

## Henry Ford Health System Publication List - February 2010

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### Anesthesiology

Kim, D. and R. Wadley (2010). "Variability in Techniques and Patient Safety Protocols in Discography: A National Multispecialty Survey of International Spine Intervention Society Members." J Spinal Disord Tech **Epub Ahead of Print.** [Article Request Form](#)

Department of Anesthesiology, Division of Pain Medicine, Henry Ford Medical Center, Detroit, MI.

STUDY DESIGN: National survey. OBJECTIVE: (1) Characterize the way discography is being carried out and by which specialties. (2) Quantify adherence to the International Spine Intervention Society (ISIS) guidelines. (3) To see if there is experience or specialty differences in technique. BACKGROUND: Discography is a controversial diagnostic tool that attempts to correlate disc morphology to concordant pain. It is increasingly performed by different specialties as a prelude to fusion, disc replacement, and percutaneous intradiscal procedures. A consensus committee of the ISIS has published guidelines for performing discography to increase diagnostic accuracy, standardize technique, and improve patient safety. This survey wishes to see how closely these guidelines are followed. METHODS: In all, 500 members of the ISIS were randomly selected to receive a 13-item questionnaire. The questions included the following demographic information: specialty, number of discograms in 1 year (<15, 15-50, >50). Patient safety questions included the following: use of preoperative antibiotics, intradiscal antibiotics, postoperative antibiotics, and use of double needle technique. Technical questions included the following: needle entry on the opposite site of symptoms, injecting the control disc first, using manometry to record opening pressure, using manometry to record pressure on pain reproduction, injecting discs adjacent to the painful disc, and using pain assessment forms. Comparison of responses was made between specialties. Responses to the questions were also compared based on the number of procedures performed per year. RESULTS: The response rate to the questionnaire was 34.6%. Of the 173 respondents, the following specialties were represented: 100 (57.8%) Anesthesiology, 53 (30.6%) Physical Medicine and Rehabilitation (PMR), 16 (9.2%) Radiology, 4 (2.3%) Other. Number of procedures carried out was as follows: <15 (22.54%), 15 to 50 (50.86%), >50 (26.58%). The adherence to patient safety guidelines were as follows: preoperative antibiotics (83.81%), intradiscal antibiotics (84.97%), postprocedure antibiotics (9.82%), use of double needle technique (64.16%). The adherence to technical guidelines were as follows: optional use of computed tomography scan (64.78%), pain assessment sheet (66.47%), entering on the side opposite symptoms (48.55%), manometry for opening pressure (65.31%), manometry of pain reproduction pressure (72.25%), injecting a control disc first (78.61%), injecting discs adjacent to the painful disc (56.64%). Significant differences across Anesthesiology, PMR, and Radiology were detected for computed tomography, intradiscal antibiotics, opening pressure, pain assessment form, and pain pressure measurement. There was no effect of volume of procedures done on overall adherence to guidelines. A significant interaction between specialty and number of procedures performed was detected for

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compliance with intradiscal antibiotics ( $P=0.092$ ), opening pressure ( $P=0.027$ ), and pain pressure ( $P=0.029$ ) for respondents with >50 procedures. Respondents in Radiology were approximately 98% less likely to use intradiscal antibiotics compared with those in Anesthesiology (odds ratio, 0.019; 95% confidence interval, 0.001-0.264). PMR respondents were approximately 83% less likely than Anesthesiologists to use opening pressure (odds ratio, 0.168; 95% confidence interval, 0.035-0.82) when procedures were <15 per year. CONCLUSIONS: Discography is being performed by multiple different specialties: Anesthesiology, PMR, Radiology (highest to lowest in number, respectively). Overall adherence to guidelines pertaining to infection control was fair except for double needle technique which was poor. Adherence to guidelines that affect the diagnostic value was poor. There is specialty variation in adherence to guidelines and to a lesser extent volume based effect on compliance.

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### **Biostatistics & Research Epidemiology**

Berenson, K., A. Ogbonnaya, R. Casciano, D. Makenbaeva, E. Mozaffari, L. Lamerato and J. Corbelli (2010). "Economic consequences of ACS-related rehospitalizations in the US." Current Medical Research and Opinion **26**(2): 329-336. [Article Request Form](#)

[Berenson, Karina; Ogbonnaya, Augustina; Casciano, Roman] Analyt Int, New York, NY 10018 USA. [Makenbaeva, Dinara] Bristol Myers Squibb Co, Plainsboro, NJ USA. [Mozaffari, Essy] Sanofi Aventis, Bridgewater, NJ USA. [Lamerato, Lois] Henry Ford Hosp, Detroit, MI 48202 USA. [Corbelli, John] SUNY, Buffalo Sch Med & Biomed Sci, Williamsville, NY USA. [Corbelli, John] Buffalo Cardiol & Pulm Associates PC, Buffalo, NY USA.

Berenson, K, Analyt Int, 24 W 40th St, New York, NY 10018 USA. [kberenson@analyticaintl.com](mailto:kberenson@analyticaintl.com)

Objective: To examine economic consequences related to rehospitalization following initial acute coronary syndrome (ACS) treatment in United States managed care settings. Study design: Retrospective observational studies. Research design and methods: Retrospective observational studies were conducted on two managed care populations to examine medical encounter insurance claims and charges for ACS-related rehospitalizations following an index hospitalization for new onset ACS (2002-2007). All charges were adjusted to year 2007 United States Dollars (USDs). Main outcome measures: The main outcomes for this study were the direct charges related to ACS rehospitalizations as captured in two separate medical encounter claims databases. Results: Of the 11,266 ACS patients identified for analysis in the health system plan, 3588 (32%) had at least one ACS rehospitalization. Of the 97,177 ACS patients enrolled in the nationally representative managed care database, 32,578 (34%) had at least one ACS-related rehospitalization. Multivariate analyses demonstrated that coronary artery bypass graft (CABG) was the strongest predictor of increased charges during the recurrence in both populations ( $p<0.0001$ ). When controlling for length of stay (LOS) in the model, CABG remained a significant predictor of increased charges, while percutaneous coronary intervention (PCI) and stent insertion became even stronger predictors of increased charges. Conclusions: The costs associated with ACS-related rehospitalizations in a real-world setting are high, even when controlling for known cost drivers such as length of stay.

