

Henry Ford Health System Publication List May 2009

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

Allergy & Immunology

Misiak, R. T., G. Wegienka, S. Havstad, D. R. Ownby, C. C. Johnson and E. M. Zoratti (2009). "Specific allergic sensitization in parents and their 18-year-old offspring in the Suburban Detroit Childhood Allergy Study." J Allergy Clin Immunol **123**(6): 1401-6 e2. [PDF Full-Text](#)

Department of Internal Medicine, Division of Allergy, Henry Ford Hospital, Henry Ford Health System, Detroit, MI 48202, USA. rmisiak1@hfhs.org

BACKGROUND: Allergic sensitization is increased among offspring of sensitized parents. OBJECTIVE: We sought to evaluate whether 18-year-old offspring are likely to have the same allergic sensitizations as their parents. METHODS: Eighteen-year-old participants in an unselected birth cohort and their parents were tested for total and increased (>0.35 kU/L) levels of allergen-specific IgE to 6 allergens: Dermatophagoides farinae, dog, cat, grass, ragweed, and Alternaria alternata. RESULTS: In 316 parent-teen triads parental sensitization to any of 6 allergens was associated with teen sensitization to any of those same allergens. An increased risk of matched sensitization (ie, a teen has an increased risk of being sensitized to the same specific allergen as their parent) was found after adjusting for the spouse's sensitivities and adjusting for other allergens (ie, the parent had an allergic sensitization but not to the particular allergen under analysis). Risk of maternal matched sensitization with their teen to cat (adjusted odds ratio [aOR], 2.1; 95% CI, 1.0-4.5), grass (aOR, 2.5; 95% CI, 1.2-5.2), and A alternata (aOR, 2.4; 95% CI, 1.1-5.5) was increased when compared with that seen in teens without parental allergen-specific sensitization. Similarly, a higher than expected risk of paternal matched sensitization with their teen to dog (aOR, 2.7; 95% CI, 1.3-5.9), D farinae (aOR, 2.7; 95% CI, 1.4-5.1), and grass (aOR, 2.7; 95% CI, 1.5-5.9) was observed. CONCLUSION: Parental allergen-specific IgE increases the likelihood of sensitization to the same allergen in young adult offspring.

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Biostatistics & Research Epidemiology

Cassidy-Bushrow, A. E., R. Krajenta, G. S. Richardson and D. Hudgel (2009). "Neighborhood-Level Deprivation Does Not Explain the Association of African-American Ethnicity with Sleep Apnea Severity." Sleep **32**: 0678. [Article Request Form](#)

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Hours
8:30am-7:30pm M-Th
8:30am-5:00pm F

Biostatistics & Research Epidemiology

Moore, K. M., S. Andrade, A. Cassidy-Bushrow, S. Dublin, R. Greenlee, C. Nakasato, R. Platt, M. M. Raebel, C. Rolnick, D. H. Smith and J. S. Brown (2009). "Variation in Icd-9 Diagnosis Coding within and across Health Systems." Value in Health **12**(3): A24-A24. [PDF Full-Text](#) (Scroll down to page A24)

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Biostatistics & Research Epidemiology

Stern, L., L. Lamerato, A. Ogbonnaya, S. H. Ong, V. C. Munk and A. Charney (2009). "Use of Renin System Agents among Hypertension Patients with Renal Disease in a Managed Care Setting." Value in Health **12**(3): A161-A161. [PDF Full-Text](#) (Scroll down to page 161)

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Bone & Joint Center

Vaidya, R., J. Carp, S. Bartol, N. Ouellette, S. Lee and A. Sethi (2009). "Lumbar Spine Fusion in Obese and Morbidly Obese Patients." Spine **34**(5): 495-500. [PDF Full-Text](#)

Study Design. Single-center retrospective study. Objective. The aim of the study was to compare the surgical experience, clinical outcomes, and effect on body weight between obese and morbidly obese patients undergoing lumbar spine fusion surgery. Summary of Background Data. Obese and morbidly obese patients undergoing spinal fusion surgery are a challenge to the operating surgeon. Only few reports are available on the perioperative data in this group of patients. Further, it is unknown if the degree of obesity has an effect on the surgical experience and clinical outcomes including body weight. Methods. A retrospective study of 63 patients undergoing lumbar spinal fusion was carried out. The main inclusion criteria were a body mass index (BMI) equal to or greater than 30. Information recorded included surgical set-up time, surgical time, blood loss, American Association of Anesthesiologists score, and surgical complications. At follow-up, the Oswestry Disability Index and visual analog scale for back and leg pain were recorded along with a pain diagram and radiographic evaluation. Results. The obese group had lower American Association of Anesthesiologists scores. The surgical time was dependent on the number of levels fused and was independent of the BMI. Blood loss during surgery was marginally greater in the obese patients. Neither group showed significant change in weight and BMI. Clinical outcomes showed improvement in visual analog scale for back and leg pain with some improvement in Oswestry scores and were independent of the BMI of the patient. The incidence of postoperative complications was significant in 45% of morbidly obese and 44% of obese patients. Conclusion. Obese and morbidly obese patients have multiple comorbidities, and the spinal surgeon should be prepared to encounter perioperative complexities. Operative times are longer in comparison with normal weight patients with a higher incidence of postoperative complications. No weight loss occurs after spinal surgery.

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Cardiology

Al-Mallah, M. H., H. Hatahet, J. L. Cavalcante and S. Khanal (2009). "Low admission LDL-cholesterol is associated with increased 3-year all-cause mortality in patients with non ST segment elevation myocardial infarction." Cardiol J **16**(3): 227-33. [Article Request Form](#)

Division of Cardiology, Henry Ford Heart and Vascular Institute, Detroit, MI 48202, USA.
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BACKGROUND: The relationship between admission low-density lipoprotein (LDL) levels and long-term outcomes has not been established in patients with acute coronary syndrome. We tested the hypothesis that patients who develop non-ST segment elevation myocardial infarction (NSTEMI) despite low LDL have a worse cardiovascular outcome in the long term. METHODS: Patients admitted with NSTEMI between 1 January 1997 and 31 December 2000 and with fasting lipid profiles measured within 24 hours of admission were selected for analysis. Baseline characteristics and 3-year all-cause mortality were compared between the patients with LDL above and below the median. Multivariate analysis was used to determine the predictors of all-cause mortality, and adjusted survival was analyzed using the Cox proportional hazard model. RESULTS: Of the total of 517 patients, 264 had LDL \leq 105 mg/dL and 253 had LDL > 105 mg/dL. There was no difference in age, gender, severity of coronary artery disease, and left ventricular ejection fraction between the

2 groups. Thirty-six percent of patients with LDL \leq 105 mg/dL and 24% of patients with LDL $>$ 105 mg/dL were on lipid-lowering therapy on admission. After 3 years, patients with admission LDL \leq 105 mg/dL had higher all-cause mortality rate compared to patients with LDL $>$ 105 mg/dL (14.8% vs. 7.1%, $p = 0.005$). The higher all-cause mortality persisted (OR 1.8, 95% CI 1.0-3.5, $p = 0.05$) even after adjustment for confounding variables. **CONCLUSIONS:** In our cohort, lower LDL-cholesterol at admission was associated with decreased 3-year survival in patients with NSTEMI. Whether this was a result of current therapy or a marker for worse baseline characteristics needs to be studied further.

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Cardiology

Armstrong, P. W., Y. L. Fu, C. M. Westerhout, M. P. Hudson, K. W. Mahaffey, H. D. White, T. G. Todaro, P. X. Adams, P. E. G. Aylward and C. B. Granger (2009). "Baseline Q-Wave Surpasses Time From Symptom Onset as a Prognostic Marker in ST-Segment Elevation Myocardial Infarction Patients Treated With Primary Percutaneous Coronary Intervention." Journal of the American College of Cardiology **53**(17): 1503-1509. [PDF Full-Text](#)

Objectives We assessed the incremental value of baseline Q waves over time from symptom onset as a marker of clinical outcome in ST-segment elevation myocardial infarction (STEMI). **Background** Time from symptom onset is a central focus in STEMI patients. The presence of Q waves on the baseline electrocardiogram (ECG) has been suggested to be of incremental value to time from symptom onset in evaluating clinical outcomes. **Methods** We evaluated baseline Q waves and ST-segment resolution 30 min after primary percutaneous intervention (PCI) ECGs in 4,530 STEMI patients without prior infarction. Additionally, peak biomarkers; 90-day mortality; and the composite of death, congestive heart failure (CHF), or cardiogenic shock were assessed. **Results** Fifty-six percent of patients had baseline Q waves: they were older, more frequently male and diabetic, and had a more advanced Killip class. Patients with baseline Q waves had greater mortality and a higher composite rate of death, CHF, and shock versus patients without baseline Q waves at 90 days (5.3% vs. 2.1% and 12.1% vs. 4.8%, respectively, both $p < 0.001$). Complete ST-segment resolution was highest, whereas 90-day mortality and the composite outcome were lowest among those randomized \leq 3 h without baseline Q waves. After multivariable adjustment, baseline Q-wave but not time from symptom onset was significantly associated with a 78% relative increase in the hazard of 90-day mortality and a 90% relative increase in the hazard of death, shock, and CHF. **Conclusions** Baseline Q waves in STEMI patients treated with primary PCI provide an independent prognostic marker of clinical outcome. These data might be useful in designing future clinical trials as well as in evaluating patients for triage and potential transfer for planned primary PCI.

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Cardiology

Ghali, J. K., J. Wikstrand, D. J. Van Veldhuisen, B. Fagerberg, S. Goldstein, A. Hjalmarson, P. Johansson, J. Kjekshus, L. Ohlsson, O. Samuelsson, F. Waagstein and H. Wedel (2009). "The Influence of Renal Function on Clinical Outcome and Response to beta-Blockade in Systolic Heart Failure: Insights From Metoprolol CR/XL Randomized Intervention Trial in Chronic HF (MERIT-HF)." Journal of Cardiac Failure **15**(4): 310-318. [PDF Full-Text](#)

Background: Limited information is available on the risk and impact of renal dysfunction on the response to beta-blockade and mode of death in systolic heart failure (HF). **Methods and Results:** Renal function was estimated with glomerular filtration rate (eGFR) using the simplified Modification of Diet in Renal Disease (MDRD) equation. Patients from the Metoprolol CR/XL Controlled Randomized Intervention Trial in Chronic HF (MERIT-HF) were divided into 3 renal function subgroups (MDRD formula): eGFR(MDRD) $>$ 60 ($n = 2496$), eGFR(MDRD) 45 to 60 ($n = 976$), and eGFR(MDRD) $<$ 45 mL/min per 1.73m² body surface area ($n = 493$). Hazard ratio (HR) was estimated with Cox proportional hazards models adjusted for prespecified risk factors. Placebo patients with eGFR $<$ 45 had significantly higher risk than those with eGFR $>$ 60: HR for all-cause mortality, 1.90 (95% confidence interval [CI], 1.28 to 2.81) comparing placebo patients with eGFR $<$ 45 and eGFR $>$ 60, and for the combined end point of all-cause mortality/hospitalization for worsening HF (time to first event): HR, 1.91 (95% CI, 1.44 to 2.53). No significant increase in risk with decreased renal function was observed for those randomized to metoprolol controlled release (CR)/extended release (XL) due to a highly significant decrease in risk on metoprolol CR/XL in those with eGFR $<$ 45. For total mortality, metoprolol CR/XL vs placebo: HR, 0.41 (95% CI, 0.25 to 0.68; $P < .001$) in those with eGFR $<$ 45 compared with HR, 0.71 (95% CI, 0.54 to 0.95; $P < .021$) for those with eGFR $>$ 60; corresponding data for the combined end point was HR, 0.44 (95% CI, 0.31 to 0.63; $P < .0001$) and HR, 0.75 (0.62 to 0.92; $P = .005$, respectively; $P = .095$ for

interaction by treatment for total mortality; $P = .011$ for combined end point). Metoprolol CR/XL was well tolerated in all 3 renal function subgroups. Conclusions: Renal function as estimated by eGFR was a powerful predictor of death and hospitalizations from worsening HF. Metoprolol CR/XL was at least as effective in reducing death and hospitalizations for worsening HF in patients with eGFR < 45 as in those with eGFR > 60 .

