treatment with VELCADE significantly reduced infarct volume, whereas tPA alone did not reduce infarct volume and aggravated blood-brain barrier disruption in aged rats compared with saline-treated rats. However, the combination treatment significantly enhanced the reduction of infarct volume, which was associated with an increase in endothelial nitric oxide synthase activity compared with saline-treated rats. Additionally, the combination treatment promoted thrombolysis and did not increase the incidence of hemorrhage transformation. VELCADE significantly reduced lesion volume in wild-type mice but failed to significantly reduce lesion volume in endothelial nitric oxide synthase knockout mice. Conclusions-Treatment with VELCADE exerts a neuroprotective effect in aged rats after stroke. The combination of VELCADE with the low-dose tPA further amplifies the neuroprotective effect. Endothelial nitric oxide synthase at least partly contributes to VELCADE-mediated neuroprotection after stroke. (Stroke. 2010;41:1001-1007.)

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Neurology

Zhang, R. L., M. Chopp, L. F. Jiang, C. Roberts, M. Wei and Z. G. Zhang (2010). "Mash1 Lineage Cells Contribute to Ischemia Induced Neurogenesis and Oligodendrogenesis." Stroke **41**(4): E251-E251. [Article Request Form](#)

[Zhang, Ruilan; Chopp, Michael; Jiang, Longfei; Roberts, Cindi; Wei, Mei; Zhang, Zheng Gang] Henry Ford Hosp, Detroit, MI 48202 USA.

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Neurosurgery

Chang, V., P. Hartzfeld, M. Langlois, A. Mahmood and D. Seyfried (2010). "Outcomes of cranial repair after craniectomy - Clinical article." Journal of Neurosurgery **112**(5): 1120-1124. [PDF Full-Text](#)

[Chang, Victor; Hartzfeld, Paul; Mahmood, Asim; Seyfried, Donald] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI 48202 USA. [Langlois, Marianne] Baystate Hlth Syst, Div Neurosurg, Springfield, MA USA.

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Object. Hemicraniectomy is a commonly practiced neurosurgical intervention with a wide range of indications and clinical data supporting its use. The extensive use of this procedure directly results in more cranioplasties to repair skull defects. The complication rate for cranial repair after craniectomy seems to be higher than that of the typical elective craniotomy. This finding prompted the authors to review their experience with patients undergoing cranial repair. **Methods.** The authors performed a retrospective review of 212 patients who underwent cranial repair over a 13-year period at their institution. A database tracking age, presenting diagnosis, side of surgery, length of time before cranial repair, bone graft material used, presence of a ventricular shunt, presence of a postoperative drain, and complications was created and analyzed. **Results.** The overall complication rate was 16.4% (35 of 213 patients). Patients 0-39 years of age had the lowest complication rate of 8% ($p = 0.028$). For patients 40-59 years of age and older than 60, complication rates were 20 and 26%, respectively. Patients who originally presented with traumatic injuries had a lower rate of complications than those who did not (10 vs 20%; $p = 0.049$). Conversely, patients who presented with tumors had a higher complication rate than those without (38 vs 15%; $p = 0.027$). Patients who received autologous bone graft placement had a statistically significant lower risk of postoperative infection (4.6 vs 18.4%; $p = 0.002$). Patients who underwent cranioplasty with a 0-3 month interval between operations had a complication rate of 9%, 3-6 months 18.8%, and > 6 months 26%. Pairwise comparisons showed that the difference between the 0-3 month interval and the > 6-month interval was significant ($p = 0.007$). The difference between the 0-3 month interval and the 4-6 month interval showed a trend ($p = 0.07$). No difference was detected between the 4-6 month interval and > 6-month interval ($p = 0.35$). **Conclusions.** The overall rate of complications related to cranioplasty after craniectomy is not negligible, and certain factors may be associated with increased risk. Therefore, when evaluating the need to perform a large decompressive craniectomy, the surgeon should also be aware that the patient is not only subject to the risks of the initial operation, but also the risks of subsequent cranioplasty. (DOI: 10.3171/2009.6.JNS09133)

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Neurosurgery

Slavin, S., B. Gesuntheit, N. Ashkenasi, R. Bakimer-Kleiner, B. Gowda-Kurkalli, C. Karageorgiou, N. Kronfeld, S. Cazacu, S. Finnins, H. K. Lee and C. Brodie (2010). "Clinical and Future Application of Autologous Multipotential Mesenchymal Stromal Stem Cells for the Treatment of Neurological Diseases." Human Gene Therapy 21(5): 646-646. [Article Request Form](#)

[Slavin, S.; Gesuntheit, B.; Ashkenasi, N.; Bakimer-Kleiner, R.; Gowda-Kurkalli, B.] Int Ctr Cell Therapy & Canc Immunotherapy CTCl, Tel Aviv, Israel. [Karageorgiou, C.] Gen Hosp G Gennimatas, Dept Neurol, Athens, Greece. [Kronfeld, N.; Brodie, C.] Bar Ilan Univ, Mina & Everard Goodman Fac Life Sci, Ramat Gan, Israel. [Cazacu, S.; Finnins, S.; Lee, H-K; Brodie, C.] Henry Ford Hosp, Dept Neurosurg, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. slavin@CTClcenter.com

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Neurosurgery

Thomas, S. L., R. Alam, N. Lemke, L. R. Schultz, J. A. Gutierrez and S. A. Rempel (2010). "PTEN augments SPARC suppression of proliferation and inhibits SPARC-induced migration by suppressing SHC-RAF-ERK and AKT signaling." Neuro Oncol **Epub Ahead of Print**. [PDF Full-Text](#)

Barbara Jane Levy Laboratory of Molecular Neuro-Oncology, Hermelin Brain Tumor Center, Department of Neurosurgery (S.L.T., R.A., N.L., S.A.R.), Department of Biostatistics and Research Epidemiology (L.R.S.), and Department of Pathology (J.A.G.), Henry Ford Hospital, Detroit, Michigan.

SPARC (secreted protein acidic and rich in cysteine) is expressed in all grades of astrocytoma, including glioblastoma (GBM). SPARC suppresses glioma growth but promotes migration and invasion by mediating integrin and growth factor receptor-regulated kinases and their downstream effectors. PTEN (phosphatase and tensin homolog deleted on chromosome 10), which is commonly lost in primary GBMs, negatively regulates proliferation and migration by inhibiting some of the same SPARC-mediated signaling pathways. This study determined whether PTEN reconstitution in PTEN-mutant, SPARC-expressing U87MG cells could further suppress proliferation and tumor growth but inhibit migration and invasion in SPARC-expressing cells in vitro

and in vivo, and thereby prolong survival in animals with xenograft tumors. In vitro, PTEN reduced proliferation and migration in both SPARC-expressing and control cells, with a greater suppression in SPARC-expressing cells. PTEN reconstitution suppressed AKT activation in SPARC-expressing and control cells but suppressed the SHC-RAF-ERK signaling pathway only in SPARC-expressing cells. Importantly, coexpression of SPARC and PTEN resulted in the smallest, least proliferative tumors with reduced invasive capacity and longer animal survival. Furthermore, direct inhibition of the AKT and SHC-RAF-ERK signaling pathways suppressed the proliferation and migration of SPARC-expressing cells in vitro. These findings demonstrate that PTEN reconstitution or inhibition of signaling pathways that are activated by the loss of PTEN provide potential therapeutic strategies to inhibit SPARC-induced invasion while enhancing the negative effect of SPARC on tumor growth.