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### **Biostatistics & Research Epidemiology**

Hensley Alford, S. M., R. E. Lappin, L. Peterson and C. C. Johnson (2009). "Pregnancy associated smoking behavior and six year postpartum recall." Matern Child Health J **13**(6): 865-72. [PDF Full-Text](#)

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BACKGROUND: This study examined predictors and behaviors of pregnancy-related smoking among women who belonged to a private health maintenance organization and the recall accuracy of pregnancy-related smoking behaviors after 6-years. METHODS: A cohort of 725 pregnant women was followed for six years. Major predictors for smoking behavior before, during, and one-year following pregnancy were determined. In addition, accuracy of recall six years postpartum of smoking behavior at the time of pregnancy and one-year postpartum was tested. RESULTS: Mother's education, asthma status, amount of pre-pregnancy smoking, gravidity, and father's smoking status were important in the prediction of pregnancy associated smoking. Agreement for recall of smoking behavior during pregnancy (6 year recall) and one-year postpartum (5 year recall) were 90% and 91%, respectively. CONCLUSIONS: Despite potentially adverse outcomes, a proportion

of women continue to smoke throughout pregnancy. A number of variables proved to be important predictors of pregnancy associated smoking behavior. These factors should be considered by smoking cessation programs targeting women of reproductive age. Additionally, there was substantial agreement for maternal recall at six years postpartum of smoking behavior at the time of pregnancy and one-year postpartum. This should be considered in retrospective study designs that are primarily based on maternal recall of smoking behaviors before, during, and following pregnancy.

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### **Biostatistics & Research Epidemiology**

Levin, A. M., I. Datta, J. Yang, M. C. Iannuzzi, P. M. McKeigue, B. A. Rybicki and C. L. Gray-McGuire (2009). "Ancestry Informative Markers and Family-Based Association." Genetic Epidemiology **33**(8): 107. [Article Request Form](#)

[Levin, Albert M.; Datta, Indrani; Yang, James; Rybicki, Benjamin A.] Henry Ford Hlth Syst, Detroit, MI USA. [Iannuzzi, Micheal C.] SUNY Upstate Med Univ, Syracuse, NY USA. [McKeigue, Paul M.] Univ Edinburgh, Western Gen Hosp, Edinburgh EH8 9YL, Midlothian, Scotland. [Gray-McGuire, Courtney L.] Oklahoma Med Res Fdn, Oklahoma City, OK USA.

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### **Biostatistics & Research Epidemiology**

McNeal, C. J., T. Dajani, D. Wilson, A. E. Cassidy-Bushrow, J. B. Dickerson and M. Ory (2010). "Hypercholesterolemia in Youth: Opportunities and Obstacles to Prevent Premature Atherosclerotic Cardiovascular Disease." Current Atherosclerosis Reports **12**(1): 20-28. [PDF Full-Text](#)

[McNeal, Catherine J.] Scott & White Mem Hosp & Clin, Dept Pediat, Div Cardiol, Temple, TX 76502 USA. [McNeal, Catherine J.] Scott & White Mem Hosp & Clin, Dept Internal Med, Temple, TX 76502 USA. [Dajani, Tala; Wilson, Don] Phoenix Childrens Hosp, Div Endocrinol & Diabet, Phoenix, AZ 85016 USA. [Cassidy-Bushrow, Andrea E.] Henry Ford Hosp, Dept Biostat & Res Epidemiol, Detroit, MI 48202 USA. [Dickerson, Justin B.] Oregon Dept Human Serv, Salem, OR 97301 USA. [Ory, Marcia] Sch Rural Publ Hlth, Dept Social & Behav Hlth, College Stn, TX 77843 USA. McNeal, CJ, Scott & White Mem Hosp & Clin, Dept Pediat, Div Cardiol, 2401 S 31st St, Temple, TX 76502 USA. [cmcneal@swmail.sw.org](mailto:cmcneal@swmail.sw.org) [tdajani@phoenixchildrens.com](mailto:tdajani@phoenixchildrens.com) [dpwilson@phoenixchildrens.com](mailto:dpwilson@phoenixchildrens.com) [acassid1@hfhs.org](mailto:acassid1@hfhs.org) [justin.b.dickerson@state.or.us](mailto:justin.b.dickerson@state.or.us) [mory@srph.tamhsc.edu](mailto:mory@srph.tamhsc.edu)

Treatment of hypercholesterolemia in youth is predicated on the knowledge that we can identify those youth with this atherosclerotic risk factor most likely to develop premature cardiovascular disease. Unfortunately, this is not the case. Before we can adequately address appropriate lipid-lowering therapies in this special population, we must address and resolve current barriers related to screening and diagnosis. In this article, we describe some of the opportunities and obstacles that clinicians and policy makers confront when applying the current pediatric guidelines focused on screening and treating hypercholesterolemia in the pediatric population.

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### **Biostatistics & Research Epidemiology**

Sukhanova, A., D. P. Ritzwoller, G. Alexander, J. H. Calvi, C. Carlier, J. B. McClure, S. Rolnick and C. Johnson (2009). "Cost analyses of a web-based behavioral intervention to enhance fruit and vegetable consumption." International Journal of Behavioral Nutrition and Physical Activity **6**. [PDF Full-Text](#)

[Sukhanova, Anna; Ritzwoller, Debra P.] Kaiser Permanente, Inst Hlth Res, Denver, CO USA. [Alexander, Gwen; Johnson, Christine] Henry Ford Hlth Syst & Hosp, Detroit, MI USA. [Calvi, Josephine H.] Kaiser Permanente, Ctr Hlth Res, Atlanta, GA USA. [Carlier, Carola] Univ Michigan, Ann Arbor, MI 48109 USA. [McClure, Jennifer B.] Grp Hlth Res Inst, Seattle, WA USA. [Rolnick, Sharon] HealthPartners Res Fdn, Minneapolis, MN USA. Sukhanova, A, Kaiser Permanente, Inst Hlth Res, Denver, CO USA. [anna.sukhanova@kp.org](mailto:anna.sukhanova@kp.org) [debra.ritzwoller@kp.org](mailto:debra.ritzwoller@kp.org) [galexan2@hfhs.org](mailto:galexan2@hfhs.org) [josephine.calvi@kp.org](mailto:josephine.calvi@kp.org) [ccarlier@umich.edu](mailto:ccarlier@umich.edu) [mcclure.j@ghc.org](mailto:mcclure.j@ghc.org) [cheri.j.rolnick@healthpartners.com](mailto:cheri.j.rolnick@healthpartners.com) [cjohnso1@hfhs.org](mailto:cjohnso1@hfhs.org)

Background: The purpose of this paper is to evaluate costs associated with the online intervention trial, Making Effective Nutritional Choices for Cancer Prevention (MENU), and to connect the findings to the study outcomes. Methods: Using prospective data collected during the MENU development and implementation phases, we estimated overall costs per person, incremental costs for the three arms of the MENU intervention, and incremental costs per change in fruit and vegetable (F&V) consumption across the studied population. The MENU study was conducted in five HMO sites of the Cancer Research Network. The number of eligible study participants who were enrolled in the study was 2,540. Recruited participants were randomized into (1) an untailed website program, (2) tailored website program, or (3) tailored web program plus personalized counseling (HOBI) via email. The primary measures for these analyses include the total intervention costs, average cost per participant, and the average cost per mean change in daily intake of F&V, stratified by study arm. Results: The mean change in F&V consumption was greater in both the tailored arm and statistically higher in the HOBI arm relative to the untailed arm. The untailed arm achieved +2.34 servings increase vs. the tailored website arm (+2.68) and the HOBI arm (+2.80) servings increase. Total intervention costs for MENU participants who completed the 12-month follow-up assessment, by study arm, were estimated to be \$197,197 or \$110 respectively. This translates to \$69 per participant in the untailed web site intervention, \$81 per participant in the tailored website intervention, and \$184 per participant in the HOBI intervention and a cost per average change in F&V consumption to be \$35, \$27 and \$61 respectively. Conclusions: Providing personalized "tailored" messages and additional personalized support via email generated an additional \$12-\$115 per participant, over the untailed web program. Incremental increases in F&V consumption associated with the email support arm were associated with considerable increases in intervention costs, suggesting that the most cost effective arm of the MENU study by servings gained was the tailored website.