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Center for Health Services Research

Tunceli, K., H. Zeng, Z. A. Habib and L. K. Williams (2009). "Long-term projections for diabetes-related work loss and limitations among U.S. adults." *Diabetes Res Clin Pract* **83**(1): e23-5. [Article Request Form](#)

Center for Health Services Research, Henry Ford Hospital, Detroit, MI 48202, USA.

We used data from the U.S. National Health Interview Survey to estimate the effect of diabetes on labor market outcomes. In the year 2050 an estimated 1.46 million U.S. adults will not be working; 597,000 will be work disabled; and 780,000 will have work limitations as a result of diabetes.

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Dermatology

Hornyak, T. J., S. L. Jiang, E. A. Guzman, B. N. Scissors, C. Tuchinda, H. B. He, J. D. Neville and F. M. Strickland (2009). "Mitf dosage as a primary determinant of melanocyte survival after ultraviolet irradiation." *Pigment Cell & Melanoma Research* **22**(3): 307-318.

[PDF Full-Text](#)

Microphthalmia-associated transcription factor (Mitf) is essential for melanocyte development and function and regulates anti-apoptotic Bcl2 expression. We hypothesized that cellular deficiency of Mitf can influence melanocyte survival in response to ultraviolet (UV) radiation. Primary melanocyte cultures were prepared from neonatal wild-type mice and congenic animals heterozygous for Mitf mutations Mitf (mi-vga9/+) and Mitf(Mi-wh/+), and exposed to UV irradiation. Wild-type melanocytes were more resistant to UV-induced apoptosis than melanocytes partially deficient in Mitf activity, as determined by relative levels of intracellular melanin and relative activation of Mitf target genes Tyr, Tyrp1, Dct, and Cdk2. Comparative experiments with wild-type cells and congenic albino melanocytes demonstrated that these differences are not due to differences in melanin content, implicating Mitf as a primary determinant of UV-dependent melanocyte survival. Mitf activity correlated directly with resistance to UV-induced apoptosis in melanocytes. Mitf was important not only for regulating the expression of anti-apoptotic Bcl-2 following UV irradiation, but also the expression of the pro-apoptotic BH3-only Bad protein and activation of the extrinsic apoptotic pathway. Hence, Mitf is a multifaceted regulator of UV-induced apoptosis in melanocytes.

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Dermatology

Tierney, E., A. Barker, J. Ahdout, C. W. Hanke, R. L. Moy and D. J. Kouba (2009). "Photodynamic Therapy for the Treatment of Cutaneous Neoplasia, Inflammatory Disorders, and Photoaging." *Dermatologic Surgery* **35**(5): 725-746. [PDF Full-Text](#)

Photodynamic therapy (PDT) has demonstrated high efficacy, minimal side effects, and improved cosmetic outcome when used for the treatment of actinic keratoses (AK), basal cell carcinoma (BCC), squamous cell carcinoma, and photoaging. To review the literature on the use of PDT in dermatologic surgery using MEDLINE. Published clinical studies using PDT in the treatment of AKs yield overall efficacy rates ranging from 50% to 71% with one treatment to as high as 88% to 90% with two or more treatments. For superficial BCC, initial clearance rates were 76% to 97%, and for Bowen's disease, initial clearance rates ranged from 72% to 94% overall. The use of PDT for photorejuvenation is a relatively new application of this technology, which has shown promise in improving the appearance of fine lines, pigmentary variation, and telangiectasias. The advantages of photodynamic therapy include the capacity for noninvasive targeted therapy through topical application of aminolevulinic acid and methyl aminolevulinic acid, with outstanding cosmetic results. Although the theory behind the use of chemical photosensitizers and ultraviolet light to treat a wide variety of skin disorders is straightforward, the practical application of this technology is evolving. Additional research into the precise mechanisms of action for specific photosensitizers and optimal light sources will be highly beneficial to

the advancement of this technology. The authors have indicated no significant interest with commercial supporters.

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Dermatology

Tierney, E., B. H. Mahmoud, C. Hexsel, D. Ozog and I. Hamzavi (2009). "Randomized Control Trial for the Treatment of Hidradenitis Suppurativa with a Neodymium-Doped Yttrium Aluminium Garnet Laser." [Dermatol Surg](#) **EPub Ahead of Print**. [PDF Full-Text](#)

Center for Multicultural Dermatology, Department of Dermatology, Henry Ford Hospital, Detroit, Michigan.

BACKGROUND Hidradenitis suppurativa (HS) is a chronic suppurative condition for which there is limited efficacy of medical and surgical treatments. **OBJECTIVE** To assess whether the 1,064-nm neodymium-doped yttrium aluminium garnet (Nd:YAG) laser is an effective treatment for HS. **MATERIALS AND METHODS** Prospective, randomized, controlled study for patients with stage II to III HS disease (n=22). A series of 3 monthly laser sessions were performed. Treatment response was measured before each laser session and 1 month after the completion of laser treatment (HS Lesion, Area, and Severity Index (HS-LASI) scale). A modification was made to include symptoms (erythema, edema, pain, and purulent discharge; modified HS-LASI, 0-3 scale). **RESULTS** The percentage change in HS severity after 3 months of treatment was -65.3% over all anatomic sites, -73.4% inguinal, -62.0% axillary, and -53.1% inframammary. For all anatomic sites combined and each individual anatomic site, the change in HS severity from baseline to month 3 was statistically significant at the treated sites (p<.02 for modified HS-LASI and HS-LASI) but not at the control sites (p>.05 for modified HS-LASI and HS-LASI). **CONCLUSIONS** The long-pulse Nd:YAG laser is effective for treatment of HS. The effectiveness of Nd:YAG laser, a hair epilation device, supports the primary follicular pathogenesis of the condition. The authors have indicated no significant interest with commercial supporters.

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Dermatology

Zhou, L., K. H. Seo, H. K. Wong and Q. S. Mi (2009). "MicroRNAs and immune regulatory T cells." [International Immunopharmacology](#) **9(5)**: 524-527. [Article Request Form](#)

MicroRNAs (miRNAs)-mediated RNA interference are emerging as an important regulatory pathway for various biological processes, including development, differentiation, and homeostasis. Accumulated evidence suggests that miRNAs regulate T cell and B cell differentiation, proliferation, and apoptosis. Deletion of miRNAs in hematopoietic stem cells or in thymus disrupts T cell homeostasis and results in autoimmunity and abnormal cytokine production. Regulatory T cells are potent immune regulators. In this mini-review, we provide a brief overview of the important roles of miRNAs in the development and function of T cells, especially in immune regulatory T cells.

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Diagnostic Radiology

Fourgas, E., J. Craig, A. Bouffard and M. van Holsbeeck (2009). "Ultrasound of the Elbow: Surface Anatomy, Common Pathology and Positioning of the Ultrasound Transducer (CME Credit Available)." [American Journal of Roentgenology](#) **192(5)**. [Article Request Form](#)

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Diagnostic Radiology

Masuda, E. and D. Myers (2009). "Portal Vein Thrombosis: A Multimodality Approach to the Diagnosis of Bland vs. Malignant Thrombi (CME Credit Available)." [American Journal of Roentgenology](#) **192(5)**. [Article Request Form](#)

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Diagnostic Radiology

Merchant, K., E. Masuda, G. Fundaro and N. Beydoun (2009). "MRI Detected Breast Cancers with False Negative Mammograms." [American Journal of Roentgenology](#) **192**(5).

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Diagnostic Radiology

Rad, A. M., A. S. Iskander, B. Janic, R. A. Knight, A. S. Arbab and H. Soltanian-Zadeh (2009). "AC133+ progenitor cells as gene delivery vehicle and cellular probe in subcutaneous tumor models: a preliminary study." [BMC Biotechnol](#) **9**: 28. PMC2669076.

[PDF Full-Text](#)

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BACKGROUND: Despite enormous progress in gene therapy for breast cancer, an optimal systemic vehicle for delivering gene products to the target tissue is still lacking. The purpose of this study was to determine whether AC133+ progenitor cells (APC) can be used as both gene delivery vehicles and cellular probes for magnetic resonance imaging (MRI). In this study, we used superparamagnetic iron oxide (SPIO)-labeled APCs to carry the human sodium iodide symporter (hNIS) gene to the sites of implanted breast cancer in mouse model. In vivo real time tracking of these cells was performed by MRI and expression of hNIS was determined by Tc-99m pertechnetate (Tc-99m) scan. RESULTS: Three million human breast cancer (MDA-MB-231) cells were subcutaneously implanted in the right flank of nude mice. APCs, isolated from fresh human cord blood, were genetically transformed to carry the hNIS gene using adenoviral vectors and magnetically labeled with ferumoxides-protamine sulfate (FePro) complexes. Magnetically labeled genetically transformed cells were administered intravenously in tumor bearing mice when tumors reached 0.5 cm in the largest dimension. MRI and single photon emission computed tomography (SPECT) images were acquired 3 and 7 days after cell injection, with a 7 Tesla animal MRI system and a custom built micro-SPECT using Tc-99m, respectively. Expression of hNIS in accumulated cells was determined by staining with anti-hNIS antibody. APCs were efficiently labeled with ferumoxide-protamine sulfate (FePro) complexes and transduced with hNIS gene. Our study showed not only the accumulation of intravenously administered genetically transformed, magnetically labeled APCs in the implanted breast cancer, but also the expression of hNIS gene at the tumor site. Tc-99m activity ratio (tumor/non-tumor) was significantly different between animals that received non-transduced and transduced cells ($P < 0.001$). CONCLUSION: This study indicates that genetically transformed, magnetically labeled APCs can be used both as delivery vehicles and cellular probes for detecting in vivo migration and homing of cells. Furthermore, they can potentially be used as a gene carrier system for the treatment of tumor or other diseases.

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Emergency Medicine

Goyal, N. and D. K. Gupta (2009). "In Response to "A Prospective, Randomized Trial of an Emergency Department Observation Unit for Acute Onset Atrial Fibrillation"." [Annals of Emergency Medicine](#) **53**(5): 695-696. [PDF Full-Text](#)

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Endocrinology & Metabolism

Bhadada, S. K. and D. S. Rao (2009). "Hyperparathyroidism-Jaw Tumor Syndrome." [Endocrine Practice](#) **15**(3): 276-277. [PDF Full-Text](#)

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Endocrinology & Metabolism

Kruger, D. F. (2008). "Integrating innovative tools into the management of type 2 diabetes to improve patient self-management." [J Am Acad Nurse Pract](#) **20 Suppl 1**: 17-20. [PDF Full-Text](#) (Scroll down to page 17)

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Family Medicine

Williams, B. C., B. Simons, S. Schooley and D. Gordon (2009). "A Blog and Student-Centered Seminars Facilitated Reflective Learning in Caring for Underserved Patients." Journal of General Internal Medicine **24**: 222-222. [PDF Full-Text](#) (Scroll down to page 222)

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Gastroenterology

McHutchison, J. G., G. T. Everson, S. C. Gordon, I. M. Jacobson, M. Sulkowski, R. Kauffman, L. McNair, J. Alam and A. J. Muir (2009). "Telaprevir with Peginterferon and Ribavirin for Chronic HCV Genotype 1 Infection." New England Journal of Medicine **360**(18): 1827-1838. [PDF Full-Text](#)

BACKGROUND Current therapy for chronic hepatitis C virus (HCV) infection is effective in less than 50% of patients infected with HCV genotype 1. Telaprevir, a protease inhibitor specific to the HCV nonstructural 3/4A serine protease, rapidly reduced HCV RNA levels in early studies. **METHODS** We randomly assigned patients infected with HCV genotype 1 to one of three telaprevir groups or to the control group. The control group (called the PR48 group) received peginterferon alfa-2a (180 mu g per week) and ribavirin (1000 or 1200 mg per day, according to body weight) for 48 weeks, plus telaprevir-matched placebo for the first 12 weeks (75 patients). The telaprevir groups received telaprevir (1250 mg on day 1 and 750 mg every 8 hours thereafter) for 12 weeks, as well as peginterferon alfa-2a and ribavirin (at the same doses as in the PR48 group) for the same 12 weeks (the T12PR12 group, 17 patients) or for a total of 24 weeks (the T12PR24 group, 79 patients) or 48 weeks (the T12PR48 group, 79 patients). The primary outcome was a sustained virologic response (an undetectable HCV RNA level 24 weeks after the end of therapy). **RESULTS** The rate of sustained virologic response was 41% (31 of 75 patients) in the PR48 group, as compared with 61% (48 of 79 patients) in the T12PR24 group (P = 0.02), 67% (53 of 79 patients) in the T12PR48 group (P = 0.002), and 35% (6 of 17 patients) in the T12PR12 group (this group was exploratory and not compared with the control group). Viral breakthrough occurred in 7% of patients receiving telaprevir. The rate of discontinuation because of adverse events was higher in the three telaprevir-based groups (21%, vs. 11% in the PR48 group), with rash the most common reason for discontinuation. **CONCLUSIONS** Treatment with a telaprevir-based regimen significantly improved sustained virologic response rates in patients with genotype 1 HCV, albeit with higher rates of discontinuation because of adverse events. (ClinicalTrials.gov number, NCT00336479.)