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Neurosurgery

Xiong, Y., A. Mahmood, C. Qu, H. Kazmi, Z. G. Zhang, C. T. Noguchi, T. Schallert and M. Chopp (2010). "Erythropoietin improves histological and functional outcomes after traumatic brain injury in mice in the absence of the neural erythropoietin receptor." J Neurotrauma **27**(1): 205-15. 2824224. [PDF Full-Text](#)

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

Erythropoietin (EPO), essential for erythropoiesis, provides neuroprotection. The EPO receptor (EPOR) is expressed in both neural and non-neural cells in the brain. This study was designed to test the hypothesis that EPO provides beneficial therapeutic effects, even in the absence of the neural EPOR. In this study, EPOR-null mice were rescued with selective EpoR expression driven by the endogenous EpoR promoter in hematopoietic tissue, but not in the neural cells. Anesthetized young adult female EPOR-null and wild-type mice were subjected to traumatic brain injury (TBI) induced by controlled cortical impact. EPO (5000 U/kg) or saline was intraperitoneally administered at 6 h and 3 and 7 days post-injury. Sensorimotor and spatial learning functions were assessed. Expression of EPOR and its downstream signal proteins were evaluated by Western blot analysis. Our data demonstrated that EPO treatment significantly reduced cortical tissue damage and hippocampal cell loss, and improved spatial learning following TBI in both the wild-type and EPOR-null mice. EPO treatment significantly improved sensorimotor functional recovery, with better outcomes in the wild-type mice. EPO treatment upregulated anti-apoptotic proteins (p-Akt and Bcl-XL) in the ipsilateral hippocampus and cortex of the injured wild-type and EPOR-null mice. These data demonstrate that EPO significantly provides neuroprotection following TBI, even in the absence of EPOR in the neural cells, suggesting that its therapeutic benefits may be mediated through vascular protection.

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Neurosurgery

Yu, L. Y., S. Krishnamurthy, H. Chang and J. J. Wasenko (2010). "Congenital maturing immature intraventricular teratoma." Clinical Imaging **34**(3): 222-225. [Article Request Form](#)

[Yu, Liyuan; Wasenko, John J.] State Univ New York Upstate Med Univ, Dept Radiol, Syracuse, NY 13210 USA. [Krishnamurthy, Satish] Henry Ford Hosp, Dept Neurosurg, Detroit, MI 48202 USA. [Chang, Howard] Michigan State Univ, Dept Neurol, E Lansing, MI 48824 USA.

Wasenko, JJ, State Univ New York Upstate Med Univ, Dept Radiol, 750 E Adams St, Syracuse, NY 13210 USA.

We report a case of a maturing immature intraventricular teratoma in a neonate. The computed tomography and magnetic resonance imaging and pathologic findings are described. The relevant literature is reviewed and management is discussed. (C) 2010 Elsevier Inc. All rights reserved.

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Pathology

Dulai, M. S., D. V. Caccamo, A. L. Briley, M. S. B. Edwards, P. C. Fisher and N. L. Lehman (2010). "Intramedullary papillary ependymoma with choroid plexus differentiation and cerebrospinal fluid dissemination to the brain Case report." Journal of Neurosurgery-Pediatrics **5**(5): 511-517. [PDF Full-Text](#)

[Dulai, Mohanpal S.; Briley, Anita L.; Lehman, Norman L.] Stanford Univ, Med Ctr, Dept Pathol, Stanford, CA 94305 USA. [Edwards, Michael S. B.; Fisher, Paul C.] Stanford Univ, Med Ctr, Dept Neurosurg, Stanford, CA 94305 USA. [Fisher, Paul C.] Stanford Univ, Med Ctr, Dept Neurol, Stanford, CA 94305 USA. [Fisher, Paul C.] Stanford Univ, Med Ctr, Dept Pediat, Stanford, CA 94305 USA. [Caccamo, Dario V.] Sutter Med Ctr, Dept Pathol, Sacramento, CA USA.
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This 8-year-old girl presented with a papillary ependymoma in the thoracic spinal cord. Resection was followed by recurrence at the primary site and later in the lumbosacral thecal sac, followed by cerebrospinal fluid dissemination to the brain approximately 5 years after her initial presentation. The tumor showed cytological and immunohistochemical features overlapping those of classic ependymomas and choroid plexus tumors similar to those seen in uncommon supratentorial papillary ependymomas. also known as papillary tumors of the pineal region. The histopathological and clinical courses of this rare spinal papillary ependymoma exhibiting mixed ependymal and choroid plexus like differentiation are discussed. (DOI: 10.3171/2009.12.PEDS09130)

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Pathology

Meier, F. A. and B. Jones (2010). "Patient safety and sources of error in point-of-care testing." *J Lab Med* **34**(3): 141-7. [Article Request Form](#)

Patient safety is the project of reducing medical errors by creating and enforcing standards of practice, tracking and publishing errors to guide countermeasures, improving information transfer, and fostering increased accountability among healthcare providers. Errors in point-of-care testing (POCT) can be practical, cognitive, or axiological (the latter are errors of judgment). Countermeasures to errors in POCT have been organized into a laboratory ethos of test operator training and competence demonstration, explicit written procedures, routine quality control, recorded, verified, and retrievable patient results, and external proficiency testing. Three characteristics of POCT can defeat these countermeasures: technical limitations of POCT methods, the rapid availability of their results, and the tendency of these results to change patient care immediately. In the United States, government regulations of POCT have not been a success, but government mandated accreditation programs have been more effective. Laboratorians who monitor of POCT - called in the United States point-of-care test coordinators - have been essential to reporting and tracking POCT errors. They have exploited electronic information transfer to do so and to increase accountability for POCT among clinician test operators. Although a modified version of Gerald Kost's taxonomy of sources of errors offers a systematic approach to POCT error classification, major preventable adverse events (called "sentinel events" in the United States) tend to drive POCT patient safety. This circumstance has stressed the importance of clinical contexts. Tight glycemic control using POCT whole blood glucose is the example with which we illustrate the challenges to patient safety, from the technical limitations, rapid result availability, and impact on therapy, characteristic of POCT.

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Pathology

Nakhleh, R. E., L. G. Bekeris, R. J. Souers, F. A. Meier and J. A. Tworek (2010). "Surgical Pathology Case Reviews Before Sign-Out A College of American Pathologists Q-Probes Study of 45 Laboratories." *Archives of Pathology & Laboratory Medicine* **134**(5): 740-743.
[PDF Full-Text](#)