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### **Biostatistics & Research Epidemiology**

Yang, J. J. (2010). "Distribution of Fisher's combination statistic when the tests are dependent." Journal of Statistical Computation and Simulation **80**(1-2): 1-12. [Article Request Form](#)

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Many questions in multivariate analysis involve the situation when the number of variables is greater than the available sample size. Combination test statistics provides one method to deal with this situation. However, the properties of this approach have not been fully investigated. In this article, an approximation to the null distribution of fisher's method of combining one-sided test statistics was investigated using the pairwise correlations. The unbiased variance estimate of the combination test statistic is derived. A Monte Carlo study indicates that the new approximation provides a closer type-I error rate than other existing methods.

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### **Cardiology**

Al-Mallah, M. H., K. M. Chinnaiyan, A. Abidov, D. Share and G. Raff (2009). "Coronary CT Angiography and Racial Differences in Post-Test Resource Utilization: The ACIC Registry." Circulation **120**(18): S343-S343. [Article Request Form](#)

[Al-Mallah, Mouaz H.] Henry Ford Hosp, Detroit, MI 48202 USA. [Chinnaiyan, Kavitha M.; Abidov, Aiden; Raff, Gilbert] William Beaumont Hosp, Royal Oak, MI 48072 USA. [Share, David] Univ Michigan, Ann Arbor, MI 48109 USA.

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### **Cardiology**

Chinnaiyan, K. M., A. Abidov, M. Al-Mallah, G. L. Raff, P. A. Marcovitz and C. L. Grines (2009). "Effect of Gender on Management of Suspected Coronary Artery Disease After Coronary CT Angiography." Circulation **120**(18): S344-S344. [Article Request Form](#)

[Chinnaiyan, Kavitha M.; Abidov, Aiden; Raff, Gilbert L.; Marcovitz, Pamela A.; Grines, Cindy L.] William Beaumont Hosp, Royal Oak, MI 48072 USA. [Al-Mallah, Mouaz] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Cardiology**

Gerson, M. C., J. H. Caldwell, K. Ananthasubramaniam, I. P. Clements, M. J. Henziava, A. Amanullah and A. F. Jacobson (2009). "Influence of Diabetes Mellitus on Prognostic Utility of Imaging of Myocardial Sympathetic Innervation in Heart Failure Patients: Further Observations From ADMIRE-HF." Circulation **120**(18): S348-S348. [Article Request Form](#)

[Gerson, Myron C.] Univ Cincinnati, Coll Med, Cincinnati, OH USA. [Caldwell, James H.] Univ Washington, Seattle, WA 98195 USA. [Ananthasubramaniam, Karthik] Henry Ford Hosp, Detroit, MI 48202 USA. [Clements, Ian P.] Mayo Clin, Rochester, MN USA. [Henziava, Milena J.] Mt Sinai Med Ctr, New York, NY 10029 USA. [Amanullah, Aman] Albert Einstein Med Ctr, Philadelphia, PA 19141 USA. [Jacobson, Arnold F.] GE Healthcare, Princeton, NJ USA.

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### **Cardiology**

Jackson, E., M. Moscucci, D. E. Smith, D. Share, S. Dixon, A. Greenbaum and H. S. Gurm (2009). "Is Gender Still Relevant to the Outcome of Patients Undergoing Primary Percutaneous Coronary Intervention for ST-Elevation Myocardial Infarction in the Contemporary Era? Insights From the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2)." Circulation **120**(18): S421-S422. [Article Request Form](#)

[Jackson, Elizabeth; Smith, Dean E.; Share, David; Gurm, Hitinder S.] Univ Michigan, Med Ctr, Ann Arbor, MI USA. [Moscucci, Mauro] Univ Miami, Miller Med Cntr, Miami, FL USA. [Dixon, Simon] William Beaumont Hosp, Royal Oak, MI 48072 USA. [Greenbaum, Adam] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Cardiology**

Kadish, A. H., K. Nademanee, K. Volosin, S. Krueger, S. Neelagaru, N. Raval, O. Obel, S. Weiner, M. Wish, P. Carson, K. Ellenbogen, R. Bourge, M. Parides, R. Chiacchierini, R. Goldsmith, S. Goldstein, Y. Mika, D. Burkhoff and W. Abraham (2009). "Cardiac Contractility Modulation Improves Exercise Tolerance in NYHA Class III Patients With Narrow QRS and EF Between 25 and 35%: A Subgroup Analysis of the FIX-HF-5 Study." Circulation **120**(18): S824-S824. [Article Request Form](#)

[Kadish, Alan H.] Northwestern Univ, Mem Hosp, Chicago, IL 60611 USA. [Nademanee, Koonlawee] Pacific Rim EP, Inglewood, CA USA. [Volosin, Kent] Univ Penn, Philadelphia, PA 19104 USA. [Krueger, Steven] Bryan LGH, Lincoln, NE USA. [Neelagaru, Suresh] Lone Star Arrhythmia, Amarillo, TX USA. [Raval, Nirav] St Josephs Rsch Inst, Atlanta, GA USA. [Obel, Owen] UT SW, Dallas, TX USA. [Weiner, Stanislav] Tyler CVC, Tyler, TX USA. [Wish, Marc] Inova Arrhythmia Associates, Fairfax, VA USA. [Carson, Peter] Washington VAMC, Washington, DC USA. [Ellenbogen, Kenneth] Virginia Commonwealth Univ, Med Coll Virginia, Richmond, VA 23298 USA. [Bourge, Robert] Univ Alabama, Birmingham, AL USA. [Parides, Michael] Mt Sinai Sch Med, New York, NY USA. [Chiacchierini, Richard] RP Chiacchierini & Associates, Rockville, MD USA. [Goldsmith, Rochelle] Columbia Univ, New York, NY USA. [Goldstein, Sidney] Henry Ford Hosp, Detroit, MI 48202 USA. [Mika, Yuval; Burkhoff, Daniel] Impulse Dynam, Orangeburg, NY USA. [Abraham, William] Ohio State Univ, Columbus, OH 43210 USA.