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Gastroenterology

Moonka, D. K. and A. Kapke (2009). "The Influence of Induction Therapy on Patient Survival after Liver Transplantation as a Function of Baseline Renal Function." American Journal of Transplantation **9**: 231-231. [Article Request Form](#)

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Hypertension & Vascular Research

Bignone, I., A. Sabattini, M. D'Ambrosio, G. Melendi, D. Verdi and R. Diez (2009). "Inappropriate use of antibiotics and education." Archivos Argentinos De Pediatria **107**(2): 191-192. [Article Request Form](#)

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Hypertension & Vascular Research

Mendez, M. (2009). "CBP and p300 in renin homeostasis: can they drive the fate?" American Journal of Physiology-Heart and Circulatory Physiology **296**(5): H1213-H1214. [PDF Full-Text](#)

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Infectious Diseases

Boster, A., S. Hreha, J. R. Berger, F. Bao, R. Penmesta, A. Tselis, C. Endress, I. Zak, J. Perumal, C. Caon, J. Vazquez, K. L. Tyler, M. K. Racke, S. Millis and O. Khan (2009). "Progressive Multifocal Leukoencephalopathy and Relapsing-Remitting Multiple Sclerosis." Archives of Neurology **66**(5): 593-599. [PDF Full-Text](#)

Objective: To identify clinical and magnetic resonance imaging (MRI) features that distinguish progressive multifocal leukoencephalopathy (PML) from relapsing-remitting multiple sclerosis (RRMS). Design: Retrospective medical record review. Setting: Two urban teaching hospitals in Detroit, Michigan. Patients: Forty-five confirmed PML cases and 100 patients with RRMS. Main Outcome Measures: Clinical and MRI features distinguishing PML from RRMS. Results: Overall, monosymptomatic presentations were more common in multiple sclerosis (MS) than PML (85% vs 47%; $P < .01$). However, patients with PML presented more often with hemiparesis (24% vs 5%; $P = .001$) and altered mentation (19% vs 0%; $P < .0001$), whereas brainstem (2% vs 18%; $P = .007$) presentations were more common in patients with RRMS. Spinal cord and optic neuritis presentations were seen in 18% and 33% of patients with RRMS, respectively, but not in patients with PML ($P < .0001$). Brain MRI scans, available in 35 (78%) PML cases, revealed 7 lesion types. Large, confluent T2-weighted lesions (74% vs 2%; $P < .0001$) and deep gray matter lesions (31% vs 7%; $P < .001$) were more frequent in patients with PML than patients with RRMS. Crescentic cerebellar lesions (23% vs 0%; $P < .001$) were seen only in patients with PML. Gadolinium-enhancing (23%), transcallosal (9%), and periventricular (9%) lesions were noted in patients with PML. Brain magnetization transfer ratio (MTR) was low in both PML and MS lesions. However, normal-appearing brain tissue MTR in PML was higher than normal-appearing brain tissue MTR in RRMS (44.15% vs 41.04%; $P = .002$), suggesting that PML may be relatively more focal than MS. Conclusions: There appear to be differences between the clinical and MRI characteristics of PML and RRMS, which may help distinguish new MS activity from PML. Magnetization transfer ratio studies may provide additional clues in improving early detection of PML in patients with preexisting MS and warrant further investigation.

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Infectious Diseases

Johnson, L. E., K. Reyes and M. J. Zervos (2009). "Resources for Infection Prevention and Control on the World Wide Web." Clinical Infectious Diseases **48**(11): 1585-1595. [PDF Full-Text](#)

This review summarizes infection prevention resources on the Internet. Web sites are presented in 8 categories: guidelines, policies, and regulatory bodies; health care-associated infection and multidrug-resistant organisms; surveillance, reporting, and initiatives; antibiotic use; employee health; long-term care facilities; facility and environmental infection control; and professional societies, educational opportunities, and listserves. For example, links to the National Surgical Quality Improvement Program and National Healthcare Safety Network reports are provided among resources for infection surveillance, reporting, and initiatives. A link to guidelines for infection prevention in health care workers is listed with other information regarding employee health. The Web address for the Society for Healthcare Epidemiology of America guidelines for infection control in long-term care facilities is listed with resources for long-term care facilities. Guidelines for construction and environmental services are summarized with other information regarding facility and environmental infection control. This review summarizes the most useful and up-to-date infection prevention resources on the Internet and will simplify the search for pertinent information.

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Infectious Diseases

Moore, C. L., A. Hingwe, S. M. Donabedian, M. B. Perri, S. L. Davis, N. Z. Haque, K. Reyes, D. Vager and M. J. Zervos (2009). "Comparative evaluation of epidemiology and outcomes of methicillin-resistant Staphylococcus aureus (MRSA) USA300 infections causing community- and healthcare-associated infections." Int J Antimicrob Agents **EPub Ahead of Print**. [Article Request Form](#)

Henry Ford Health System, 2799 West Grand Boulevard, Detroit, MI 48202, USA.

Methicillin-resistant Staphylococcus aureus (MRSA) USA300 clone is commonly found in the community and is being increasingly reported in the healthcare setting. A retrospective analysis was conducted to compare the epidemiology and outcomes between community-associated (CA) and healthcare-associated (HA) USA300 MRSA infections. The study enrolled 160 subjects with USA300 MRSA infections (47.5% CA-MRSA and 52.5% HA-MRSA). Failure in the HA group was higher (38.1%) compared with the CA group (23.7%) (P=0.05). Predictors of failure included male gender, age, presence of any co-morbidity, coronary artery disease, chronic kidney disease, history of MRSA, previous admission, fluoroquinolone exposure, HA infection and osteomyelitis (P<=0.05). Independent predictors of failure were osteomyelitis, history of MRSA, male gender and pneumonia. Recurrent disease was found in 32.6% of cases. Overall, USA300 MRSA most commonly causes infection of the skin and skin structure, however, 20% of subjects can experience more invasive disease with infection of the bloodstream, lung or bone. Failure rates are higher in subjects with healthcare risk factors or if the infection was acquired in the hospital, with these subjects experiencing more invasive infections such as bacteraemia, pneumonia or osteomyelitis.

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Internal Medicine

Arnaout, K., G. Abou Dagher, S. Rancour, M. Younes, E. Kawar and A. Lukowski (2009). "Bickerstaff Brainstem Encephalitis: A Rare Variant of Guillian-Barre Syndrome." Journal of General Internal Medicine **24**: 295-296. [PDF Full-Text](#) (Scroll down to page 295)

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Internal Medicine

Garcia-Sayan, E., W. Astorne, Z. Habib, J. Han, W. Morse and S. S. Kaatz (2009). "Integrating Blogs into Medical Education: A Novel Approach to Journal Club." Journal of General Internal Medicine **24**: 231-232. [PDF Full-Text](#) (Scroll down to page 231)

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Internal Medicine

Gonzalez, H., E. C. Ayala, R. D. Wong, A. N. Lucar, S. Kaatz and M. A. Y. Huang (2009). "Effect of QTc Interval on Liver Transplantation in End Stage Liver Disease Patients." American Journal of Transplantation **9**: 691-691. [Article Request Form](#)

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Internal Medicine

Huaman, M. A., R. V. Araujo-Castillo, G. Soto, J. M. Neyra, J. A. Quispe, M. F. Fernandez, C. C. Mundaca and D. L. Blazes (2009). "Impact of two interventions on timeliness and data quality of an electronic disease surveillance system in a resource limited setting (Peru): a prospective evaluation." BMC Med Inform Decis Mak **9**: 16. PMC2667397. [PDF Full-Text](#)

US Naval Medical Research Center Detachment, Lima, Peru. mhuaman1@hfhs.org

BACKGROUND: A timely detection of outbreaks through surveillance is needed in order to prevent future pandemics. However, current surveillance systems may not be prepared to accomplish this goal, especially in resource limited settings. As data quality and timeliness are attributes that improve outbreak detection capacity, we assessed the effect of two interventions on such attributes in Alerta, an electronic disease surveillance system in the Peruvian Navy. METHODS: 40 Alerta reporting units (18 clinics and 22 ships) were included in a 12-week prospective evaluation project. After a short refresher course on the notification process, units were randomly assigned to either a phone, visit or control group. Phone group sites were called three hours before the biweekly reporting deadline if they had not sent their report. Visit group sites received supervision visits on weeks 4 & 8, but no phone calls. The control group sites were not contacted by phone or visited. Timeliness and data quality were assessed by calculating the percentage of reports sent on time and percentage of errors per total number of reports, respectively. RESULTS: Timeliness improved in the phone group from 64.6% to 84% in clinics (+19.4 [95% CI, +10.3 to +28.6]; p < 0.001) and from 46.9% to 77.3% on ships (+30.4 [95% CI, +16.9 to +43.8]; p < 0.001). Visit and control groups did not show significant changes in timeliness. Error rates decreased in the visit group from 7.1% to 2% in clinics (-5.1 [95% CI, -8.7 to -1.4]; p = 0.007), but only from 7.3% to 6.7% on ships (-0.6 [95% CI, -2.4 to +1.1]; p = 0.445). Phone and control groups did not show significant improvement in data quality. CONCLUSION: Regular phone reminders significantly

improved timeliness of reports in clinics and ships, whereas supervision visits led to improved data quality only among clinics. Further investigations are needed to establish the cost-effectiveness and optimal use of each of these strategies.

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Internal Medicine

Nikolic, D., K. Rangelov and S. S. Kaatz (2009). "Management of Massive Infected Pancreatic Pseudocyst." Journal of General Internal Medicine **24**: 329-329. [PDF Full-Text](#) (Scroll down to page 329)

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Internal Medicine

Tapia, M. G. and K. Baker-Genaw (2009). "Interstitial Pneumonitis during Treatment with Nitrofurantoin." Journal of General Internal Medicine **24**: 323-323. [PDF Full-Text](#) (Scroll down to page 323)

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Nephrology

Boudville, N. C., O. Djurdjev, I. C. Macdougall, A. L. de Francisco, G. Deray, A. Besarab, P. E. Stevens, R. G. Walker, P. Urena, P. Inigo, R. Minutolo, Y. S. Haviv, K. Yeates, M. L. Aguera, J. M. Macrae and A. Levin (2009). "Hemoglobin Variability in Nondialysis Chronic Kidney Disease: Examining the Association with Mortality." Clin J Am Soc Nephrol **Epub Ahead of Print**. [Article Request Form](#)

School of Medicine and Pharmacology, University of Western Australia, and Department of Renal Medicine, Sir Charles Gairdner Hospital, Perth, Western Australia, Australia; Department of Medicine, Division of Nephrology, St. Paul's Hospital, University of British Columbia, Vancouver, British Columbia, Canada; Department of Renal Medicine, King's College Hospital, London, United Kingdom; Servicio de Nefrologia, Hospital Universitario Valdecilla, Santander, Spain; ||Department of Nephrology, Hospitalier Pitie-Salpetriere, Paris, France; paragraph signDepartment of Medicine, Division of Nephrology and Hypertension, Henry Ford Health System, Detroit, Michigan; **Department of Renal Medicine, Kent and Canterbury Hospital, Canterbury, United Kingdom; Department of Nephrology, Royal Melbourne Hospital, Melbourne, Victoria, Australia; Service de Nephrologie Dialyse, Clinique du Landy, Saint Ouen, France; Servicio de Nefrologia, Hospital Clinico Universitario "Lozano Blesa," Zaragoza, Spain; ||||Department of Nephrology, Second University of Naples, Naples, Italy; paragraph sign paragraph signDivision of Nephrology, Hadassah-Hebrew University Medical Center, Jerusalem, Israel; ***Department of Medicine, Queen's University, Kingston, Ontario, Canada; Servicio de Nefrologia, Hospital Univeritario Reina Sofia, Cordoba, Spain; and Division of Nephrology, Foothills Medical Centre, Calgary, Alberta, Canada.