[Nakhleh, Raouf E.] Mayo Clin, Dept Pathol, Jacksonville, FL 32224 USA. [Bekeris, Leonas G.] Phoenixville Hosp, Dept Pathol, Phoenixville, PA USA. [Souers, Rhona J.] Coll Amer Pathologists, Dept Stat, Northfield, IL USA. [Meier, Frederick A.] Henry Ford Hlth Syst, Dept Pathol, Detroit, MI USA. [Tworek, Joseph A.] St Josephs Mercy Hosp, Dept Pathol, Ann Arbor, MI USA.
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Context.-To avoid errors many surgical pathology services mandate review of a case by a second pathologist before reports are released (signed out). Objective.-To study the extent and characteristics of such review. Design.-Participants retrospectively examined up to 400 cases to identify a maximum of 30 cases reviewed by

at least one additional pathologist before sign-out. For each case, participants documented the organ system, primary disease type, number of additional pathologists consulted, and the reason for case review. The main outcome measure was the fraction of surgical pathology cases that underwent second pathologist review before sign-out. Results.-From 45 laboratories, examination of 18 032 surgical pathology cases yielded 1183 (6.6%) cases that had been reviewed before sign-out. The median laboratory reviewed 8.2% of cases. Three-fifths of reviews focused on 4 organ systems: gastrointestinal (20.5%), breast (16.0%), skin (12.7%), and female genital tract (10.0%). Malignant neoplasm far exceeded all other categories of disease in reviewed cases (45.3%). Cases were reviewed by one additional pathologist 78% of the time. Two dominant reasons for case review emerged: difficult diagnosis (46.2%) and audit required by departmental policy (43.0%). Most laboratories (71%) had departmental policies regarding review of cases. These laboratories reviewed cases about 33% more often than laboratories without policies (9.6% versus 6.5%). Conclusions.-Review of selected surgical pathology cases before sign-out is widely accepted with 71% of participant laboratories following policies to this effect. About 1 case in 15 (6.6%) were reviewed with the median laboratory of participants reviewing about 1 in 12 (8.2%). (Arch Pathol Lab Med. 2010;134:740-743)

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Pharmacy

Edwin, S. B., D. L. Jennings and J. S. Kalus (2010). "An Evaluation of the Early Pharmacodynamic Response After Simultaneous Initiation of Warfarin and Amiodarone." Journal of Clinical Pharmacology **50**(6): 693-698. [PDF Full-Text](#)

[Jennings, Douglas L.; Kalus, James S.] Henry Ford Hosp, Dept Pharm, Detroit, MI 48202 USA. [Edwin, Stephanie B.] Univ Michigan, Dept Pharm, Ann Arbor, MI 48109 USA.

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Amiodarone inhibits the metabolism of warfarin. Previous studies characterizing this drug interaction have focused on the effect of adding amiodarone to stable doses of warfarin. The objective of this study was to assess whether simultaneous initiation of warfarin and amiodarone results in early alteration of the international normalized ratio (INR) response to warfarin. Patients initiated on warfarin and amiodarone during the same hospitalization were included in the amiodarone (AMIO) group. Patients initiated on warfarin alone (n = 42) were identified for the CONTROL group. The AMIO and CONTROL groups were matched based on age, gender, and ejection fraction <40% using propensity score matching (final n = 18 patients per group). Total and average daily warfarin dose was lower in the AMIO group, yet INR values were similar on each day between the 2 groups. More patients in the AMIO group had an INR greater than 2 during the 5-day observation period as compared to the CONTROL group. In addition, there were trends toward greater deviation from INR values expected with a 5-mg daily warfarin dose among AMIO group patients. Simultaneous initiation of warfarin and amiodarone leads to an enhanced pharmacodynamic response to warfarin early in therapy. Although these data should be viewed as hypothesis generating, cautious dosing and monitoring with simultaneous initiation of warfarin and amiodarone may be warranted.

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Pharmacy

Kalus, J. S. (2010). "Pharmacotherapeutic decision-making for patients with atrial fibrillation." Am J Health Syst Pharm **67**(9 Suppl 5): S17-25. [PDF Full-Text](#)

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PURPOSE: To discuss the therapeutic goals in patients with atrial fibrillation (AF); antithrombotic, rate-control, and rhythm-control medications used in these patients; rationale for choosing between rate-control and rhythm-control strategies; and safety, efficacy, and patient-specific considerations in choosing among established antiarrhythmic medications for these patients. **SUMMARY:** The three primary goals for patients with AF are prevention of thromboembolic stroke, heart rate control, and rhythm control. Warfarin is more effective than aspirin for stroke prevention in patients with AF, and it is recommended for patients at high risk for stroke. However, warfarin is underused, especially in elderly patients. Diltiazem, verapamil, beta-blockers, digoxin, and amiodarone may be used for rate control; the choice among these agents is based on the patient's blood pressure and the presence of certain underlying diseases. Rhythm-control strategies for patients with AF offer no advantage over rate-control strategies in terms of mortality or quality of life, and they are associated with a higher rate of hospitalization. Exercise tolerance is greater with rhythm control, however. The choice among antiarrhythmic agents for maintenance of sinus rhythm after cardioversion is based on safety, efficacy, and the presence of underlying structural heart disease (e.g., heart failure, coronary artery

disease, hypertension with or without left ventricular hypertrophy) and renal impairment. **CONCLUSION:** Careful consideration of patient-specific characteristics and the differences in safety and efficacy among antithrombotic, rate-control, and rhythm-control medications is needed to optimize treatment of and outcomes in patients with AF.

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Pharmacy

Toth, N. R., R. M. Chambers and S. L. Davis (2010). "Implementation of a care bundle for antimicrobial stewardship." *American Journal of Health-System Pharmacy* **67**(9): 746-749.

[PDF Full-Text](#)

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Purpose. The impact of an antibiotic-use care bundle on compliance with quality indicators was evaluated. **Methods.** Patients admitted to the internal medicine or surgery floor of a tertiary care center who were receiving an antipseudomonal beta-lactam, vancomycin, a fluoroquinolone, linezolid, an aminoglycoside, or any combination of these agents were included in the study. The study consisted of two phases: intervention (when a stewardship pharmacist was involved in patient care) and control (when no stewardship pharmacist was involved). The stewardship pharmacist completed interventions via prospective audit and suggested changes to empirical and definitive antimicrobials, monitored patients' cultures and antimicrobial therapy daily, and provided education on the institution's antibiogram. The primary outcome measured was compliance with the care bundle's quality indicators, which included documentation of treatment rationale, collection of appropriate culture specimens according to institutional and national guidelines, appropriate empirical selection of antibiotics according to institutional and national guidelines at initiation of antibiotic therapy and deescalation, and selection of appropriate agents for definitive therapy during antimicrobial therapy. **Results.** A total of 160 patients and 442 antibiotic orders were evaluated. During the intervention phase, 168 interventions were made, with an acceptance rate of 91%. The rate of appropriate deescalation rose from 72% to 90% ($p = 0.01$). Compliance with all quality indicators rose from 16% to 43% ($p < 0.001$). **Conclusion.** Implementation of an antimicrobial stewardship program care bundle on two patient care units was associated with improved rates of compliance with quality indicators.

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Radiation Oncology

Ali, M. M., B. Janic, A. Babajani-Feremi, N. R. Varma, A. S. Iskander, J. Anagli and A. S. Arbab (2010). "Changes in vascular permeability and expression of different angiogenic factors following anti-angiogenic treatment in rat glioma." *PLoS One* **5**(1): e8727. 2806917.

[PDF Full-Text](#)

Cellular and Molecular Imaging Laboratory, Department of Radiology, Henry Ford Hospital, Detroit, Michigan, United States of America.