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### **Cardiology**

Keteyian, S. J., J. L. Fleg, C. A. Brawner and I. L. Pina (2010). "Role and benefits of exercise in the management of patients with heart failure." Heart Fail Rev **EPub Ahead of Print**. [PDF Full-Text](#)

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Initial research established the feasibility of exercise training in patients with heart failure, as well as associated physiological benefits. This review summarizes the findings from over two dozen single-site studies that address the effect of exercise training on exercise capacity and cardiovascular and peripheral function. In addition, it incorporates the results from two meta-analyses and a recently completed multi-center trial, all of which studied the effects of exercise training on clinical outcomes. The major conclusions from these studies are that exercise training is safe; improves health status and exercise capacity; helps attenuate much of the abnormal pathophysiology that develops with heart failure; and yields a modest reduction in clinical events. The magnitude of the clinical benefits appears related to the volume of exercise completed. Future research is needed to identify which patient subgroups might benefit the most from exercise training, the optimal exercise dose or load needed to lessen disease-related symptoms and maximize clinical benefit, and the effects of exercise training in patients with heart failure and preserved left ventricular systolic function.

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### **Cardiology**

Lanfear, D., M. C. Kontos, F. M. Tang, S. Daugherty, P. G. Jones and J. A. Spertus (2009). "Biomarker Elevations Late After Myocardial Infarction and Association With Health Status." Circulation **120**(18): S393-S393. [Article Request Form](#)

[Lanfear, David] Henry Ford Hosp, Detroit, MI 48202 USA. [Kontos, Michael C.] Virginia Commonwealth Univ Med Coll Virginia, Charlottesville, VA USA. [Tang, Fengming; Jones, Philip G.; Spertus, John A.] St Lukes Hosp, Mid Amer Heart Inst, Kansas City, MO 64111 USA. [Daugherty, Stacie] Univ Colorado, Hlth Sci Ctr, Denver, CO USA.

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### **Cardiology**

Lanfear, D., K. Wells, J. Campbell, O. Uju-Eke, D. Favro, D. Wu, H. Phatak, E. L. Peterson and L. K. Williams (2009). "Reversibility of Worsened Renal Function During Acute Heart Failure Hospitalization and Association With Subsequent Outcomes." Circulation **120**(18): S485-S485. [Article Request Form](#)

[Lanfear, David; Wells, Karen; Campbell, Janis; Uju-Eke, Oluchi; Favro, David; Peterson, Edward L.; Williams, L. Keoki] Henry Ford Hosp, Detroit, MI 48202 USA. [Wu, David; Phatak, Hemant] Merck, Whitehouse Stn, NJ USA.

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### **Cardiology**

Myers, J., R. L. Goldsmith, S. J. Keteyian, C. A. Brawner, J. K. Ehrman, D. A. Brazil, H. Aldred, S. Hallenbeck and D. Burkhoff (2009). "The Ventilatory Anaerobic Threshold in Heart Failure: A Multi-Center Evaluation of Reliability." Circulation **120**(18): S549-S550. [Article Request Form](#)

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

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### **Cardiology**

Sabbah, H. N., M. Wang, A. Jiang, I. Ilsar, R. C. Gupta and S. Rastogi (2009). "Long-term Monotherapy With Ivabradine Improves Left Ventricular Function and Prevents Progressive Chamber Remodeling in Dogs With Moderate Heart Failure." Circulation **120**(18): S867-S868. [Article Request Form](#)

[Sabbah, Hani N.; Wang, Mengjun; Jiang, Alice; Ilsar, Itamar; Gupta, Ramesh C.; Rastogi, Sharad] Henry Ford Hosp, Detroit, MI 48202 USA.

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## Cardiology

Sabbah, H. N., M. J. Wang, A. Jiang, I. Ilsar, M. S. Sabbah, S. Helgerson, R. Peterson, N. Tarazona and R. Lee (2009). "Circumferential Mid-Ventricular Intramyocardial Injections of Alginate Hydrogel Improve Left Ventricular Function and Prevent Progressive Remodeling in Dogs With Chronic Heart Failure." Circulation **120**(18): S912-S912. [Article Request Form](#)

[Sabbah, Hani N.; Wang, Mengjun; Jiang, Alice; Ilsar, Itamar; Sabbah, Michael S.] Henry Ford Hosp, Detroit, MI 48202 USA. [Helgerson, S.; Peterson, R.; Tarazona, N.] Symphony Med Inc, Laguna Hills, CA USA. [Lee, R.] UCSF, San Francisco, CA USA.

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## Cardiology

Sharma, K., J. J. Rivera, M. J. Budoff, R. Blankstein, M. H. Al-Mallah, N. D. Wong, L. J. Shaw, J. Carr, D. O'Leary, J. A. Lima, M. Szklo, R. S. Blumenthal and K. Nasir (2009). "Relationship of Premature Family History of Coronary Heart Disease With Coronary Artery Calcium Progression in the Multi-Ethnic Study of Atherosclerosis." Circulation **120**(18): S537-S538. [Article Request Form](#)

[Sharma, Kavita; Rivera, Juan J.; Lima, Joao A.; Szklo, Moyses; Blumenthal, Roger S.; Nasir, Khurram] Johns Hopkins Univ, Baltimore, MD USA. [Budoff, Matthew J.] Univ Calif Los Angeles, Harbor Med Ctr, Los Angeles Biomed Res Inst, Torrance, CA 90509 USA. [Blankstein, Ron] Brigham & Womens Hosp, Boston, MA 02115 USA. [Al-Mallah, Mouaz H.] Henry Ford Hosp, Detroit, MI 48202 USA. [Wong, Nathan D.] Univ Calif Irvine, Irvine, CA USA. [Shaw, Leslee J.] Emory Univ, Atlanta, GA 30322 USA. [Carr, Jeffrey] Wake Forest Univ, Winston Salem, NC 27109 USA. [O'Leary, Daniel] Caritas Carney Hosp, Dorchester, MA USA.

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## Cardiology

Sinno, M. C., A. A. Alsheikh-Ali, R. Mokdad, M. Zaidan, J. Chattahi and M. H. Al-Mallah (2009). "Diagnostic Accuracy of Electrocardiographic Criteria for Left Ventricular Hypertrophy: Comparison With Computed Tomography." Circulation **120**(18): S673-S673. [Article Request Form](#)

[Mokdad, Rana; Zaidan, Mohammad; Chattahi, Joseph; Al-Mallah, Mouaz H.] Henry Ford Hosp, Detroit, MI 48202 USA. [Alsheikh-Ali, Alawi A.] Tufts New England Med Cntr, Boston, MA USA.