BACKGROUND AND OBJECTIVES: Anemia and hemoglobin (Hb) variability are associated with mortality in hemodialysis patients who are on erythropoiesis-stimulating agents (ESA). Our aim was to describe the degree of Hb variability present in nondialysis patients with chronic kidney disease (CKD), including those who were not receiving ESA, and to investigate the association between Hb variability and mortality. **DESIGN, SETTING, PARTICIPANTS, & MEASUREMENTS:** Hb variability was determined using 6 mo of "baseline" data between January 1, 2003, and October 31, 2005. A variety of definitions for Hb variability were examined to ensure consistency and robustness. **RESULTS:** A total of 6165 patients from 22 centers in seven countries were followed for a mean of 34.0 +/- 15.8 mo; 49% were prescribed an ESA. There was increased Hb variability with ESA use; the residual SD of Hb was 4.9 +/- 4.4 g/L in patients who were not receiving an ESA, compared with 6.8 +/- 4.8 g/L. Hb variability was associated with a small but significantly increased risk for death per g/L residual SD, irrespective of ESA use. Multivariate linear regression model explained only 11% of the total variance of Hb variability. **CONCLUSIONS:** Hb variability is increased in patients who have CKD and are

receiving ESA and is associated with an increased risk for death (even in those who are not receiving ESAs). This analysis cannot determine whether Hb variability causally affects mortality. Thus, the concept of targeting Hb variability with specific agents needs to be examined within the context of factors that affect both Hb variability and mortality.

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Nephrology

Thalla, R., D. Kim, K. K. Venkat and R. Parasuraman (2009). "Sequestration of active *Cryptococcus neoformans* infection in the parathyroid gland despite prolonged therapy in a renal transplant recipient." [Transpl Infect Dis](#) **EPub Ahead of Print**. [PDF Full-Text](#)

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

Disseminated cryptococcal infection occurs mainly in the immunocompromised host, particularly in those with impaired cellular immunity. The treatment outcome depends not only on the duration and choice of antifungal therapy, but also on the activity of the organism to persist in different parts of the body despite therapy. We present a case of persistence of cryptococcal infection in the parathyroid gland in a kidney transplant recipient. A 38-year-old male renal transplant recipient diagnosed to have disseminated cryptococcosis was treated with discontinuation of immunosuppression, amphotericin B, and flucytosine for 2 weeks, and fluconazole subsequently. Dialysis was initiated when graft function deteriorated after discontinuation of immunosuppression. The patient showed no clinical signs of active cryptococcal infection on fluconazole therapy. One year after the diagnosis of cryptococcosis, and still on fluconazole, he underwent parathyroidectomy, for severe secondary hyperparathyroidism. Surprisingly, active cryptococcal infection with necrotizing granulomatous inflammation was demonstrated in the parathyroid, despite being on therapy. This patient illustrates that persistence of fungal infection despite prolonged therapy can occur in unusual sites such as the parathyroid and may be a source for future recurrence and dissemination.

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Neurology

Chen, J., X. Cui, A. Zacharek, C. Roberts and M. Chopp (2009). "eNOS Mediates TO90317 Treatment-Induced Angiogenesis and Functional Outcome After Stroke in Mice." [Stroke](#) **EPub Ahead of Print**. [Article Request Form](#)

From the Department of Neurology, Henry Ford Hospital, Detroit, Mich; and the Department of Physics, Oakland University, Rochester, Mich.

BACKGROUND AND PURPOSE: TO901317, a synthetic liver X receptor agonist, elevates high-density lipoprotein cholesterol (HDL-C) in mice. We tested the hypothesis that TO901317 treatment of stroke promotes angiogenesis and vascular maturation and improves functional outcome after stroke by increasing endothelial nitric oxide synthase (eNOS) phosphorylation. **METHODS:** C57BL/6J mice were subjected to middle cerebral artery occlusion and were treated with or without TO901317 (30 mg/kg) starting 24 hours after middle cerebral artery occlusion and daily for 14 days. **RESULTS:** TO901317 significantly increased serum HDL-C level, promoted angiogenesis and vascular stabilization in the ischemic brain, and improved functional outcome after stroke. The increased HDL-C level significantly correlated with functional recovery after stroke. TO901317 also increased eNOS phosphorylation in the ischemic brain. Mechanisms underlying the TO901317-induced angiogenesis were investigated using eNOS knockout (eNOS^{-/-}) mice. TO901317 treatment of eNOS^{-/-} mice significantly increased HDL-C level but failed to increase angiogenesis and functional outcome after stroke. In vitro studies demonstrated that TO901317 and HDL-C significantly increased capillary tube formation and promoted eNOS phosphorylation activity in cultured mouse brain endothelial cells compared with nontreatment controls. However, TO901317 and high-density lipoprotein treatment-induced capillary tube formation were absent in eNOS-deficient mouse brain endothelial cell. **CONCLUSIONS:** These data indicate that TO901317 treatment increases serum HDL-C level, which promotes angiogenesis through eNOS and leads to improvement of functional outcome after stroke.

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Neurology

Ishii, R., L. Canuet, A. Herdman, A. Gunji, M. Iwase, H. Takahashi, T. Nakahachi, M. Hirata, S. E. Robinson, C. Pantev and M. Takeda (2009). "Cortical oscillatory power changes during auditory oddball task revealed by spatially filtered magnetoencephalography." Clinical Neurophysiology **120**(3): 497-504. [PDF Full-Text](#)

Objective: To investigate the neural sources and associated changes in oscillatory activity involved in auditory attention and memory updating processing using spatially filtered magnetoencephalography. Methods: We recorded magnetic responses during an auditory oddball task in 12 normal subjects. Synthetic aperture magnetometry (SAM)-permutation analysis was used to visualize the multiple brain regions associated with event-related magnetic fields (ERFs), and event-related oscillations during target detection processing. Results: SAM-permutation results showed the topographical distribution of N1m over the bilateral primary auditory cortex. Post-stimulus delta (1.5-4 Hz) activity sources, likely related to the P300 slow-waveform, were distributed over the tight frontocentral and parietal regions. Source locations of theta (4-8 Hz) and alpha (8-13 Hz) event-related synchronization (ERS) were identified over the dorsolateral and medial prefrontal cortex. We visualized bilateral central-Rolandic suppressions for mu (8-15 Hz), beta (15-30 Hz), and low-gamma (30-60 Hz) activities, more dominant in the hemisphere contralateral to the moving hand (button-pressing in response to target stimuli). Conclusions: Prefrontal theta and alpha ERS, and frontocentral-parietal delta ERS are functionally-parietal engaged in auditory attention and memory updating process. Significance: Spatially filtered MEG is valuable for detection and source localization of task-related changes in the ongoing oscillatory activity during oddball tasks.

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Neurology

Lewitt, P. A., D. Jennings, K. E. Lyons, R. Pahwa, A. L. Rabinowicz, J. Wang, M. Guarnieri, J. P. Hubble and H. Murck (2009). "Pharmacokinetic-pharmacodynamic crossover comparison of two levodopa extension strategies." Mov Disord **Epub Ahead of Print**. [PDF Full-Text](#)

Departments of Neurology, Henry Ford Hospital and Wayne State University School of Medicine, Detroit, Michigan, USA.

Controlled-release carbidopa and levodopa (CL-CR) and the combination of carbidopa, levodopa, and entacapone (CLE) are used for extending levodopa (L-dopa) effects. In a randomized, open-label crossover study of 17 PD subjects with wearing-off responses, we compared 8-hour L-dopa pharmacokinetics (PK) and clinical effects after two doses of CL-CR (50 and 200 mg, respectively) and CLE (37.7, 150, 200 mg, respectively). PK analysis revealed the anticipated near-equivalent mean L-dopa area-under-the-concentration-curve values (639,490 ng min/mL for two doses of CLE, and 662,577 for CL-CR, $P = 0.86$). The mean hourly fluctuation index for L-dopa concentration was 235% for CLE and 196% for CL-CR ($P = 0.004$). The mean maximal concentration for the first CLE dose was 1,926 +/- 760 ng/mL and for CL-CR, 1,840 +/- 889 ($P = 0.33$). During the PK studies, the mean time that L-dopa concentration was $\geq 1,000$ ng/mL for CLE was 291 +/- 88 minutes and for CL-CR, 306 +/- 86 ($P = 0.33$). The mean percent-time in "off" state was 18% for CLE and 28% for CL-CR ($P = 0.017$), "on state without dyskinesia" was 64% for CLE and 65% for CL-CR ($P = 0.803$), and "on state with nontroublesome dyskinesia" was 18% for CLE and 7% for CL-CR ($P = 0.03$). Despite less "off" time with CLE, both formulations demonstrated similar mean PK values and marked intersubject PK variability. (c) 2009 Movement Disorder Society.

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Neurology

Li, Y. and M. Chopp (2009). "Marrow stromal cell transplantation in stroke and traumatic brain injury." Neurosci Lett **456**(3): 120-3. [PDF Full-Text](#)

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

There is a paucity of therapies for most central nervous system (CNS) disorders. Bone marrow stromal cells (MSCs) are a mixed cell population, including stem and progenitor cells, and are currently a strong candidate for cell-based therapy in "brain attack", including stroke, and traumatic brain injury (TBI), since they are easily

isolated and can be expanded in culture from patients without ethical and technical problems. Although it has been suggested that trans-differentiation of MSCs into cells of neural lineage may occur in vitro, no one has yet observed that MSCs give rise to fully differentiated and functional neurons in vivo. The overwhelming body of data indicate that bioactive factors secreted by MSCs in response to the local environment underlie the tissue restorative effects of MSCs. The MSCs that are employed in this therapy are not necessarily stem cells, but progenitor and differentiated cells that escape immune system surveillance and survive in the CNS even for transplantation of allogeneic or xenogeneic MSCs. The injured CNS is stimulated by the MSCs to amplify its intrinsic restorative processes. Treatment of damaged brain with MSCs promotes functional recovery, and facilitates CNS endogenous plasticity and remodeling. The current mini-review is mainly based on our data and focuses on possible cellular and molecular mechanisms of interaction of MSCs with glia, neurons and vessels after brain attack. The transplantation of MSCs opens up new avenues of cell therapy and may provide an effective treatment for various CNS diseases.