BACKGROUND: Anti-angiogenic treatments of malignant tumors targeting vascular endothelial growth factor receptors (VEGFR) tyrosine kinase are being used in different early stages of clinical trials. Very recently, VEGFR tyrosine kinase inhibitor (Vetanalib, PTK787) was used in glioma patient in conjunction with chemotherapy and radiotherapy. However, changes in the tumor size, tumor vascular permeability, vascular density, expression of VEGFR2 and other angiogenic factors in response to PTK787 are not well documented. This study was to determine the changes in tumor size, vascular permeability, fractional plasma volume and expression of VEGFR2 in PTK787 treated U-251 glioma rat model by in vivo magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT). The findings were validated with histochemical and western blot studies. **METHODOLOGIES AND PRINCIPAL FINDINGS:** Seven days after implantation of U251 glioma cells, animals were treated with either PTK787 or vehicle-only for two weeks, and then tumor size, tumor vascular permeability transfer constant ($K(\text{trans})$), fractional plasma volume (fPV) and expression of VEGFR2 and other relevant angiogenic factors were assessed by in vivo MRI and SPECT (Tc-99m-HYNIC-VEGF), and by immunohistochemistry and western blot analysis. Dynamic contrast-enhanced MRI (DCE-MRI) using a high molecular weight contrast agent albumin-(GdDTPA) showed significantly increased

K(trans) at the rim of the treated tumors compared to that of the central part of the treated as well as the untreated (vehicle treated) tumors. Size of the tumors was also increased in the treated group. Expression of VEGFR2 detected by Tc-99m-HYNIC-VEGF SPECT also showed significantly increased activity in the treated tumors. In PTK787-treated tumors, histological staining revealed increase in microvessel density in the close proximity to the tumor border. Western blot analysis indicated increased expression of VEGF, SDF-1, HIF-1alpha, VEGFR2, VEGFR3 and EGFR at the peripheral part of the treated tumors compared to that of central part of the treated tumors. Similar expression patterns were not observed in vehicle treated tumors. CONCLUSION: These findings indicate that PTK787 treatment induced over expression of VEGF as well as the Flk-1/VEGFR2 receptor tyrosine kinase, especially at the rim of the tumor, as proven by DCE-MRI, SPECT imaging, immunohistochemistry and western blot.

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Radiation Oncology

Al-Mallah, M. H., A. Sitek, S. C. Moore, M. Di Carli and S. Dorbala (2010). "Assessment of myocardial perfusion and function with PET and PET/CT." Journal of Nuclear Cardiology **17(3)**: 498-513. [PDF Full-Text](#)

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Radiation Oncology

Blankstein, R., M. K. Murphy, K. Nasir, G. S. Gazelle, J. C. Batlle, M. Al-Mallah, L. Shturman, U. Hoffmann, R. C. Cury, S. Abbara, T. J. Brady and T. H. Lee (2010). "Perceived Usefulness of Cardiac Computed Tomography as Assessed by Referring Physicians and Its Effect on Patient Management." American Journal of Cardiology **105(9)**: 1246-1253. [PDF Full-Text](#)

[Blankstein, Ron; Shturman, Leon; Hoffmann, Udo; Cury, Ricardo C.; Abbara, Suhny; Brady, Thomas J.] Massachusetts Gen Hosp, Cardiac MR PET CT Program, Dept Radiol, Boston, MA 02114 USA. [Blankstein, Ron; Shturman, Leon; Hoffmann, Udo; Cury, Ricardo C.; Abbara, Suhny; Brady, Thomas J.] Massachusetts Gen Hosp, Div Cardiol, Boston, MA 02114 USA. [Murphy, Meagan K.] Massachusetts Gen Hosp, Dept Med, Boston, MA 02114 USA. [Gazelle, G. Scott; Batlle, Juan C.] Massachusetts Gen Hosp, Dept Radiol, Boston, MA 02114 USA. [Gazelle, G. Scott] Massachusetts Gen Hosp, Inst Technol Assessment, Boston, MA 02114 USA. [Blankstein, Ron] Brigham & Womens Hosp, Dept Med & Radiol, Noninvas Cardiovasc Imaging Program, Boston, MA 02115 USA. [Nasir, Khurram] Johns Hopkins Univ, Ciccarone Prevent Cardiol Ctr, Baltimore, MD USA. [Al-Mallah, Mouaz] Henry Ford Hosp, Detroit, MI 48202 USA. [Cury, Ricardo C.] Baptist Cardiac & Vasc Inst, Miami, FL USA. [Lee, Thomas H.] Partners HealthCare, Boston, MA USA. Blankstein, R, Massachusetts Gen Hosp, Cardiac MR PET CT Program, Dept Radiol, Boston, MA 02114 USA. rblankstein@partners.org

Despite the growing use of computed tomographic angiography (CTA), the effect on patient management is less clear. We sought to determine the perceived usefulness of the results provided by CTA and to assess whether and how it influences patient management. Comprehensive prospective data were collected from 184 consecutive patients who presented for clinical CTA for the evaluation of coronary artery disease from March to July 2008. In addition, a detailed survey was sent to each referring physician for each patient examined to assess whether they found the results of the CTA useful and whether it had any influence on subsequent patient management. Of 184 CTA examinations, which had been ordered by 82 different providers, 108 surveys (59%) were completed by 53 different physicians. No significant differences were found in either the patient or provider characteristics for the completed versus noncompleted surveys. Of the 184 CTA examinations, the severity of coronary disease detected by CTA was severe for 26%, mild to moderate in 47%, and not present in 27% of the patients. Clinicians considered the test results to be useful in virtually all cases and thought the results led to significant risk reclassification in 58% of the patients. If CTA had not been available, the clinicians indicated that they would have ordered an invasive test for 46% of the patients and noninvasive tests for 32%. After CTA, changes in medical therapies were made for 31%, invasive angiography

was planned for 19%, and noninvasive testing was scheduled for 6% of the patients. In conclusion, of 53 different referring clinicians from different medical specialties, CTA was considered to almost always be useful; however, the effect on subsequent medical management was more variable. (C) 2010 Elsevier Inc. All rights reserved. (Am J Cardiol 2010;105:1246-1253)

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Radiation Oncology

Huang, Y., M. Joiner, B. Zhao, Y. Liao and J. Burmeister (2010). "Dose convolution filter: incorporating spatial dose information into tissue response modeling." Med Phys **37**(3): 1068-74. [Article Request Form](#)

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PURPOSE: A model is introduced to integrate biological factors such as cell migration and bystander effects into physical dose distributions, and to incorporate spatial dose information in plan analysis and optimization. **METHODS:** The model consists of a dose convolution filter (DCF) with single parameter sigma. Tissue response is calculated by an existing NTCP model with DCF-applied dose distribution as input. The authors determined sigma of rat spinal cord from published data. The authors also simulated the GRID technique, in which an open field is collimated into many pencil beams. **RESULTS:** After applying the DCF, the NTCP model successfully fits the rat spinal cord data with a predicted value of sigma = 2.6 +/- 0.5 mm, consistent with 2 mm migration distances of remyelinating cells. Moreover, it enables the appropriate prediction of a high relative seriality for spinal cord. The model also predicts the sparing of normal tissues by the GRID technique when the size of each pencil beam becomes comparable to sigma. **CONCLUSIONS:** The DCF model incorporates spatial dose information and offers an improved way to estimate tissue response from complex radiotherapy dose distributions. It does not alter the prediction of tissue response in large homogenous fields, but successfully predicts increased tissue tolerance in small or highly nonuniform fields.