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## Cardiology

Tisdale, J. E., B. R. Overholser, K. M. Sowinski, H. A. Wroblewski, K. Amankwa, S. Borzak, J. R. Kingery, R. Coram, D. P. Zipes, D. A. Flockhart and R. J. Kovacs (2009). "Increased Myocardial Sensitivity to I-Kr Inhibition in Patients With Heart Failure Due to Left Ventricular Systolic Dysfunction." Circulation **120**(18): S640-S640. [Article Request Form](#)

[Tisdale, James E.; Overholser, Brian R.; Sowinski, Kevin M.; Wroblewski, Heather A.; Amankwa, Kwadwo] Purdue Univ, Indianapolis, IN USA. [Borzak, Steven] Henry Ford Hosp, Detroit, MI 48202 USA. [Kingery, Joanna R.] Clarian Hlth Partners, Indianapolis, IN USA. [Coram, Rita; Zipes, Douglas P.; Flockhart, David A.; Kovacs, Richard J.] Indiana Univ, Indianapolis, IN 46204 USA.

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## Cardiology

Travin, M., K. Ananthasubramaniam, M. J. Henzlova, I. P. Clements, A. Amanullah and A. F. Jacobson (2009). "Imaging of Myocardial Sympathetic Innervation for Prediction of Cardiac and All-cause Mortality in Heart Failure Patients: Analyses From the ADMIRE-HF Trial." Circulation **120**(18): S350-S350. [Article Request Form](#)

[Travin, Mark] Montefiore Med Ctr, New York, NY USA. [Ananthasubramaniam, Karthik] Henry Ford Hosp, Detroit, MI 48202 USA. [Henzlova, Milena J.] Mt Sinai Med Ctr, New York, NY 10029 USA. [Clements, Ian P.] Mayo Clin, Rochester, MN USA. [Amanullah, Aman] Albert Einstein Med Ctr, Philadelphia, PA 19141 USA. [Jacobson, Arnold F.] GE Healthcare, Princeton, NJ USA.

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### **Cardiology**

Wang, M. J., I. Ilsar, R. C. Gupta, A. Jiang, M. S. Sabbah, K. Dye and H. N. Sabbah (2009). "Intravenous GP531, an Adenosine Regulating Agent, Improves Left Ventricular Function in Dogs With Chronic Heart Failure." Circulation **120**(18): S853-S853. [Article Request Form](#)

[Wang, Mengjun; Ilsar, Itamar; Gupta, Ramesh C.; Jiang, Alice; Sabbah, Michael S.; Dye, Kaitlin; Sabbah, Hani N.] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Cardiology**

Wang, M. J., I. Ilsar, A. Jiang, M. S. Sabbah, R. C. Gupta, T. D. Cowart, R. Mazhari and H. N. Sabbah (2009). "Acute Intravenous Infusion of CXL-1020, a Nitroxyl Donor, Improves Left Ventricular Function in Dogs With Advanced Heart Failure." Circulation **120**(18): S852-S852. [Article Request Form](#)

[Wang, Mengjun; Ilsar, Itamar; Jiang, Alice; Sabbah, Michael S.; Gupta, Ramesh C.; Sabbah, Hani N.] Henry Ford Hosp, Detroit, MI 48202 USA. [Cowart, T. D.; Mazhari, Reza] Cardioxyl Pharmaceut Inc, Hunt Valley, MD USA.

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### **Dermatology**

Bi, X., J. Gu, Z. Guo, S. Tao, Y. Wang, L. Tang, J. Wu and Q. Mi (2010). "Different Pathways Are Involved in Arsenic-Trioxide-Induced Cell Proliferation and Growth Inhibition in Human Keratinocytes." Skin Pharmacology and Physiology **23**(2): 68-78. [PDF Full-Text](#)

[Bi, X.; Gu, J.; Guo, Z.; Tao, S.; Wang, Y.; Tang, L.; Wu, J.] Mil Med Coll 2, Changhai Hosp, Dept Dermatol, Shanghai 200433, Peoples R China. [Mi, Q.] Henry Ford Hosp, Dept Dermatol, Dept Med, Henry Ford Hlth Syst, Immunol Program, Detroit, MI 48202 USA.

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Background: Arsenic is a carcinogen that is associated with an increased risk of human skin cancer. On the other hand, arsenic trioxide (As<sub>2</sub>O<sub>3</sub>) has potential anticancer activity against a wide range of carcinomas. The mechanisms involved in these two opposing processes remain unclear. Methods: We used normal human keratinocytes (NHK), the human keratinocyte HaCaT cell line and human epidermal carcinoma cells (A431 cell line) to investigate potential pathways involved in the effects on cell proliferation and growth inhibition by different concentrations of As<sub>2</sub>O<sub>3</sub>. Results: At low concentrations (0.5-32 μM), As<sub>2</sub>O<sub>3</sub> enhanced keratinocyte proliferation and regulated the expression of about 172 genes. Among them, cell cycling pathway genes (including CDK4 and E2F1) were significantly upregulated. At high concentrations (0.5-10 μM), As<sub>2</sub>O<sub>3</sub> inhibited cell growth in NHK and HaCaT cells, but not in A431 cells. As<sub>2</sub>O<sub>3</sub> significantly induced NHK and HaCaT apoptosis through the activation of caspase-3, as well as cell cycle arrest at the G<sub>2</sub>-M phase. Conclusion: Our data suggest that different pathways are involved in As<sub>2</sub>O<sub>3</sub>-mediated proliferation and growth inhibition. In addition, skin carcinoma cells were resistant to As<sub>2</sub>O<sub>3</sub>-induced cell growth inhibition and apoptosis when compared to NHK and HaCaT cells. Therefore, As<sub>2</sub>O<sub>3</sub> may not be appropriate for treatment of skin carcinomas.

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### **Dermatology**

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

[Lim, Henry W.; Sage, Robert J.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.  
Lim, HW, Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.

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## **Dermatology**

Menter, A., N. J. Korman, C. A. Elmets, S. R. Feldman, J. M. Gelfand, K. B. Gordon, A. Gottlieb, J. Y. M. Koo, M. Lebwohl, H. W. Lim, A. S. Van Voorhees, K. R. Beutner and R. Bhushan (2010). "Guidelines of care for the management of psoriasis and psoriatic arthritis Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy." Journal of the American Academy of Dermatology **62**(1): 114-135.