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Neurology

Senderek, J., S. M. Garvey, M. Krieger, V. Guergueltcheva, A. Urtizbera, A. Roos, M. Elbracht, C. Stendel, I. Tournev, V. Mihailova, H. Feit, J. Tramonte, P. Hedera, K. Crooks, C. Bergmann, S. Rudnik-Schoneborn, K. Zerres, H. Lochmuller, E. Seboun, J. Weis, J. S. Beckmann, M. A. Hauser and C. E. Jackson (2009). "Autosomal-Dominant Distal Myopathy Associated with a Recurrent Missense Mutation in the Gene Encoding the Nuclear Matrix Protein, Matr3." *American Journal of Human Genetics* **84**(4): 511-518. [PDF Full-Text](#)

Distal myopathies represent a heterogeneous group of inherited skeletal muscle disorders. One type of adult-onset, progressive autosomal-dominant distal myopathy, frequently associated with dysphagia and dysphonia (vocal cord and pharyngeal weakness with distal myopathy [VCPDM]), has been mapped to chromosome 5q31 in a North American pedigree. Here, we report the identification of a second large VCPDM family of Bulgarian descent and fine mapping of the critical interval. Sequencing of positional candidate genes revealed precisely the same nonconservative S85C missense mutation affecting an interspecies conserved residue in the MATR3 gene in both families. MATR3 is expressed in skeletal muscle and encodes matrin 3, a component of the nuclear matrix, which is a proteinaceous network that extends throughout the nucleus. Different disease related haplotype signatures in the two families provided evidence that two independent mutational events at the same position in MATR3 cause VCPDM. Our data establish proof of principle that the nuclear matrix is crucial for normal skeletal muscle structure and function and put VCPDM on the growing list of monogenic disorders associated with the nuclear proteome.

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Neurology

Zachry, W. M., Q. D. Doan, J. D. Clewell and B. J. Smith (2009). "Case-control analysis of ambulance, emergency room, or inpatient hospital events for epilepsy and antiepileptic drug formulation changes." *Epilepsia* **50**(3): 493-500. [PDF Full-Text](#)

Purpose: Although antiepileptic drugs (AEDs) with multisource generic alternatives are becoming more prevalent, no case-control studies have been published examining multisource medication use and epilepsy-related outcomes. This study evaluated the association between inpatient/emergency epilepsy care and the occurrence of a recent switch in AED formulation. Methods: A case-control analysis was conducted utilizing the Ingenix LabRx Database. Eligible patients were 12-64 years of age, received 145 days of AEDs in the preindex period, had continuous eligibility for 6 months preindex, and no prior inpatient/emergency care. Cases received care between 7/1/2006 and 12/31/2006 in an ambulance, emergency room, or inpatient hospital with a primary epilepsy diagnosis. Controls had a primary epilepsy diagnosis in a physician's office during the same period. The index date was the earliest occurrence of care in each respective setting. Cases and controls were matched 1: 3 by epilepsy diagnosis and age. Odds of a switch between "A-rated" AEDs within 6 months prior to index were calculated. Results: Cases (n = 416) had 81% greater odds of having had an A-rated AED formulation switch [odds ratio (OR) = 1.81; 95% confidence interval (CI) = 1.25 to 2.63] relative to controls (n = 1248). There were no significant differences between groups regarding demographics or diagnosis. Significant differences were found with regard to medical coverage type (case Medicaid 4.6%, control Medicaid = 1.8%, p = 0.002). Post hoc analysis results excluding Medicaid recipients remained significant and concordant with the original analysis. Discussion: This analysis found an association between patients receiving epilepsy care in an emergency or inpatient setting and the recent occurrence of AED formulation switching involving A-rated generics.

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Neurology

Zhang, C. Z., C. S. Kang, Y. P. You, P. Y. Pu, W. D. Yang, P. Zhao, G. X. Wang, A. L. Zhang, Z. F. Jia, L. Han and H. Jiang (2009). "Co-suppression of miR-221/222 cluster suppresses human glioma cell growth by targeting p27(kip1) in vitro and in vivo." International Journal of Oncology **34**(6): 1653-1660. [Article Request Form](#)

MicroRNAs are short regulatory RNAs that negatively modulate protein expression at a post-transcriptional level. Emerging evidence suggests that altered regulation of miRNA may be involved in the pathogenesis of several types of cancers. In the current study, an inverse relationship between the expression of miR-221/miR-222 and the cell cycle inhibitor p27(Kip1) was identified in U251 glioma cells. Co-suppression of miR-221/222 directly resulted in the up-regulation of p27(Kip1) in the tested cells, consequently, affects their, growth potential by reducing a G1 to S shift in the cell cycle. Consistently, miR-221/222 knocked-down through antisense 2(1)-OME-oligonucleotides increased p27(Kip1) in U251 glioma subcutaneous mice and strongly reduced tumor growth in vivo through up regulation of p27(Kip1). Our results suggest that miR-221/222 is a regulator of the tumor suppressor gene p27(Kip1), and co-suppression of miR-221/222 expression in advanced gliomas may inhibit glioma cell proliferation by a mechanism involving the up-regulation of p27(Kip1) in vitro and in vivo.

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Neurology

Zhang, R. L., M. Chopp, S. R. Gregg, Y. Toh, C. Roberts, Y. Letourneau, B. Buller, L. Jia, P. N. D. S and Z. G. Zhang (2009). "Patterns and dynamics of subventricular zone neuroblast migration in the ischemic striatum of the adult mouse." J Cereb Blood Flow Metab **Epub Ahead of Print**. [Article Request Form](#)

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

The migratory behavior of neuroblasts after a stroke is poorly understood. Using time-lapse microscopy, we imaged migration of neuroblasts and cerebral vessels in living brain slices of adult doublecortin (DCX, a marker of neuroblasts) enhanced green fluorescent protein (eGFP) transgenic mice that were subjected to 7 days of stroke. Our results show that neuroblasts originating in the subventricular zone (SVZ) of adult mouse brain laterally migrated in chains or individually to reach the ischemic striatum. The chains were initially formed at the border between the SVZ and the striatum by neuroblasts in the SVZ and then extended to the striatum. The average speed of DCX-eGFP-expressing cells within chains was 28.67±1.04 μm/h, which was significantly faster ($P<0.01$) than the speed of the cells in the SVZ (17.98±0.57 μm/h). Within the ischemic striatum, individual neuroblasts actively extended or retracted their processes, suggestive of probing the immediate microenvironment. The neuroblasts close to cerebral blood vessels exhibited multiple processes. Our data suggest that neuroblasts actively interact with the microenvironment to reach the ischemic striatum by multiple migratory routes.

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Neurology

Zhang, X., X. Zheng, F. Jiang, Z. G. Zhang, M. Katakowski and M. Chopp (2009). "Dual-color fluorescence imaging in a nude mouse orthotopic glioma model." J Neurosci Methods **Epub Ahead of Print**. [Article Request Form](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI, USA; Department of Surgical Oncology, Affiliated Hospital, North China Coal Medical University, Tangshan City, Hebei, PR China.

We sought to establish a new orthotopic glioma model of nude mice by transfer of DsRed2, a red fluorescent protein gene, to malignant glioma cells and to perfuse the tissue with fluorescein isothiocyanate (FITC) dextran in vivo, which would permit the concurrent detection of brain tumor invasion and angiogenesis in vivo by fluorescence microscopy. 9L or U87 malignant glioma cells with DsRed2 expression were intracerebrally

injected into the nude mice. FITC-dextran was administered intravenously to the mice bearing DsRed2-9L or DsRed2-U87 cells immediately before they were sacrificed at 10 days or 15 days after the implantation, respectively. Coronal vibratome sections were examined using 2D and 3D fluorescence microscopy and the results were compared with those examined by routine hematoxylin and eosin (H & E) staining. Angiogenesis induced by glioma was confirmed by two-dimensional and three-dimensional imaging analysis. DsRed2 fluorescence clearly demarcated the primary tumor margins and readily allowed for the visualization of local invasion at the single-cell level in the brain adjacent to tumor. We found that a few tumor cells migrated from the tumor mass along the aberrant microvasculature, but did not extend out of the angiogenic areas. However, locally invasive foci were very difficult to detect by H & E staining. We demonstrated, for the first time, that abnormal vascular structure and glioma cells can be visualized concurrently by fluorescence microscopy. This method is superior to H & E staining for the detection and study of physiologically relevant patterns of brain tumor invasion and angiogenesis in vivo.

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Neurology

Zheng, X., F. Jiang, M. Katakowski, Z. G. Zhang, Q. E. Lu and M. Chopp (2009). "ADAM17 promotes breast cancer cell malignant phenotype through EGFR-PI3K-AKT activation." *Cancer Biol Ther* **8**(11). [Article Request Form](#)

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

A disintegrin and metalloproteinase-17 (ADAM17) is involved in proteolytic ectodomain shedding of several membrane-bound growth factors and cytokines. The expression and activity of ADAM17 increase under some pathological conditions such as stroke and glioma. ADAM17 promotes neural progenitor cell migration and contributes to stroke-induced neurogenesis after stroke and brain tumor growth and invasion. In the present study, we sought to elucidate whether ADAM17 contributes to breast cancer progression and its mechanisms. To this end, we examined the role of ADAM17 in the proliferation, invasion and tube formation of MDA-MB-231 breast cancer cells in vitro. Stable transfection of the MDA-MB-231 cell line with either a plasmid for overexpression of human ADAM17, or a siRNA to ADAM17 was employed in this study to establish high or low ADAM17 expression in breast cancer cells, respectively. For study of mechanism, the ADAM17 inhibitor TAPI-2 and the PI3K-AKT inhibitor LY294002 were used to counteract high ADAM17 expression or the activated PI3K-AKT pathway. Proliferation of MDA-MB-231 breast cancer cells were tested by MTT, Bromodeoxyuridine incorporation assay, growth curve and sulforhodamine B assay. Matrigel invasion assays were used to assess the ability of MDA-MB-231 cells to penetrate the Extra Cellular Matrix. A Matrigel tube formation assay was performed to test capillary tube formation ability. EGFR-PI3K-Akt pathway activation in MDA-MB-231 cells under different ADAM17 expression levels were tested by western blot and ELISA. Our data show that ADAM17 promotes the MDA-MB-231 malignant phenotype by increased proliferation, invasion and angiogenesis. TGF α , VEGF secretion and VEGF expression was increasing by ADAM17 and counteracted by ADAM17 siRNA, TAPI-2 and LY294002 in MDA-MB-231 cells. ADAM17 activated, whereas ADAM17 siRNA, TAPI-2 and LY294002 deactivated the EGFR-PI3K-AKT signal pathway, which correlated with MDA-MB-231 cell malignant phenotype changes. This study suggests ADAM17 contributes to breast cancer progression through activation of the EGFR-PI3K-AKT signal pathway.

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Neurosurgery

Lomonaco, S. L., S. Finniss, C. Xiang, A. Decarvalho, F. Umansky, S. N. Kalkanis, T. Mikkelsen and C. Brodie (2009). "The induction of autophagy by gamma-radiation contributes to the radioresistance of glioma stem cells." *Int J Cancer* **125**(3): 717-722. [PDF Full-Text](#)

William and Karen Davidson Laboratory of Cell Signaling and Tumorigenesis, Department of Neurosurgery, Hermelin Brain Tumor Center, Henry Ford Hospital, Detroit, MI.

Malignant gliomas are characterized by a short median survival which is largely impacted by the resistance of these tumors to chemo- and radiotherapy. Recent studies suggest that a small subpopulation of cancer stem cells, which are highly resistant to gamma-radiation, has the capacity to repopulate the tumors and contribute to their malignant progression. gamma-radiation activates the process of autophagy and inhibition of this process increases the radiosensitivity of glioma cells; however, the role of autophagy in the resistance of

glioma stem cells (GSCs) to radiation has not been yet reported. In this study we examined the induction of autophagy by gamma-radiation in CD133+ GSCs. Irradiation of CD133+ cells induced autophagy within 24-48 hr and slightly decreased the viability of the cells. gamma-radiation induced a larger degree of autophagy in the CD133+ cells as compared with CD133- cells and the CD133+ cells expressed higher levels of the autophagy-related proteins LC3, ATG5 and ATG12. The autophagy inhibitor bafilomycin A1 and silencing of ATG5 and beclin1 sensitized the CD133+ cells to gamma-radiation and significantly decreased the viability of the irradiated cells and their ability to form neurospheres. Collectively, these results indicate that the induction of autophagy contributes to the radioresistance of these cells and autophagy inhibitors may be employed to increase the sensitivity of CD133+ GSCs to gamma-radiation.