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Radiation Oncology

Movsas, B., C. J. Langer, H. J. Ross, L. H. Wang, R. M. Jotte, S. Feigenberg, F. Xu, C. H. Huang, M. J. Monberg and C. K. Obasaju (2010). "Randomized Phase II Trial of Cisplatin, Etoposide, and Radiation Followed by Gemcitabine Alone or by Combined Gemcitabine and Docetaxel in Stage III A/B Unresectable Non-small Cell Lung Cancer." Journal of Thoracic Oncology **5**(5): 673-679. [PDF Full-Text](#)

[Movsas, Benjamin] Henry Ford Hlth Syst, Dept Radiat Oncol, Detroit, MI 48202 USA. [Langer, Corey J.] Univ Penn, Philadelphia, PA 19104 USA. [Ross, Helen J.] Mayo Clin, Scottsdale, AZ USA. [Wang, Luhua] Canc Hosp, Beijing, Peoples R China. [Wang, Luhua] Inst CAMS & PUMC, Beijing, Peoples R China. [Jotte, Robert M.] Rocky Mt Canc Ctr, Denver, CO USA. [Feigenberg, Steve] Fox Chase Canc Ctr, Philadelphia, PA 19111 USA. [Xu, Feng] Sichuan Univ, W China Hosp, Chengdu 610064, Sichuan, Peoples R China. [Huang, Chao H.] Kansas City VA Med Ctr, Kansas City, MO USA. [Monberg, Matthew J.; Obasaju, Coleman K.] Lilly USA, Indianapolis, IN USA.

Movsas, B, Henry Ford Hlth Syst, Dept Radiat Oncol, 2799 W Grand Blvd, Detroit, MI 48202 USA. bmovsas1@hfhs.org

Purpose: Southwest Oncology Group 9504 demonstrated the feasibility and potential benefit of docetaxel consolidation after etoposide, cisplatin, and radiotherapy in patients with locally advanced non-small cell lung cancer. Our study assessed consolidation with either gemcitabine alone or with docetaxel after identical chemoradiation as used in Southwest Oncology Group 9504. **Methods:** Patients with stage III non-small cell lung cancer and good performance status were included. Treatment consisted of concurrent cisplatin 50 mg/m² on days 1 and 8 plus etoposide 50 mg/m² on days 1 to 5 for two 28-day cycles plus radiotherapy (62 Gy, 2 Gy daily in 31 fractions over 7 weeks), followed by randomization to either gemcitabine 1000 mg/m² on days 1 and 8 (G) or gemcitabine 1000 mg/m² on days 1 and 8 plus docetaxel 75 mg/m² on day 1 (GD) every 21 days for three cycles. **Results:** Eighty-three patients were entered, 81 received induction therapy, and 64 were randomized (32 in each arm). Grade 3 or four events, including neutropenia (56.3% vs. 28.1%, p = 0.03), anemia (18.8% vs. 3.1%, p = 0.05), and fatigue (15.6% vs. 6.3%, p = NS), were more frequent with GD compared with G. Among all patients, median survival from registration was 20.8 months (95% confidence interval: 16.4-33.8), and 2-year survival was 46.7% (95% confidence interval: 35.6-57.1). From randomization, median progression-free survival was 5.4 months for G and 13.4 months for GD, and

median survival was 16.1 months for G and 29.5 months for GD. Two-year survival rates were 40.6% for G and 55.7% for GD. Conclusion: The doublet, as expected, resulted in more toxicity, particularly myelosuppression and fatigue. Survival associated with the GD treatment arm of this trial exceeds that of previously reported trials.

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Radiation Oncology

Siddiqui, F., K. Bae, C. J. Langer, J. C. Coyne, V. Gamerman, R. Komaki, H. Choy, W. J. Curran, D. Watkins-Bruner and B. Movsas (2010). "The influence of gender, race, and marital status on survival in lung cancer patients: analysis of Radiation Therapy Oncology Group trials." J Thorac Oncol **5**(5): 631-9. [PDF Full-Text](#)

Department of Radiation Oncology, Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202, USA.

OBJECTIVE: A meta-analysis was conducted to determine the influence of gender, race, and marital status on overall survival (OS) in Radiation Therapy Oncology Group nonoperative non-small cell lung cancer trials. **MATERIALS AND METHODS:** Data from 1365 patients treated on nine prospective Radiation Therapy Oncology Group studies activated during the 1990s were analyzed. Impact of gender, marital status, and race was considered in the Cox proportional hazards models. Age, Karnofsky performance status, weight loss, stage, histology, location of primary tumor, biologic equivalent dose, deviation from protocol dose, and education level were adjusted in the model. A two-sided p value <0.05 was considered statistically significant. **RESULTS:** Males had significantly higher mortality than females adjusted for other covariates (hazard ratio [HR] 1.22, 95% confidence interval 1.08 -1.38). Race and marital status were not independently predictive for OS. Single females had significantly better OS than single males (HR 0.72), and married males had lower OS than single females (HR 1.36). **CONCLUSIONS:** These results suggest that although certain subgroups of gender, race, and/or marital status have better outcomes with respect to OS; gender seems to be the most significant factor influencing survival results among nonoperative non-small cell lung cancer patients.

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Radiation Oncology

Zhong, H., J. Kim and I. J. Chetty (2010). "Analysis of deformable image registration accuracy using computational modeling." Med Phys **37**(3): 970-9. [Article Request Form](#)

Department of Radiation Oncology, Henry Ford Health System, Detroit, Michigan 48202, USA.
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Computer aided modeling of anatomic deformation, allowing various techniques and protocols in radiation therapy to be systematically verified and studied, has become increasingly attractive. In this study the potential issues in deformable image registration (DIR) were analyzed based on two numerical phantoms: One, a synthesized, low intensity gradient prostate image, and the other a lung patient's CT image data set. Each phantom was modeled with region-specific material parameters with its deformation solved using a finite element method. The resultant displacements were used to construct a benchmark to quantify the displacement errors of the Demons and B-Spline-based registrations. The results show that the accuracy of these registration algorithms depends on the chosen parameters, the selection of which is closely associated with the intensity gradients of the underlying images. For the Demons algorithm, both single resolution (SR) and multiresolution (MR) registrations required approximately 300 iterations to reach an accuracy of 1.4 mm mean error in the lung patient's CT image (and 0.7 mm mean error averaged in the lung only). For the low gradient prostate phantom, these algorithms (both SR and MR) required at least 1600 iterations to reduce their mean errors to 2 mm. For the B-Spline algorithms, best performance (mean errors of 1.9 mm for SR and 1.6 mm for MR, respectively) on the low gradient prostate was achieved using five grid nodes in each direction. Adding more grid nodes resulted in larger errors. For the lung patient's CT data set, the B-Spline registrations required ten grid nodes in each direction for highest accuracy (1.4 mm for SR and 1.5 mm for MR). The numbers of iterations or grid nodes required for optimal registrations depended on the intensity gradients of the underlying images. In summary, the performance of the Demons and B-Spline registrations have been quantitatively evaluated using numerical phantoms. The results show that parameter selection for optimal accuracy is closely related to the intensity gradients of the underlying images. Also, the result that the DIR algorithms produce much lower errors in heterogeneous lung regions relative to homogeneous (low intensity

gradient) regions, suggests that feature-based evaluation of deformable image registration accuracy must be viewed cautiously.

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Sleep Medicine

Roth, T., R. M. Benca and M. Erman (2010). "An introduction to the clinical correlates of disrupted slow-wave sleep." J Clin Psychiatry **71**(4): e09. [Article Request Form](#)

Department of Sleep Medicine, Henry Ford Hospital, Detroit, and Department of Psychiatry, University of Michigan College of Medicine, Ann Arbor, USA.

Chronic sleep deficits have been shown to lead to problems with cognition and memory, and evidence supports an association between deficits in slow-wave sleep and a variety of clinical and psychiatric disorders. Improving sleep architecture through an increase in slow-wave sleep, with or without increases in total time asleep, may lead to improvements in these associated disorders. Further research and the development of novel sleep therapies, both pharmacologic and nonpharmacologic, are needed.