[PDF Full-Text](#)

[Menter, Alan] Baylor Univ, Med Ctr, Psoriasis Res Ctr, Dallas, TX USA. [Korman, Neil J.] Univ Hosp Case Med Ctr, Murdough Family Ctr Psoriasis, Dept Dermatol, Cleveland, OH USA. [Elmets, Craig A.] Univ Alabama, Dept Dermatol, Birmingham, AL USA. [Feldman, Steven R.] Wake Forest Univ, Bowman Gray Sch Med, Dept Dermatol, Winston Salem, NC 27103 USA. [Gelfand, Joel M.] Univ Penn, Dept Dermatol, Philadelphia, PA 19104 USA. [Gelfand, Joel M.] Univ Penn, Ctr Clin Epidemiol & Biostat, Philadelphia, PA 19104 USA. [Gordon, Kenneth B.] Northwestern Univ, Fienberg Sch Med, Div Dermatol, Chicago, IL 60611 USA. [Gordon, Kenneth B.] Northwestern Univ, Fienberg Sch Med, Dept Dermatol, Chicago, IL 60611 USA. [Gottlieb, Alice] Tufts Univ, Sch Med, Tufts Med Ctr, Boston, MA 02111 USA. [Koo, John Y. M.; Beutner, Karl R.] Univ Calif San Francisco, Dept Dermatol, San Francisco, CA 94143 USA. [Lebwohl, Mark] Mt Sinai Sch Med, Dept Dermatol, New York, NY USA. [Lim, Henry W.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA. [Van Voorhees, Abby S.] Univ Penn, Dept Dermatol, Philadelphia, PA 19104 USA. [Beutner, Karl R.] Anacor Pharmaceut Inc, Palo Alto, CA USA. [Bhushan, Reva] Amer Acad Dermatol, Schaumburg, IL USA. Bhushan, R, 930 E Woodfield Rd, Schaumburg, IL 60173 USA. [rbhushan@aad.org](mailto:rbhushan@aad.org)

Psoriasis is a common, chronic, inflammatory, multisystem disease with predominantly skin and joint manifestations affecting approximately 2% of the population. In this fifth of 6 sections of the guidelines of care for psoriasis, we discuss the use of ultraviolet (LTV) light therapy for the treatment of patients with psoriasis. Treatment should be tailored to meet individual patients' needs. We will discuss in detail the efficacy and safety as well as offer recommendations for the use of phototherapy, including narrowband and broadband LNB and photochemotherapy using psoralen plus UVA, alone and in combination with topical and systemic agents. We will also discuss the available data for the use of the excimer laser in the targeted treatment of psoriasis. Finally, where available; we will summarize the available data that compare the safety and efficacy of the different forms of UV light therapy. (J Am Acad Dermatol 2010;62:114-35.)

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## **Dermatology**

Sage, R. J. and H. W. Lim (2010). "UV-based therapy and vitamin D." Dermatologic Therapy **23**(1): 72-81. [PDF Full-Text](#)

[Sage, Robert J.; Lim, Henry W.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.  
Lim, HW, Henry Ford Med Ctr, Dept Dermatol, New Ctr 1,3031 W Grand Blvd,Suite 800, Detroit, MI 48202 USA. [hlim1@hfhs.org](mailto:hlim1@hfhs.org)

The ultraviolet (UV) light spectrum has long been known to induce biologic effect on the skin. For a large number of cutaneous disorders, phototherapy and photochemotherapy are effective therapeutic options with excellent safety profiles and well-documented side effects. Despite their ease of administration and benefits, phototherapeutic treatment modalities require appropriate space for the equipment, trained staff, and patient education prior to initiating treatment. However, when the initial barriers to treatment can be overcome, UV therapy can offer patients significant relief from their cutaneous disease. Furthermore, UVB-based phototherapy can produce significant alteration to vitamin D levels. With the recent research implicating association of low vitamin D levels with a variety of health conditions, whether patients receiving phototherapy or, more specifically, those getting vitamin D supplement may be protected from these diseases remains to be established.

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## **Dermatology**

Sage, R. J. and H. W. Lim (2010). "THERAPEUTIC HOTLINE: Recommendations on photoprotection and vitamin D." *Dermatologic Therapy* **23**(1): 82-85. [PDF Full-Text](#)

[Sage, Robert J.; Lim, Henry W.] Henry Ford Hosp, Dept Dermatol, Detroit, MI 48202 USA.  
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Interest in the health benefits of vitamin D continues to increase and is at the forefront of much research and debate. Insufficient vitamin D levels have been linked in epidemiologic studies to decreased physical performance, cardiac health, autoimmune disease, neurologic disorders, colorectal and breast cancers, and total mortality. Consequently, health authorities are reviewing the most recent available data and updated recommendations on optimal vitamin D levels are pending. Daily intake of 1000 international units (IU) of vitamin D for adults and 400 IU of vitamin D for children may be appropriate for patients protecting their skin from UV radiation and can be safely obtained from diet and/or dietary supplementation. Patients should be counseled on sun protection regimens to prevent unprotected sun exposure and discouraged from using artificial tanning devices. As available information on vitamin D and its associated health benefits evolves, and as new evidence emerges, updated recommendations are sure to follow.

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## **Dermatology**

Woo, D. K. and M. J. Eide (2010). "Tanning beds, skin cancer, and vitamin D: an examination of the scientific evidence and public health implications." *Dermatologic Therapy* **23**(1): 61-71. [PDF Full-Text](#)

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Indoor tanning has become increasingly popular over the past decades, despite evidence of an increased risk of melanoma and, possibly, nonmelanoma skin cancer. Tanning bed proponents cite the health benefits of vitamin D to support indoor tanning, including concerns that reduced vitamin D levels or certain vitamin D receptor polymorphisms may be associated with increased incidence of various cancers, including cutaneous melanoma. However, most tanning devices primarily emit ultraviolet A, which is relatively ineffective in stimulating vitamin D synthesis. Health benefits can be fully dissociated from the ultraviolet exposure risks with vitamin D supplementation, although optimal levels remain to be established. Indoor tanning represents an avoidable risk factor for skin cancer, and education of the general public as well as the enactment and stricter enforcement of indoor tanning legislation are a public health imperative.

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## **Diagnostic Radiology**

Ali, M. M., B. Janic, A. Babajani-Feremi, N. R. S. Varma, A. S. M. Iskander, J. Anagli and A. S. Arbab (2010). "Changes in Vascular Permeability and Expression of Different Angiogenic Factors Following Anti-Angiogenic Treatment in Rat Glioma." *PLoS One* **5**(1). [PDF Full-Text](#)

[Ali, Meser M.; Janic, Branislava; Babajani-Feremi, Abbas; Varma, Nadimpalli R. S.; Iskander, A. S. M.; Anagli, John; Arbab, Ali S.] Henry Ford Hosp, Dept Radiol, Cellular & Mol Imaging Lab, Detroit, MI 48202 USA.  
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Background: Anti-angiogenic treatments of malignant tumors targeting vascular endothelial growth factor receptors (VEGFR) tyrosine kinase are being used in different early stages of clinical trials. Very recently, VEGFR tyrosine kinase inhibitor (Vetanalib, PTK787) was used in glioma patient in conjunction with chemotherapy and radiotherapy. However, changes in the tumor size, tumor vascular permeability, vascular density, expression of VEGFR2 and other angiogenic factors in response to PTK787 are not well documented. This study was to determine the changes in tumor size, vascular permeability, fractional plasma volume and