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Obstetrics & Gynecology

Arabi, H., H. Guan, S. Kumar, M. Cote, S. Bandyopadhyay, C. Bryant, J. Shah, F. W. Abdul-Karim, A. R. Munkarah and R. Ali-Fehmi (2009). "Impact of microsatellite instability (MSI) on survival in high grade endometrial carcinoma." *Gynecologic Oncology* **113**(2): 153-158.

[PDF Full-Text](#)

Objective. Although microsatellite instability (MSI) is a prognostic marker in colorectal cancer, its relation with prognosis in the endometrial cancer is controversial. The goal of this study is to identify the correlation between MSI and clinicopathologic markers along with survival in high grade endometrial carcinoma EC. **Methods.** Between 1995 and 2004, we identified 119 patients (57 type-I, and 62 type-II) diagnosed with high grade EC and underwent hysterectomy. Sections were immunostained using antibodies against MLH1, MSH2, and MSH6. Semi-quantitative scoring of immunoreactivity was based on percentage of tumor staining and staining intensity. Statistical analysis and Survival were assessed using the Kaplan-Meier method and Cox regression. **Result.** Tumors were considered microsatellite unstable (MSI) when at least 2/3 markers tested negative on IHC. Overall, there was no statistically significant difference in survival between patients with MSI tumors and those with microsatellite stable tumors (MSS) (p value= 0.70). However, MSI tumors which tested negative for all three markers had markedly poor survival (median survival 3 months vs 71 months, p = 0.04) when compared to MSS tumors. The risk of death was 13.2 times greater among women with MSI tumors (with 3 negative markers) compared to women with MSS tumors (OR = 13.20 95% CI 3.50-49.76). **Conclusion.** Although this study has its limitation due to the small sample size, it raises the question of the prognostic significance of MSI in high grade endometrial carcinoma. It also points to the importance of evaluating three mismatch repair genes (MLH1, MSH2, and MSH6) as a prognostic indicator.

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Other

Mavis, B., R. Pearson, G. Stewart and C. Keefe (2009). "A Work Sampling Study of Provider Activities in School-Based Health Centers." *Journal of School Health* **79**(6): 262-268. [PDF](#)

[Full-Text](#)

The purpose of this study was to describe provider activities in a convenience sample of School-Based Health Centers (SBHCs). The goal was to determine the relative proportion of time that clinic staff engaged in various patient care and non-patient care activities. All provider staff at 4 urban SBHCs participated in this study; 2 were in elementary schools, 1 in a middle school, and 1 in a school with kindergarten through grade 8. The study examined provider activity from 6 days sampled at random from the school year. Participants were asked to document their activities in 15-minute intervals from 8:00 a.m. to 5:00 p.m. A structured recording form was used that included 35 activity categories. Overall, 1492 records were completed, accounting for 2708 coded activities. Almost half (48%) of all staff activities were coded as direct patient contact, with clinic operations the second largest category. Limited variations in activities were found across clinic sites and according to season. A significant amount of provider activity was directed at the delivery of health care; direct patient care and clinic operations combined accounted for approximately 75% of clinic activity. Patient, classroom, and group education activities, as well as contacts with parents and school staff accounted for 20% of all clinic activity and represent important SBHC functions that other productivity measures such as billing data might not consistently track. Overall, the method was acceptable to professional staff as a means of tracking activity and was adaptable to meet their needs.

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Otolaryngology

Ernst, A., M. Simoff, D. Ost and F. Herth (2009). "The Emperor Wears No Clothes Response." Chest **135**(5): 1402-1403. [PDF Full-Text](#)

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Otolaryngology

Ghanem, T. (2009). "Parotid defects." Facial Plast Surg Clin North Am **17**(2): 263-9. [Article Request Form](#)

Department of Otolaryngology-Head and Neck Surgery, Oregon Health & Science University, Portland, OR, USA. TGhanem1@hfhs.org

Parotidectomy is a widely performed procedure for various indications, including benign and malignant conditions. For malignant neoplasms of the parotid gland or metastatic disease, it may be performed in conjunction with cheek or temple skin resection, facial nerve sacrifice, or composite resection of a portion of the mandible. There are various options for reconstruction depending on the extent of resection. This article discusses various reconstructive options following parotidectomy and other ablative procedures that are often performed in conjunction. Reconstruction of parotidectomy defects associated with lateral temporal bone resection is discussed elsewhere in this issue.

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Otolaryngology

Sethi, S., M. S. Benninger, M. Lu, S. Havard and M. J. Worsham (2009). "Noninvasive molecular detection of head and neck squamous cell carcinoma: an exploratory analysis." Diagn Mol Pathol **18**(2): 81-7. [PDF Full-Text](#)

Departments of Otolaryngology and Biostatistics, Henry Ford Hospital, Detroit, MI 48202, USA. ssethi1@hfhs.org

BACKGROUND: Head and neck squamous cell carcinoma (HNSCC) is a heterogeneous disease evolving through multistep carcinogenesis, one of the steps being genetic alterations. Noninvasive identification of HNSCC-specific genetic alterations using saliva would have immense potential in early diagnosis and screening, particularly among high-risk patients. **DESIGN:** In this exploratory study, a prospective cohort of 27 HNSCC and 10 healthy controls was examined to determine whether genetic alterations (losses and gains) in saliva DNA differentiated HNSCC patients from normal controls. Saliva DNA was interrogated by a candidate gene panel comprising 82 genes using the multiplex ligation-dependent probe amplification assay. **RESULTS:** Eleven genes showed some predictive ability in identifying HNSCC cases from normal controls: PMAIP1, PTPN1, ERBB2, ABCC4, UTY, DNMT1, CDKN2B, CDKN2D, NFKB1, TP53, and DCC. Statistical analysis using the Classification and Regression Tree (CART) identified 2 genes, PMAIP1 and PTPN1, which correctly discriminated all 27 HNSCC patients (100%) from normal controls. Results were validated using the leave-one-out validation approach. **CONCLUSIONS:** Noninvasive high-throughput multiplex ligation-dependent probe amplification identified discrete gene signatures that differentiated HNSCC patients from normal controls providing proof-of-concept for noninvasive HNSCC detection.

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Otolaryngology

Shonka, D. C., T. A. Ghanem, M. A. Hubbard, D. A. Barker and B. W. Kesser (2009). "Four Years of Accreditation Council of Graduate Medical Education Duty Hour Regulations: Have They Made a Difference?" Laryngoscope **119**(4): 635-639. [PDF Full-Text](#)

Objectives/Hypothesis: Measure compliance with the Accreditation Council of Graduate Medical Education (ACGME) residents' work hour regulations and evaluate their impact on patient care and residents, performance on the Otolaryngology Training Examination (OTE). **Study Design:** Retrospective review of an otolaryngology residency program's resident duty hours violations and OTE scores, and review of the associated hospital's benchmark patient data. **Methods:** Residents' duty hour violations were compiled and analyzed for individual violation, postgraduate year (PGY), and service in the program. Annual OTE scores and the department's hospital benchmark measures (inpatient mortality, inpatient length of stay, 30-day readmission rate) were compared before and after the institution of the ACGME duty hours mandate. **Results:**

The 10-hour rule was most frequently violated; residents on the oncology service and PGY-2 year were most commonly in violation. There was no difference before and after institution of the ACGME duty hours mandate in 30-day hospital readmission rates ($P = .42$), hospital mortality index ($P = .55$), length of stay ($P = .55$), OTE scores ($P = .11$, Student's t test), and graduating resident's operative volume. Conclusions: Institution of the ACGME duty hour regulations did not improve patient care as measured by the 30-day readmission rate, inhospital mortality, and patient's length of stay. Residents' performance on the OTE did not change after implementation of the ACGME rules. Further studies are warranted to assess the impact of the ACGME work hour regulations on patient care and resident-physicians training.

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Pathology

Anagli, J., Y. Han, L. Stewart, D. Yang, A. Movsisyan, K. Abounit and D. Seyfried (2009). "A novel calpastatin-based inhibitor improves postischemic neurological recovery." Biochem Biophys Res Commun **385**(1): 94-9. [PDF Full-Text](#)

Department of Pathology, Henry Ford Hospital, 1 Ford Place, 5D, Detroit, MI 48202, USA. janagli1@hfhs.org

Calpastatin, a naturally occurring protein, is the only inhibitor that is specific for calpain. A novel blood-brain barrier (BBB)-permeant calpastatin-based calpain inhibitor, named B27-HYD, was developed and used to assess calpain's contribution to neurological dysfunction after stroke in rats. Postischemic administration of B27-HYD reduced infarct volume and neurological deficits by 35% and 44%, respectively, compared to untreated animals. We also show that the pharmacologic intervention has engaged the intended biologic target. Our data further demonstrates the potential utility of SBDP145, a signature biomarker of acute brain injury, in evaluating possible mechanisms of calpain in the pathogenesis of stroke and as an adjunct in guiding therapeutic decision making.

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Pathology

Kryvenko, O., T. Christopherson, J. Wilson and N. Lehman (2009). "Primary Gliosarcoma With Ependymal Differentiation." Journal of Neuropathology and Experimental Neurology **68**(5): 117.

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Pulmonary & Critical Care Medicine

Chawla, M., T. Getzen and M. J. Simoff (2009). "Medical pneumonectomy: interventional bronchoscopic and endovascular management of massive hemoptysis due to pulmonary artery pseudoaneurysm, a consequence of endobronchial brachytherapy." Chest **135**(5): 1355-8. [PDF Full-Text](#)

Department of Medicine, Division of Pulmonary and Critical Care Medicine, Section of Interventional Pulmonology and Bronchoscopy, Henry Ford Hospital, Detroit, MI 48202, USA. chawlam1@mskcc.org

Endobronchial brachytherapy serves as an excellent adjunct to standard external beam radiation therapy. The high dose of local radiation is still used to manage airway obstructions at some institutions, despite the well-known risks of airway fistulae to the esophagus or cardiovascular structures. A less reported complication is the development of a pulmonary artery pseudoaneurysm into the mainstem bronchi. The formation of an arterial pseudoaneurysm can lead to massive hemoptysis, which often is fatal. We present a case of massive hemoptysis due to this complication of brachytherapy managed entirely through bronchoscopic and endovascular techniques.

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Pulmonary & Critical Care Medicine

Ouellette, D. R. (2009). "The Emperor Wears No Clothes." Chest **135**(5): 1402-1402. [PDF Full-Text](#)

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Radiation Oncology

Liu, D. Z., M. Ajlouni, J. Y. Jin, S. Ryu, F. Siddiqui, A. Patel, B. Movsas and I. J. Chetty (2009). "Analysis of outcomes in radiation oncology: An integrated computational platform." Medical Physics **36**(5): 1680-1689. [Article Request Form](#)

Radiotherapy research and outcome analyses are essential for evaluating new methods of radiation delivery and for assessing the benefits of a given technology on locoregional control and overall survival. In this article, a computational platform is presented to facilitate radiotherapy research and outcome studies in radiation oncology. This computational platform consists of (1) an infrastructural database that stores patient diagnosis, IMRT treatment details, and follow-up information, (2) an interface tool that is used to import and export IMRT plans in DICOM RT and AAPM/RTOG formats from a wide range of planning systems to facilitate reproducible research, (3) a graphical data analysis and programming tool that visualizes all aspects of an IMRT plan including dose, contour, and image data to aid the analysis of treatment plans, and (4) a software package that calculates radiobiological models to evaluate IMRT treatment plans. Given the limited number of general-purpose computational environments for radiotherapy research and outcome studies, this computational platform represents a powerful and convenient tool that is well suited for analyzing dose distributions biologically and correlating them with the delivered radiation dose distributions and other patient-related clinical factors. In addition the database is web-based and accessible by multiple users, facilitating its convenient application and use.