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Sleep Medicine

Roth, T., G. Zammit, A. Lankford, D. Mayleben, T. Stern, V. Pitman, D. Clark and J. L. Werth (2010). "Nonrestorative sleep as a distinct component of insomnia." Sleep **33**(4): 449-58. 2849783. [PDF Full-Text](#)

Sleep Center, Henry Ford Hospital, 2799 W. Grand Blvd, Detroit, MI 48202, USA. roth1@hfhs.org

STUDY OBJECTIVES: Explore characteristics of nonrestorative sleep (NRS) in prospectively defined subgroups of individuals with NRS symptoms, investigate whether NRS can occur independently of difficulties initiating and maintaining sleep (DIS/DMS), and determine its effect on waking function. **DESIGN:** Cross-sectional and longitudinal population-based study comparing patterns of daytime symptoms, and their persistence, in cohorts of subjects with NRS symptoms grouped according to presence or absence of DIS and DMS. **SETTING:** 28 sleep centers in the US. **PARTICIPANTS:** Subjects reporting awakening unrestored or unrefreshed at least 3 times weekly over the previous 3 months were classified, based on self-reported sleep problems, to DIS (n = 138), DMS (n = 44), DIS+DMS (n = 125), and NRS-only (no DIS or DMS; n = 192) cohorts. Eighty healthy volunteers formed a control group. **INTERVENTIONS:** None. **MEASUREMENTS AND RESULTS:** Polysomnography confirmed DIS and/or DMS in 56/138 (41%), 18/44 (41%), and 37/125 (30%) subjects in DIS, DMS, and DIS+DMS cohorts, respectively; and absence of DIS or DMS in 115/192 (60%) NRS-only subjects and 52/80 (65%) healthy volunteers. Multiple subject-reported endpoints including the Endicott Work Productivity Scale, Pittsburgh Insomnia Rating Scale, Restorative Sleep Questionnaire, and SF-36, showed that NRS-only subjects had significantly impaired daytime function relative to healthy volunteers, comparable to impairment affecting subjects with DIS and/or DMS. Symptoms persisted over 3 months. **CONCLUSIONS:** This study confirms that NRS can occur independently of other components of insomnia. Daytime symptoms were as severe in individuals with NRS-only as those whose NRS symptoms were combined with DIS or DMS.

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Surgery

Abou Abbass, A., M. Abouljoud, T. Getzen, A. Yoshida, J. Hundley, M. Kazimi, R. Slater, V. Patil and D. Y. Kim (2010). "Portal Vein Thrombosis (PVT) after Splenectomy in a Liver Transplant(LT) Patient." American Journal of Transplantation **10**: 66-66. [Article Request Form](#)

[Abou Abbass, Ahmad; Abouljoud, Marwan; Getzen, Todd; Yoshida, Atsushi; Hundley, Jonathon; Kazimi, Marwan; Slater, Robert; Patil, Vrishali; Kim, Dean Y.] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Abouljoud, M. S., M. M. Elatrache, A. Yoshida, D. Y. Kim, J. C. Hundley and M. M. Kazimi (2010). "Recurrence of Non-Alcoholic Steato-Hepatitis (NASH) and Cryptogenic Cirrhosis (CC) Following Liver Transplantation (LT) in the Context of Metabolic Syndrome." American Journal of Transplantation **10**: 67-67. [Article Request Form](#)

[Abouljoud, Marwan S.; Elatrache, Mazen M.; Yoshida, Atsushi; Kim, Dean Y.; Hundley, Jonathan C.; Kazimi, Marwan M.] Henry Ford Hlth Syst, Transplant Inst, Detroit, MI USA.

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Surgery

Cheaito, A. and M. Abouljoud (2010). "Effect of RFA and Tace on Recurrence of HCC after Liver Transplantation." American Journal of Transplantation **10**: 59-59. [Article Request Form](#)

[Cheaito, Ali; Abouljoud, Marwan] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Cheaito, A. and M. Abouljoud (2010). "Impact of Preoperative Tumor Volume and Staging of HCC on Transplant Outcomes." American Journal of Transplantation **10**: 68-68. [Article Request Form](#)

[Cheaito, Ali; Abouljoud, Marwan] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Filliung, D. R. and L. M. Bower (2010). "Medical-surgical nursing at the 86th Combat Support Hospital (2007-2009) in support of Operation Iraqi Freedom: caring for host nation patients." Mil Med **175**(5): 301-4. [Article Request Form](#)

Henry Ford Hospital, Division of Vascular Surgery (K8), 2799 W. Grand Avenue, Detroit, MI 48202, USA.

A descriptive study of the patients admitted to the host nation intermediate care ward (ICW) of the 86th Combat Support Hospital in Baghdad, Iraq was performed. A retrospective chart review was conducted of the patients admitted to the host nation ward between June 2 and September 5, 2008. One hundred and forty host nation patients were included in the study. Patient demographics, origin of admission, length of stay, and disposition of patient are reported. The types of illnesses and injuries most commonly seen as well as the most common surgical procedures are also reported. This study details the nursing care provided to host nation armed forces and civilians during a 3-month period of the deployment of the 86th CSH in Baghdad, Iraq. Information gained from this study is important for predeployment training and readiness of nurses preparing to deploy to Iraq.

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Surgery

Kim, D. Y., M. Goggins, A. B. Eisenbrey, S. Skorupski, L. Malinzak, J. Denny, A. Yoshida, A. Abou Abbass, V. Patil, R. Slater, J. Hundley, M. Kazimi and M. Abouljoud (2010). "Deceased Donor Kidney Transplantation (DDT) without Prospective Crossmatch (PC)." American Journal of Transplantation **10**: 62-62. [Article Request Form](#)

[Kim, Dean Y.; Goggins, Mariella; Eisenbrey, A. B.; Skorupski, Sharon; Malinzak, Lauren; Denny, Jason; Yoshida, Atsushi; Abou Abbass, Ahmad; Patil, Vrishali; Slater, Robert; Hundley, Jonathan; Kazimi, Marwan; Abouljoud, Marwan] Henry Ford Hosp, Transplant Inst, Detroit, MI 48202 USA.

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Surgery

Slater, R. R., A. Abou Abbass, V. Patil, J. Hundley, M. Kazimi, D. Kim, A. Yoshida and M. Abouljoud (2010). "Splenic Vein Siphon: An Under-Recognized Cause of Low Portal Flow in Liver Transplant (OLT)." American Journal of Transplantation **10**: 73-73. [Article Request Form](#)

[Slater, Robert R.; Abou Abbass, Ahmad; Patil, Vrishali; Hundley, Jonathan; Kazimi, Marwan; Kim, Dean; Yoshida, Atsushi; Abouljoud, Marwan] Henry Ford Hosp, Detroit, MI 48202 USA.

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Surgery

Slater, R. R., F. Mossa-basha, M. Abouljoud, E. Peterson, A. Yoshida, J. Hundley, M. Kazimi, A. Abou Abbass, V. Patil and D. Y. Kim (2010). "Post-Operative Hernias after Liver Transplant (OLT) with the Use of Sirolimus." American Journal of Transplantation **10**: 73-73. [Article Request Form](#)

[Slater, Robert R.; Abouljoud, Marwan; Peterson, Ed; Yoshida, Atsushi; Hundley, Jonathan; Kazimi, Marwan; Abou Abbass, Ahmad; Patil, Vrishali; Kim, Dean Y.] Henry Ford Hosp, Detroit, MI 48202 USA. [Mossa-basha, Feras] Wayne State Univ, Sch Med, Detroit, MI USA.