expression of VEGFR2 in PTK787 treated U-251 glioma rat model by in vivo magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT). The findings were validated with histochemical and western blot studies. Methodologies and Principal Findings: Seven days after implantation of U251 glioma cells, animals were treated with either PTK787 or vehicle-only for two weeks, and then tumor size, tumor vascular permeability transfer constant (K-trans), fractional plasma volume (fPV) and expression of VEGFR2 and other relevant angiogenic factors were assessed by in vivo MRI and SPECT (Tc-99m-HYNIC-VEGF), and by immunohistochemistry and western blot analysis. Dynamic contrast-enhanced MRI (DCE-MRI) using a high molecular weight contrast agent albumin-(GdDTPA) showed significantly increased K-trans at the rim of the treated tumors compared to that of the central part of the treated as well as the untreated (vehicle treated) tumors. Size of the tumors was also increased in the treated group. Expression of VEGFR2 detected by Tc-99m-HYNIC-VEGF SPECT also showed significantly increased activity in the treated tumors. In PTK787-treated tumors, histological staining revealed increase in microvessel density in the close proximity to the tumor border. Western blot analysis indicated increased expression of VEGF, SDF-1, HIF-1 alpha, VEGFR2, VEGFR3 and EGFR at the peripheral part of the treated tumors compared to that of central part of the treated tumors. Similar expression patterns were not observed in vehicle treated tumors. Conclusion: These findings indicate that PTK787 treatment induced over expression of VEGF as well as the Flk-1/VEGFR2 receptor tyrosine kinase, especially at the rim of the tumor, as proven by DCE-MRI, SPECT imaging, immunohistochemistry and western blot.

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### **Diagnostic Radiology**

Janic, B., A. M. Guo, A. S. Iskander, N. R. Varma, A. G. Scicli and A. S. Arbab (2010).

"Human cord blood-derived AC133+ progenitor cells preserve endothelial progenitor characteristics after long term in vitro expansion." PLoS One 5(2): e9173. 2820083. [PDF Full-Text](#)

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**BACKGROUND:** Stem cells/progenitors are central to the development of cell therapy approaches for vascular ischemic diseases. The crucial step in rescuing tissues from ischemia is improvement of vascularization that can be achieved by promoting neovascularization. Endothelial progenitor cells (EPCs) are the best candidates for developing such an approach due to their ability to self-renew, circulate and differentiate into mature endothelial cells (ECs). Studies showed that intravenously administered progenitors isolated from bone marrow, peripheral or cord blood home to ischemic sites. However, the successful clinical application of such transplantation therapy is limited by low quantities of EPCs that can be generated from patients. Hence, the ability to amplify the numbers of autologous EPCs by long term in vitro expansion while preserving their angiogenic potential is critically important for developing EPC based therapies. Therefore, the objective of this study was to evaluate the capacity of cord blood (CB)-derived AC133+ cells to differentiate, in vitro, towards functional, mature endothelial cells (ECs) after long term in vitro expansion. **METHODOLOGY:** We systematically characterized the properties of CB AC133+ cells over the 30 days of in vitro expansion. During 30 days of culturing, CB AC133+ cells exhibited significant growth potential that was manifested as 148-fold increase in cell numbers. Flow cytometry and immunocytochemistry demonstrated that CB AC133+ cells' expression of endothelial progenitor markers was not affected by long term in vitro culturing. After culturing under EC differentiation conditions, cells exhibited high expression of mature ECs markers, such as CD31, VEGFR-2 and von Willebrand factor, as well as the morphological changes indicative of differentiation towards mature ECs. In addition, throughout the 30 day culture cells preserved their functional capacity that was demonstrated by high uptake of Dil fluorescently conjugated-acetylated-low density lipoprotein (Dil-Ac-LDL), in vitro and in vivo migration towards chemotactic stimuli and in vitro tube formation. **CONCLUSIONS:** These studies demonstrate that primary CB AC133+ culture contained mainly EPCs and that long term in vitro conditions facilitated the maintenance of these cells in the state of commitment towards endothelial lineage.

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### **Diagnostic Radiology**

Mendiratta-Lala, M., T. Williams, N. de Quadros, J. Bonnett and V. Mendiratta (2010). "The Use of a Simulation Center to Improve Resident Proficiency in Performing Ultrasound-Guided Procedures." Acad Radiol **Epub Ahead of Print**. [Article Request Form](#)

From the Beth Israel Deaconess Hospital (M.M.-L.), One Deaconess Rd., Boston, MA 02215; Department of Radiology, Henry Ford Hospital, Detroit, MI (T.R.W., N.d.Q., J.B.); University of Michigan, West Bloomfield, MI (V.M.).

**RATIONALE AND OBJECTIVES:** With advancements in technology and push for health care reform and reduced costs, minimally invasive procedures, such as those that are ultrasound-guided, have become an essential part of radiology, and are used in many divisions of radiology. By incorporating standardized training methodologies in a risk free environment through utilization of a simulation center with phantom training, we hope to improve proficiency and confidence in procedural performance. **MATERIALS AND METHODS:** Twenty-nine radiology residents from four levels of training were enrolled in this prospective study. The residents were given written, video, and live interactive training on the basics of ultrasound-guided procedures in our simulation center on a phantom mannequin. All of the teaching materials were created by residents and staff radiologists at the institution. **RESULTS:** Residents demonstrated statistically significant improvement ( $P < .05$ ) between their pre- and posttest scores on both the written and practical examinations. They also showed a trend toward improved dexterity in the technical aspects of ultrasound-guided procedures ( $P = .07$ ) after training. On the survey questionnaire, residents confirm improved knowledge level, technical ability, and confidence levels pertaining to ultrasound-guided procedures. **CONCLUSIONS:** The use of controlled simulation based training can be an invaluable tool to improve the knowledge level, dexterity, and confidence of residents performing ultrasound-guided procedures. Additionally, a simulation model allows standardization of education.

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### **Emergency Medicine**

Coba, V., T. Andrzejewski, Y. Huang and H. Horst (2009). "Resuscitation Bundle Compliance in Severe Sepsis and Septic Shock: Better Late Than Never Still Improves Survival." Critical Care Medicine **37**(12): 903. [Article Request Form](#)

[Coba, Victor; Andrzejewski, Tanja; Huang, Yung; Horst, H.] Henry Ford Hosp, Detroit, MI USA.