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Radiation Oncology

Siddiqui, F., A. Kolozsvary, K. N. Barton, S. O. Freytag, S. L. Brown and J. H. Kim (2009). "Does hyperthermia increase adenoviral transgene expression or dissemination in tumors?" Int J Hyperthermia: 1-7. [Article Request Form](#)

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

Purpose: Viral vectors used for cancer gene therapy are usually delivered by direct intratumoral administration. We studied the role of hyperthermia (HT) in vitro and in vivo in an attempt to achieve higher transfection rates (especially, larger volume of spread). Materials and methods: Replication-deficient adenoviruses containing either the human sodium-iodide symporter (Ad5-CMV-hNIS) or green fluorescent protein (Ad5-CMV-eGFP) as reporter genes were used. For in vitro studies, human lung cancer A549 cells were transfected with the virus and assayed for hNIS expression by radioactive pertechnetate uptake or green fluorescence activity using a gamma-counter or fluoroscopy respectively in the presence and absence of HT. For in vivo studies, A549 tumors were established intramuscularly in CD1 athymic mice. The adenoviral constructs (10(10) viral particles/tumor) were injected intratumorally when the tumors reached 10-11 mm in diameter. Different timing sequences of HT were examined and viral spread was assessed using technetium-autoradiography or GFP-fluorescence microscopy. Results: In the in vitro studies, A549 cells infected with the adenoviral construct did not show any difference in gene expression level in the presence or absence of HT. In vivo, the effect of HT on the volume of gene expression in A549 tumors was highly variable with some groups of mice showing better spread in the presence of HT and others showing reduced spread with HT. Conclusion: Improvements in intratumoral adenoviral spread in response to hyperthermia were not consistently observed in a mouse tumor model using two quantitative endpoints of gene expression.

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Sleep Medicine

Bogan, R., J. Tiller, R. Yang, J. Youakim and T. Roth (2009). "Armodafinil for Excessive Sleepiness Associated with Jet Lag Disorder." Sleep **32**: 153. [Article Request Form](#)

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Sleep Medicine

Diederichs, C., T. Roehrs, M. Hyde, M. Greenwald and T. Roth (2009). "Post Surgery Patient Controlled Analgesia in Smokers and Non Smokers." Sleep **32**: 123. [Article Request Form](#)

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Sleep Medicine

Diederichs, C., T. Roehrs, R. Stout, A. Burger, M. Lumley and T. Roth (2009). "Sleepiness and Fatigue in Fibromyalgia and Rheumatoid Arthritis Patients." [Sleep](#) **32**: 1032. [Article Request Form](#)

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Sleep Medicine

Drake, C., V. Gumenyuk, C. Jefferson, C. La-Rose, L. Spear, A. Kick and T. Roth (2009). "Armodafinil in Shift Work Disorder: Normalization of the Mslt." [Sleep](#) **32**: 100. [Article Request Form](#)

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Sleep Medicine

Drake, C., A. Roth, J. Seto, S. Kluck and C. Jefferson (2009). "The Relation between Quantitative Measures of Nighttime Insomnia Symptoms and Daytime Impairment." [Sleep](#) **32**: 0777. [Article Request Form](#)

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Sleep Medicine

Fava, M., G. M. Asnis, R. Shrivastava, B. Lydiard, B. Bastani, D. Sheehan and T. Roth (2009). "Zolpidem Extended-Release Improves Sleep and Next-Day Symptoms in Comorbid Insomnia and Generalized Anxiety Disorder." [Journal of Clinical Psychopharmacology](#) **29**(3): 222-230. [PDF Full-Text](#)

A multicenter, double-blind, parallel-group study was designed to assess the efficacy and safety of zolpidem extended-release coadministered with escitalopram in patients with insomnia and comorbid generalized anxiety disorder. Patients (N = 383) received open-label escitalopram 10 mg/d and were randomized to either adjunct zolpidem extended-release 12.5 mg or placebo. The primary efficacy measure was change from baseline to week 8 in subjective total sleep time. Secondary efficacy measures included subjective sleep onset latency, number of awakenings, wake time after sleep onset, sleep quality, the Hamilton Rating Scale for Anxiety, the Beck Anxiety Inventory, the Sleep Impact Scale, the Massachusetts General Hospital Cognitive and Physical Functioning Questionnaire, and the Sheehan Disability Scale. The last-observation-carried-forward method was used to impute missing values for most efficacy measures. Safety was monitored at each visit. At week 8 and all time points, there was a significant improvement in the zolpidem extended-release/escitalopram group compared with placebo/escitalopram for total sleep time (P < 0.0001). Most of the secondary efficacy measures also significantly favored zolpidem at most visits (P < 0.0001). The most common treatment-emergent adverse events in both groups were nausea, dizziness, headache, fatigue, and dry mouth. Concurrent zolpidem extended-release/escitalopram, compared with placebo/escitalopram, significantly improved insomnia and sleep-related next-day symptoms, but not anxiety symptoms, in patients with comorbid insomnia and generalized anxiety disorder.

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Sleep Medicine

Friedman, N. P., T. Roth, K. P. Wright and C. L. Drake (2009). "Genetic and Environmental Relations between Insomnia and Intrusive Thinking: The Contribution of Sleep Reactivity to Stress." [Sleep](#) **32**: 0781. [Article Request Form](#)

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Sleep Medicine

Gumenyuk, V., T. Roth, J. E. Moran, C. Jefferson, S. M. Bowyer, N. Tepley and C. L. Drake (2009). "Cortical locations of maximal spindle activity: magnetoencephalography (MEG) study." [Journal of Sleep Research](#) **18**(2): 245-253. [PDF Full-Text](#)

The aim of this study was to determine the main cortical regions related to maximal spindle activity of sleep stage 2 in healthy individual subjects during a brief morning nap using magnetoencephalography (MEG). Eight volunteers (mean age: 26.1 +/- 8.7, six women) all right handed, free of any medical psychiatric or sleep disorders were studied. Whole-head 148-channel MEG and a conventional polysomnography montage (EEG; C3, C4, O1 and O2 scalp electrodes and EOG, EMG and ECG electrodes) were used for data collection. Sleep MEG/EEG spindles were visually identified during 15 min of stage 2 sleep for each participant. The distribution of brain activity corresponding to each spindle was calculated using a combination of independent component analysis and a current source density technique superimposed upon individual MRIs. The absolute maximum of spindle activation was localized to frontal, temporal and parietal lobes. However, the most common cortical regions for maximal source spindle activity were precentral and/or postcentral areas across all individuals. The present study suggests that maximal spindle activity localized to these two regions may represent a single event for two types of spindle frequency: slow (at 12 Hz) and fast (at 14 Hz) within global thalamocortical coherence.

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Sleep Medicine

Gumenyuk, V., L. Spear, C. Jefferson, C. La-Rose, T. Roth, O. Korzyukov and C. Drake (2009). "Armodafinil Improves Brain Activity Related to Sensory Memory and Pre-Attentive Novelty Detection in Patients with Shift Work Disorder." Sleep 32: 15. [Article Request Form](#)

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Sleep Medicine

Harris, E., T. Roehrs, M. Hyde and T. Roth (2009). "Extended Sleep in Sleepy Normals Is Analgesic." Sleep 32: 1255. [Article Request Form](#)

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Sleep Medicine

Harris, E., T. Roehrs, M. Hyde and T. Roth (2009). "A Four-Night Sleep Extension Normalizes MslT in Sleepy Normals." Sleep 32: 1256. [Article Request Form](#)

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Sleep Medicine

Hirshkowitz, M., A. Lankford, T. Roth, R. Yang and G. A. Rippon (2009). "Adjunctive Armodafinil Improves Wakefulness Throughout the Day in Cpap-Treated Patients with Excessive Sleepiness Associated with Obstructive Sleep Apnea." Sleep 32: 593. [Article Request Form](#)

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Sleep Medicine

Jarrin, D. C., J. J. McGrath, C. L. Drake, W. M. Bukowski, J. O'Loughlin and J. B. Santo (2009). "The Reliability of the Factor Structure of the Pediatric Daytime Sleepiness Scale in Both a Spanish-Colombian and French-Canadian Versions." Sleep 32: 1126. [Article Request Form](#)

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Sleep Medicine

Kessler, R. C., C. Coulouvrat, G. Hajak, T. Roth, A. C. Shillington, J. K. Walsh and A. J. Vita (2009). "American Insomnia Survey. Methodology." Sleep 32: 0812. [Article Request Form](#)

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Sleep Medicine

Kleinman, L., G. Harding, D. L. Van Brunt, K. Sarsour, A. Kalsekar, K. L. Lichstein, D. J. Buysse and T. Roth (2009). "Psychometric Validation of the Daytime Consequences of Insomnia Questionnaire." Sleep **32**: 1135. [Article Request Form](#)

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Sleep Medicine

Kleinman, V., G. Harding, D. L. Van Brunt, K. Sarsour, A. Kalsekar, K. L. Lichstein, D. J. Buysse and T. Roth (2009). "Psychometric Validation of the Assessment of Sleep Questionnaire." Sleep **32**: 1130. [Article Request Form](#)

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Sleep Medicine

Krystal, A., J. Cooper, K. Schaefer, M. Friedman and T. Roth (2009). "Weight Changes in Patients with Primary Insomnia Following Long-Term Eszopiclone Treatment." Sleep **32**: 0859. [Article Request Form](#)

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Sleep Medicine

Morin, C., A. Krystal, V. McCall, K. Schaefer, R. Claus, A. Wilson, M. Friedman, T. Roth and S. Ancoli-Israel (2009). "A Responder Analysis Using the Insomnia Severity Index in Older Adults Treated for 12 Weeks with Eszopiclone 2 Mg or Placebo." Sleep **32**: 0815. [Article Request Form](#)

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Sleep Medicine

Randall, S., R. Maan, C. Drake, T. Roehrs and T. Roth (2009). "Elevated Mslts in Insomniacs Compared to Population Controls." Sleep **32**: 0867. [Article Request Form](#)

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Sleep Medicine

Randall, S., T. Roehrs, R. Maan and T. Roth (2009). "Chronic Hypnotic Use: Risk of Rebound Insomnia." Sleep **32**: 101. [Article Request Form](#)

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Sleep Medicine

Randall, S., T. Roehrs, R. Maan and T. Roth (2009). "Chronic Hypnotic Use: Its Abuse Liability." Sleep **32**: 102. [Article Request Form](#)

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Sleep Medicine

Rosenberg, R., R. K. Bogan, R. Yang, J. Tiller, J. M. Youakim and T. Roth (2009). "Sleep Characteristics in Subjects Recruited for a Jet Lag Study." Sleep **32**: 151. [Article Request Form](#)

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Sleep Medicine

Rosenberg, R., T. Roehrs, N. Singh, F. Steinberg and T. Roth (2009). "Absence of Rebound Effects with Low-Dose Zolpidem Tartrate Sublingual Lozenge 3.5 Mg (Zsl) Prn Use: Preliminary Analysis." Sleep **32**: 0865. [Article Request Form](#)

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Sleep Medicine

Roth, T., J. Harsh, J. Walsh, R. Rosenberg, R. Yang and G. Rippon (2009). "Armodafinil Improves Wakefulness Throughout the Day in Patients with Excessive Sleepiness Associated with Narcolepsy." Sleep **32**: 0750. [Article Request Form](#)

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Sleep Medicine

Roth, T., R. Rosenberg, D. Seiden, N. Singh, F. Steinberg, S. Sakai and A. Krystal (2009). "As-Needed Treatment of Insomnia Following Motn Awakening: Clinical Efficacy of Low-Dose Zolpidem Tartrate Sublingual Lozenge." Sleep **32**: 0864. [Article Request Form](#)

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Sleep Medicine

Swanson, L., J. Arnedt, R. Rosa, M. Rosekind, G. Belenky, T. Balkin and C. Drake (2009). "Sleep, Health, and Work Outcomes for Shift Workers: Results from the 2008 Sleep in America Poll." Sleep **32**: 173. [Article Request Form](#)

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Sleep Medicine

Wright, K. P., D. F. Dinges, T. Roth, J. K. Walsh and C. A. Czeisler (2009). "Circadian Phase in Patients with Shift-Work Disorder (Swd): Influence on Nighttime Sleepiness, Performance and Daytime Sleep." Sleep **32**: 0134. [Article Request Form](#)