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Surgery

Slater, R. R., F. Mossa-Basha, E. Peterson, A. Abou Abbass, V. Patil, J. Hundley, M. Kazimi, D. Y. Kim, M. Abouljoud and A. Yoshida (2010). "Outcomes of Non-Liver Related Surgical Procedures (NLRSP) after Liver Transplant (OLT)." American Journal of Transplantation **10**: 73-73. [Article Request Form](#)

[Slater, Robert R.; Peterson, Ed; Abou Abbass, Ahmad; Patil, Vrishali; Hundley, Jonathan; Kazimi, Marwan; Kim, Dean Y.; Abouljoud, Marwan; Yoshida, Atsushi] Henry Ford Hosp, Detroit, MI 48202 USA. [Mossa-Basha, Feras] Wayne State Univ, Sch Med, Detroit, MI USA.

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Surgery

Vassiliou, M. C., P. A. Kaneva, B. K. Poulouse, B. J. Dunkin, J. M. Marks, R. Sadik, G. Sroka, M. Anvari, K. Thaler, G. L. Adrales, J. W. Hazey, J. R. Lightdale, V. Velanovich, L. L. Swanstrom, J. D. Mellinger and G. M. Fried (2010). "How should we establish the clinical case numbers required to achieve proficiency in flexible endoscopy?" American Journal of Surgery **199**(1): 121-125. [PDF Full-Text](#)

[Vassiliou, Melina C.; Kaneva, Pepa A.; Sroka, Gideon; Fried, Gerald M.] McGill Univ, Ctr Hlth, Montreal Gen Hosp, Montreal, PQ H3G 1A4, Canada. [Poulouse, Benjamin K.] Vanderbilt Univ, Nashville, TN USA. [Dunkin, Brian J.] Methodist Hosp, Houston, TX 77030 USA. [Marks, Jeffrey M.] Case Med Ctr, Cleveland, OH USA. [Sadik, Riadh] Sahlgrens Univ Hosp, Gothenburg, Sweden. [Anvari, Mehran] McMaster Univ, Hamilton, ON, Canada. [Thaler, Klaus] Univ Missouri, Columbia, MO USA. [Adrales, Gina L.] Dartmouth Hitchcock Med Ctr, Lebanon, NH 03766 USA. [Hazey, Jeffrey W.] Ohio State Univ, Columbus, OH 43210 USA. [Lightdale, Jenifer R.] Childrens Hosp Boston, Boston, MA USA. [Velanovich, Vic] Henry Ford, Detroit, MI USA. [Swanstrom, Lee L.] Legacy Hlth, Portland, OR USA. [Mellinger, John D.] Med Coll Georgia, Augusta, GA 30912 USA. Vassiliou, MC, McGill Univ, Ctr Hlth, Montreal Gen Hosp, 1650 Cedar Ave, L9-518, Montreal, PQ H3G 1A4, Canada. melina.vassiliou@mcgill.ca

BACKGROUND: Recommended procedure numbers for upper endoscopy (UE) and colonoscopy (C) are 35 and 50 for surgical residents, and 130 and 140 for gastroenterology fellows, respectively. The purpose of this study was to challenge the methods used to determine proficiency in flexible endoscopy. METHODS: Global assessment of gastrointestinal endoscopic skills (GAGES) was used to evaluate 139 procedures. Scores for UE were compared using self-reported case numbers and grouped according to requirements for each discipline. C scores were compared using the requirements to define novice and experienced endoscopists. Procedure volumes were plotted against GAGES scores. RESULTS: Three groups were compared for UE

based on case volumes: fewer than 35 cases (group 1), 35 to 130 cases (group 2), and more than 130 cases (group 3). There was no difference between group 2 (17.8 +/- 1.8) and group 3 (19.1 +/- 1.1), but both scored higher than group 1 (14.4 +/- 3.7; $P < .05$). For C, the scores were 11.8 +/- 3.8 (novices) and 18.8 +/- 1.34 (experienced; $P < .001$) at a 50-case minimum and 12.4 +/- 4.2 and 18.8 +/- 1.3 ($P < .001$) for a 140-case proficiency cut-off level, respectively. The curve of procedures versus GAGES plateaued at 50 (UE) and 75 (C). **CONCLUSIONS:** The surgical and gastroenterology case recommendations may not represent the experience needed to achieve proficiency. GAGES scores could help define proficiency in basic endoscopy. (C) 2010 Elsevier Inc. All rights reserved.

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Urology

Nguyen, H. T., R. S. Hurwitz, W. R. Defoor, E. Minevich, A. J. McAdam, J. E. Mortensen, S. M. Novak-Weekley, B. J. Minnillo and J. S. Elder (2010). "Trimethoprim In Vitro Antibacterial Activity is Not Increased by Adding Sulfamethoxazole for Pediatric Escherichia coli Urinary Tract Infection." J Urol Epub Ahead of Print. [PDF Full-Text](#)

Vattikuti Urology Institute, Henry Ford Health System, Department of Urology, Children's Hospital of Michigan, Detroit, Michigan.

PURPOSE: The combination of trimethoprim/sulfamethoxazole is often used to treat uncomplicated urinary tract infections in children. The rationale for combining trimethoprim and sulfamethoxazole is that they may act synergistically to increase antibacterial activity. However, approximately 3% of patients show allergic reactions to sulfamethoxazole, of which some are serious (liver failure and Stevens-Johnson syndrome). We determined whether adding sulfamethoxazole is necessary to increase in vitro antibacterial activity for pediatric urinary tract infection compared to that of trimethoprim alone. **MATERIALS AND METHODS:** We prospectively identified 1,298 children with urinary tract infection (greater than 100,000 cfu/ml Escherichia coli) from a total of 4 American regions. In vitro susceptibility of bacterial isolates to sulfamethoxazole, trimethoprim and trimethoprim/sulfamethoxazole was determined using disk diffusion. Ampicillin susceptibility was tested at 2 sites. At 1 site all uropathogens from consecutive urinary isolates were evaluated. **RESULTS:** E. coli susceptibility to trimethoprim was 70%, comparable to the 70% of trimethoprim/sulfamethoxazole ($p = 0.9$) and higher than the 56.9% of sulfamethoxazole ($p < 0.05$). This susceptibility pattern was without regional differences. At 2 sites susceptibility to trimethoprim was significantly higher than to ampicillin. At 1 site the susceptibility of other uropathogens to trimethoprim and trimethoprim/sulfamethoxazole was similar to that of E. coli. **CONCLUSIONS:** In children with urinary tract infection in vitro susceptibility to trimethoprim was comparable to that to trimethoprim/sulfamethoxazole and significantly higher than to sulfamethoxazole. This finding was similar at all sites. Adding sulfamethoxazole appears unnecessary and may represent a risk to patients. Trimethoprim can be used as an alternative to trimethoprim/sulfamethoxazole based on in vitro antibacterial susceptibility. Routine trimethoprim/sulfamethoxazole use for urinary tract infection should be carefully reevaluated.

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Urology

Sarveswaran, S., J. Liroff, Z. X. Zhou, A. Y. Nikitin and J. Ghosh (2010). "Selenite triggers rapid transcriptional activation of p53, and p53-mediated apoptosis in prostate cancer cells: Implication for the treatment of early-stage prostate cancer." International Journal of Oncology **36**(6): 1419-1428. [Article Request Form](#)

[Sarveswaran, Sivalokanathan; Liroff, Joshua; Ghosh, Jagadananda] Henry Ford Hlth Syst, Dept Urol, Vattikuti Urol Inst, Detroit, MI 48202 USA. [Zhou, Zongxiang; Nikitin, Alexander Yu.] Cornell Univ, Dept Biomed Sci, Ithaca, NY 14853 USA.