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Sleep Medicine

Zee, P., S. Wang-Weigand, F. Ogrinc and T. Roth (2009). "The Use of Ramelteon to Advance Sleep Timing and Melatonin Phase in Delayed Sleep Phase Disorder." Sleep **32**: 0142. [Article Request Form](#)

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Surgery

Alkortas, D., I. Bajjoka, L. Hsaiky and M. Abouljoud (2009). "The Quality of Life of Kidney Transplant Recipients Following Transplantation with Expanded Criteria Donor Versus Standard Criteria Donor Organs." American Journal of Transplantation **9**: 565-565. [Article Request Form](#)

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Surgery

Alkortas, D., I. Bajjoka, L. Hsaiky, M. Magan and M. Abouljoud (2009). "The Quality of Life of Orthotopic Liver Transplant Recipients Following Transplantation with Marginal Organs." American Journal of Transplantation **9**: 454-454. [Article Request Form](#)

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Surgery

Bajjoka, I., L. Hsaiky, K. Brown, M. Ma and M. Abouljoud (2009). "Thymoglobulin Improves Renal Function without Accelerating Hepatitis C Virus Recurrence in HCV Positive Liver Transplant Recipients." American Journal of Transplantation **9**: 262-262. [Article Request Form](#)

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Surgery

Kakkos, S. K. and G. K. Haddad (2009). "Two-stage combined basilic-brachial vein transposition." Vascular **17**(2): 96-9. [Article Request Form](#)

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

In the present report, we describe a two-stage technique of combined basilic and brachial vein transposition. Our patient had a brachial-basilic vein fistula created, but during the second stage for the transposition, a low basilic-brachial vein confluence was found. Instead of abandoning the procedure, the brachial vein was mobilized and transposed to primarily constitute a usable fistula, which subsequently was successfully used for hemodialysis. A detailed description of our technique is provided. Surgeons should be aware of this alternative procedure to maximize fistula creation rates.

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Surgery

Lin, J. C., D. Eun, A. Shrivastava, A. D. Shepard and D. J. Reddy (2009). "Total robotic ligation of inferior mesenteric artery for type II endoleak after endovascular aneurysm repair." Ann Vasc Surg **23**(2): 255 e19-21. [PDF Full-Text](#)

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, Detroit, MI 48202, USA. jlin1@hfhs.org

We present a case of totally robotic ligation of the inferior mesenteric artery (IMA) for treatment of a persistent endoleak from the IMA into the aneurysm sac after endovascular aneurysm repair (EVAR). An 84-year-old male underwent EVAR with a Gore Excluder stent graft for an asymptomatic infrarenal abdominal aortic aneurysm. Follow-up computed tomographic (CT) scan showed persistent type II endoleak from the IMA, with progressive enlargement of the aneurysm sac from 5 to 6.1 cm over an 18-month period. In this case, the patient underwent ligation of the IMA using the da Vinci Surgical System for the treatment of retrograde flow into the aneurysm sac. The total operating time was 249 min; of this, the robotic assistance time was approximately 180 min. No intraoperative complications occurred. The estimated blood loss was 50 mL and the urine output 650 mL. The patient was extubated immediately after the procedure and tolerated a regular diet the following day. He was discharged home with a urinary catheter on postoperative day 2. CT scan postoperatively and at 3-month follow-up demonstrated an occluded IMA and stabilization of the aneurysm sac size.

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Surgery

Memon, A. A., A. Patel, M. O. Goggins, R. Kurtz, S. Perrine, V. Karthikeyan, D. Kim and M. Abouljoud (2009). "Variables Affecting Predonation Renal Function by Iohalamate GFR in Living Kidney Donors." American Journal of Transplantation **9**: 602-602. [Article Request Form](#)

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Surgery

Patel, A., M. Goggins, L. Malinzek, V. Karthikeyan and K. Brady (2009). "Effect of Race on Death Censored Renal Allograft Survival in Different Donor/Recipient Pairs." American Journal of Transplantation **9**: 345-346. [Article Request Form](#)

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Surgery

Pearson, T., S. Mulgaonkar, R. Kalil, A. Patel, J. Scandling, D. Patel, H. Shidban and M. Weir (2009). "CNI Withdrawal in African Americans-1 Year Outcomes of African American Renal Transplant Recipients in the Spare-the-Nephron (STN) Trial." American Journal of Transplantation **9**: 496-496. [Article Request Form](#)

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Surgery

Pelletier, S. J., J. C. Hundley, M. J. Englesbe, A. P. Rojas, R. H. Bartlett and J. D. Punch (2009). "Liver Transplantation and ECMO-Assisted Donation after Cardiac Death." American Journal of Transplantation **9**: 263-263. [Article Request Form](#)

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Surgery

Slater, R. R., F. Mossa-Basha, A. Abou-Abbass, A. Kapke, D. Y. Kim, M. S. Abouljoud and A. Yoshida (2009). "The Impact of Surgeon Fatigue on Liver Transplant Outcomes." American Journal of Transplantation **9**: 609-610. [Article Request Form](#)

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Surgery

Weir, M., S. Mulgaonkar, T. Pearson, A. Patel, D. Patel, H. Shidban and J. Scandling (2009). "Mycophenolate Mofetil/Sirolimus Maintenance Therapy after Calcineurin Inhibitor Withdrawal in Renal Transplant Recipients: 2-Year Outcomes of the Spare-the-Nephron (STN) Trial." American Journal of Transplantation **9**: 200-201. [Article Request Form](#)

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Urology

Ficarra, V., G. Novara, W. Artibani, A. Cestari, A. Galfano, M. Graefen, G. Guazzoni, B. Guillonnet, M. Menon, F. Montorsi, V. Patel, J. Rassweiler and H. Van Poppel (2009). "Retropubic, Laparoscopic, and Robot-Assisted Radical Prostatectomy: A Systematic Review and Cumulative Analysis of Comparative Studies." European Urology **55**(5): 1037-1063. [PDF Full-Text](#)

Context: Despite the wide diffusion of laparoscopic radical prostatectomy (LRP) and robot-assisted laparoscopic radical prostatectomy (RALP), only few studies comparing the results of these techniques with the retropubic radical prostatectomy (RRP) are currently available. Objective: To evaluate the perioperative, functional, and oncologic results in the comparative studies evaluating RRP, LRP, and RALP. Evidence acquisition: A systematic review of the literature was performed in January 2008, searching Medline, Embase, and Web of Science databases. A "free-text" protocol using the term radical prostatectomy was applied. Some 4000 records were retrieved from the Medline database; 2265 records were retrieved from the Embase database; and 4219 records were retrieved from the Web of Science database. Three of the authors reviewed the records to identify comparative studies. A cumulative analysis was conducted using Review Manager software v.4.2 (Cochrane Collaboration, Oxford, UK). Evidence synthesis: Thirty-seven comparative studies were identified in the literature search, including a single, randomised, controlled trial. With regard to the perioperative outcome, LRP and RALP were more time consuming than RRP, especially in the initial steps of the learning curve, but blood loss, transfusion rates, catheterisation time, hospitalisation duration, and complication rates all favoured LRP. With regard to the functional results, LRP and RRP showed similar continence and potency rates. Similarly, no significant differences were identified between LRP and RALP, while a single, nonrandomised, prospective study suggested advantages in terms of both continence and potency recovery after RALP, compared with RRP. With regard to the oncologic outcome, LRP and RALP were associated with positive surgical margin rates similar to those of RRP. Conclusions: The quality of the available comparative studies was not excellent. LRP and RALP are followed by significantly lower blood loss and transfusion rates, but the available data were not sufficient to prove the superiority of any surgical approach in terms of functional and oncologic outcomes. Further high-quality, prospective, multicentre, comparative studies are needed.

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Urology

Krane, L. S., M. Bhandari, J. O. Peabody and M. Menon (2009). "Impact of Percutaneous Suprapubic Tube Drainage on Patient Discomfort after Radical Prostatectomy." Eur Urol EPub Ahead of Print. [PDF Full-Text](#)

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BACKGROUND: Patients undergoing radical prostatectomy (RP) traditionally require urethral catheterization for adequate bladder drainage in the postoperative period. However, many patients have significant discomfort from the urethral catheter. **OBJECTIVE:** To describe a technique of percutaneous suprapubic tube (PST) bladder drainage after robotic-assisted laparoscopic radical prostatectomy (RALP) and to evaluate patient discomfort, complications, continence, and stricture rate after this procedure. **DESIGN, SETTING, AND PARTICIPANTS:** Two hundred two patients undergoing RALP were drained with a 14F PST instead of a urethral catheter. The PST was placed robotically at the conclusion of the urethrovesical anastomosis and secured to the skin over a plastic button. Beginning on postoperative day 5, patients clamped the PST, urinated per urethra, and measured the postvoid residual (PVR) drained by PST. The PST was removed when residuals were <30cm(3) per void. The control group consisted of 50 consecutive patients undergoing RALP with urethral catheter drainage. **MEASUREMENTS:** The primary end point was catheter-associated discomfort as measured with the Faces Pain Score-Revised (FPS-R). Secondary end points included use of anticholinergics, complications related to the PST, urinary continence, and urethral stricture. **RESULTS AND LIMITATIONS:** When compared with urethral catheter patients, PST patients had significantly decreased catheter-related discomfort on postoperative days 2 and 6 ($p<0.001$). Anticholinergic medication was required by one PST and four urethral catheter patients ($p<0.001$). Ten patients required urethral catheterization for PST dislodgement ($n=5$) or urinary retention ($n=5$). No patient has developed a urethral stricture at a mean follow-up of 7 mo. **CONCLUSIONS:** PST provides adequate urinary drainage following RALP with less patient discomfort and no increased risk of urethral stricture.

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Urology

Menon, M., A. Shrivastava, M. Bhandari, R. Satyanarayana, S. Siva and P. K. Agarwal (2009). "Vattikuti Institute Prostatectomy: Technical Modifications in 2009." [Eur Urol EPub Ahead of Print](#). [PDF Full-Text](#)

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BACKGROUND: Since we last published our technique of robotic prostatectomy, we have introduced three technical refinements: superviseil nerve sparing, bladder drainage with a percutaneous suprapubic tube (PST), and limited node dissection of the obturator and internal iliac nodes in preference to the external iliac nodes in selected patients. **OBJECTIVE:** To describe selection criteria, to explain the three techniques, and to evaluate functional and oncologic results. **DESIGN, SETTING, AND PARTICIPANTS:** Single-institution study of 1151 radical prostatectomies performed from 2006 to 2008 by one surgeon. **SURGICAL PROCEDURE:** The superviseil nerve-sparing technique spares nerves from the 11-o'clock position to the 1-o'clock position. The bladder is drained with a PST rather than a urethral catheter. For low- or intermediate-risk disease, limited lymphadenectomy concentrates on the internal iliac and obturator nodes, excluding the external iliac lymph nodes. **MEASUREMENTS:** Erectile function and patient comfort were evaluated using questionnaires administered by a third party. Lymph node yield was quantified by a qualified urologist. **RESULTS AND LIMITATIONS:** At 6-18 months after surgery, 94% of men who attempted sexual intercourse were successful with a median Sexual Health Inventory For Men (SHIM) score of 18 out of 25. PST bladder drainage resulted in less patient discomfort; visual analog scores were 2 at 2 days after prostatectomy and 0 at 6 days after prostatectomy. The modified lymphadenectomy harvested few overall nodes, but it increased the yield of positive nodes >13-fold in patients with low-risk stratification (6.7% compared with 0.5%). **CONCLUSION:** In this single-institution, single-surgeon study, these modifications improved erectile function outcomes, decreased catheter-associated discomfort, and enhanced the detection of positive nodes.

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Urology

Patel, M. N., M. Bhandari, M. Menon and C. G. Rogers (2009). "Robotic-assisted partial nephrectomy." [Bju International](#) **103**(9): 1296-1311. [PDF Full-Text](#)