Ghosh, J, Henry Ford Hlth Syst, Dept Urol, Vattikuti Urol Inst, 1 Ford Pl, Detroit, MI 48202 USA.

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Supra-nutritional selenium supplementation has emerged as an attractive new approach to intervene in a range of human cancers, in particular prostate cancer. However, scanty information is currently available on molecular mechanisms underlying selenium's anticancer action. The tumor suppressor p53 plays an important role in preventing transformation by transcriptional regulation of a range of genes that are involved in vital cell functions such as DNA repair, cell cycle arrest, and induction of apoptosis. Here we report that incubation of LNCaP human prostate cancer cells (p53 +/-) with a natural form of selenium triggers rapid transcriptional

activation of p53, and up-regulation of the expression of p53-target genes as well as induction of miR-34 class of microRNAs. Moreover, blocking p53 function by transfection of cells with a dominant-negative, mutated p53 gene, or by siRNA, significantly reduced selenium-induced expression of p53-target genes and induction of apoptosis. Since majority of the early-stage human prostate cancers bear functional p53 gene (P53+/+) our findings indicate that the anticancer action of selenium may involve transactivation of p53 as a potential mechanism, and suggest that selenite may be useful not only for prevention but also for treatment of human prostate cancer.

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Urology

Sarveswaran, S., C. E. Myers and J. Ghosh (2010). "MK591, a leukotriene biosynthesis inhibitor, induces apoptosis in prostate cancer cells: Synergistic action with LY294002, an inhibitor of phosphatidylinositol 3'-kinase." Cancer Letters **291**(2): 167-176. [Article Request Form](#)

[Sarveswaran, Sivalokanathan; Ghosh, Jagadananda] Henry Ford Hlth Syst, Vattikuti Urol Inst, Detroit, MI 48202 USA. [Myers, Charles E.] Amer Inst Dis Prostate, Charlottesville, VA USA.

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MK591 is a synthetic compound which specifically inhibits the activity of 5-Lox and is currently under development for the treatment of asthma. We observed that human prostate cancer cells treated with MK591 undergo apoptosis within hours of treatment. Apoptosis involves severe morphological alteration, externalization of phosphatidyl-serine, cleavage of PARP, and degradation of chromatin-DNA. MK591 also induced rapid activation of the stress kinase, c-Jun N-terminal kinase (JNK), which plays an important role in the apoptosis process. The phosphatidylinositol 3'-kinase-Akt/protein kinase B (PI3K/Akt) axis is a well-known pro-survival pathway which prevents apoptosis through defined anti-apoptotic mechanisms in a variety of cancer cells. Interestingly, we observed that MK591 triggers apoptosis in prostate cancer cells without inhibition of PI3K-Akt, or ERK. Moreover, it was observed that MK591 and LY294002 (an inhibitor of PI3K) exert synergistic effect in inducing apoptosis in prostate cancer cells. Altogether, these findings indicate that 5-Lox inhibition-induced apoptosis in prostate cancer cells occurs without inhibition of PI3K-Akt, or ERK, and suggest for the existence of an Akt- and ERK-independent survival mechanism(s) in these cancer cells maintained via signals generated by metabolites of 5-Lox. (C) 2009 Elsevier Ireland Ltd. All rights reserved.

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Urology

Siddiqui, S. A., L. S. Krane, A. Bhandari, M. N. Patel, C. G. Rogers, H. Stricker, J. O. Peabody and M. Menon (2010). "The Impact of Previous Inguinal or Abdominal Surgery on Outcomes After Robotic Radical Prostatectomy." Urology **75**(5): 1079-1082. [PDF Full-Text](#)

[Siddiqui, Sameer A.; Krane, Louis S.; Bhandari, Akshay; Patel, Manish N.; Rogers, Craig G.; Stricker, Hans; Peabody, James O.; Menon, Mani] Henry Ford Hosp, Vattikuti Urol Inst, Detroit, MI 48202 USA.

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OBJECTIVES To evaluate our experience with robotic radical prostatectomy (RRP) in the setting of previous inguinal or abdominal surgery. **METHODS** From a prospective cohort of 3950 consecutive patients who underwent transperitoneal RRP between September 2001 and September 2008, we identified 1049 (27%) patients with a history of abdominal or inguinal surgery. Demographic data including body mass index, age at the time of surgery, serum prostate-specific antigen, and clinical stage were prospectively recorded. Clinical endpoints measured included estimated blood loss (EBL), console time, total operative time, and perioperative complications. Degree of adhesiolysis at the time of surgery was graded into minor, moderate, or large. **RESULTS** In comparing patients with previous abdominal or inguinal surgery with no surgery, there were no differences in EBL (150 vs 151 mL, $P = .79$), total operative time (158 minutes v second 155 minutes, $P = .15$), body mass index (27.8 vs 27.4, $P = .2$), preoperative prostate-specific antigen (6.1 vs 6.3, $P = .07$) and clinical stage ($P = .71$). A total of 243 (24%) of patients with previous surgery required adhesiolysis vs 246 (8%) of patients with no previous surgery ($P < .001$). Appendectomy was the most common previous surgery identified (11%). Patients with a previous history of colectomy had the highest incidence of adhesiolysis (72%). A total of 5 bowel injuries were recorded in the cohort of 3950 patients; of these 3 patients had a history of prior abdominal surgery. **CONCLUSIONS** Previous abdominal or inguinal surgery is not a contraindication to RRP.

The majority of these patients can have their procedure safely performed without an increased risk of complications. UROLOGY 75: 1079-1082, 2010. (C) 2010 Elsevier Inc.

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Urology

Sivanandam, A., S. Murthy, S. H. Kim, E. R. Barrack and G. P. Veer Reddy (2010). "Role of Androgen Receptor in Prostate Cancer Cell Cycle Regulation: Interaction with Cell Cycle Regulatory Proteins and Enzymes of DNA Synthesis." Curr Protein Pept Sci **Epub Ahead of Print**. [Article Request Form](#)

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The androgen receptor (AR) plays a critical role in proliferation and viability of prostate cancer cells. Therefore, suppressing AR activity by androgen deprivation or anti-androgen treatment has been the frontline therapy for over six decades. However, these treatment strategies are not curative and patients succumb to castration-resistant disease. Although AR is evidently critical for proliferation of prostate cancer cells, very little is known about its mechanism of action in this process. Over the years, the role of AR in prostate cancer cell proliferation and viability has been studied by focusing primarily on its role as a transcription factor. However, recent observations indicate that besides its role as a transcription factor, AR interacts physically with components of the pre-replication complex (pre-RC) and DNA replication machinery (replisome). These interactions may enable AR to exert control over the process of DNA synthesis. In addition, alterations in the proteins that interact with AR in complexes required for DNA synthesis could lead to the development of hormone-refractory prostate cancer. These observations suggest a paradigm shift for the role of AR in proliferation of prostate cancer cells from its role as a transcription factor to a non-transcriptional role as a component of the replication machinery, interacting with cell cycle regulatory proteins and enzymes of DNA synthesis. We propose that a detailed understanding of the structural interactions between AR and the components of pre-RC and replisome may lead to the development of new strategies for the treatment of prostate cancer.

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