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### **Emergency Medicine**

Donnino, M. W., M. Cocchi, E. Carney, J. Saliccoli, N. Joyce, S. Farris, J. Mackenhauer and J. Miller (2009). "Severity and Outcome of Post-Cardiac Arrest Syndrome: A Tale of Two Cities." Circulation **120**(18): S1472-S1472. [Article Request Form](#)

[Donnino, Michael W.; Cocchi, Michael; Carney, Erin; Saliccoli, Justin; Joyce, Nina; Mackenhauer, Julie] Beth Israel Deaconess Med Ctr, Boston, MA 02215 USA. [Farris, Sarah; Miller, Joseph] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Emergency Medicine**

Hartmann, O., J. Landsberg, C. Mueller, R. Nowak, P. Ponikowski, M. Moeckel, C. Hogan, A. H. B. Wu, M. Richards, G. S. Filippatos, S. Di Somma, I. S. Anand, L. Ng, S. X. Neath, R. Christenson, J. McCord, N. G. Morgenthaler, R. Engineer, A. Bergmann, S. D. Anker, A. S. Maisel and F. W. Peacock (2009). "Procalcitonin Identifies Acute Heart Failure Biomarkers in Patients with Acute Heart Failure in Need of Antibiotic Therapy: Observational Results from the Bach (Biomarkers in Acute Heart Failure) Trial." Thorax **64**: A62-A62. [Article Request Form](#)

[Hartmann, O.; Morgenthaler, N. G.; Bergmann, A.] BRAHMS Aktiengesell, Hennigsdorf, Germany. [Landsberg, J.; Wu, A. H. B.; Neath, S. X.] Univ Calif San Diego, San Diego, CA 92103 USA. [Mueller, C.] Univ Basel Hosp, CH-4031 Basel, Switzerland. [Nowak, R.; McCord, J.] Henry Ford Hlth Syst Detroit, Detroit, MI USA. [Ponikowski, P.] Mil Hosp, Wroclaw, Poland. [Moeckel, M.; Anker, S. D.] Campus Virchow Klinikum, Charite Med Sch, Berlin, Germany. [Hogan, C.] Virginia Commonwealth Univ, Richmond, VA USA. [Richards, M.] Univ Otago, Christchurch, New Zealand. [Filippatos, G. S.] Univ Athens, Hosp Attikon, Athens, Greece. [Di Somma, S.] Univ Roma La Sapienza, St Andrea Hosp, Rome, Italy. [Anand, I. S.] VA Minneapolis, Minneapolis, MN USA. [Ng, L.] Univ Leicester, Leicester, Leics, England. [Christenson, R.] Univ Maryland,

Baltimore, MD 21201 USA. [Engineer, R.; Peacock, F. W.] Cleveland Clin Fdn, Cleveland, OH 44195 USA. [Maisel, A. S.] VA San Diego Healthcare Syst, San Diego, CA USA.

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### **Emergency Medicine**

Paxton, J. H. and I. S. Rubinfeld (2010). "Medical Errors Education: A Prospective Study of a New Educational Tool." [Am J Med Qual](#) **EPub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Hospital, Detroit, MI.

Medical errors training is an important yet often overlooked aspect of medical education. A medical errors educational session was developed for rotating medical students (MSs) with prospective analysis of the educational tool. Students completed the same 12-question test before and after the educational session and a long-term posttest 1 to 12 months later. Control students who did not take part in the session completed the test twice with a 6-month interval. In all, 51 students completed a pretest and a short-term posttest, and 35 students completed a long-term posttest. Test scores for the study group increased significantly from a pretest mean of 29.3% to a short-term posttest mean of 73.7% ( $P < .001$ ) and a long-term posttest mean of 49.1% ( $P < .001$ ). Long-term test scores for 24 control group students were significantly lower ( $P < .001$ ). This brief educational intervention led to statistically significant improved performance in general understanding of medical errors and could be a useful tool to enhance MS awareness and proactive handling of medical errors.

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### **Emergency Medicine**

Sasson, C., J. Forman, D. Krass, M. Macy, A. J. Hegg, B. F. McNally and A. L. Kellermann (2010). "A Qualitative Study to Understand Barriers to Implementation of National Guidelines for Prehospital Termination of Unsuccessful Resuscitation Efforts." [Prehosp Emerg Care](#) **EPub Ahead of Print**. [Article Request Form](#)

From the Department of Emergency Medicine (CS, MM), University of Michigan (DK), Ann Arbor, Michigan; the Veterans Affairs Center for Clinical Management and Research (JF), Ann Arbor, Michigan; the Department of Emergency Medicine (AJH), Henry Ford Health System, Detroit, Michigan; and the Department of Emergency Medicine (BFMcN, ALK), Emory University, Atlanta, Georgia.

**Abstract Background.** The American Heart Association's (AHA's) Advanced Cardiac Life Support guidelines act as the national standards for termination of resuscitation (TOR) in cases of refractory out-of-hospital cardiac arrest. However, local emergency medical services (EMS) implementation of these guidelines has been nonuniform. **Objective.** To identify the operational issues within local EMS systems that may serve as barriers or facilitators to full acceptance of national guidelines for prehospital TOR in appropriate circumstances. **Methods.** We conducted three focus groups at the January 2008 National Association of EMS Physicians (NAEMSP) annual meeting. Snowball sampling was used to recruit 19 physicians, two EMS providers, one research director, one nurse, and one medical student attending the conference. Two reviewers analyzed the data in an iterative process to identify recurrent and unifying themes. **Results.** We identified three distinct stakeholder groups whose current beliefs and practices may influence local implementation of TOR: EMS providers with variations in education and work culture; EMS medical directors with responsibility but little authority; and online medical control physicians who do not communicate effectively with the other groups. Our focus group participants suggested that national organizations, such as the AHA and the American College of Emergency Physicians, may serve a role in overcoming the overarching barriers of communication, standardized educational requirements, and coordination of local services. **Conclusion.** We have identified operational barriers that may impede implementation of TOR guidelines. Three influential stakeholder groups will need to work with national organizations to overcome these local barriers.

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### **Emergency Medicine**

Sen, A., A. Hegg, S. Strote and J. Miller (2009). "Inferior Vena Cava Collapsibility Index Predicts Diagnosis of Acute Heart Failure." [Critical Care Medicine](#) **37**(12): 198. [Article Request Form](#)

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### **Emergency Medicine**

Sen, A., P. Hu, C. Mackenzie, R. Dutton, S. Jordan, Y. Xiao and T. Scalea (2009). "Critical Care Monitoring in the Field: Prehospital Continuous Vital Signs Acquisition Identifies Best Predictors of Life-Saving Interventions in Trauma Patients." Critical Care Medicine **37**(12): 677. [Article Request Form](#)

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### **Emergency Medicine**

Sen, A., C. Lewandowski, A. Garcia, H. Wilkie, M. Moyer and R. Nowak (2009). "Hemodynamic Data at Your Finger-Tips: Noninvasive Continuous Data Acquisition by Finger-Cuff Technology in Acute Stroke." Critical Care Medicine **37**(12): 337. [Article Request Form](#)

[Sen, Ayan; Lewandowski, Christopher; Garcia, Audwin; Wilkie, Heidi; Moyer, Michele; Nowak, Richard] Henry Ford Hosp, Detroit, MI USA.

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### **Emergency Medicine**

Sen, A., I. Rubinfeld, O. Azuh, V. Coba, P. Brady, I. Khouradji, M. Horst and J. Patton (2009). "Visensia Index Predicts Life-Saving Interventions in Pre-Hospital Trauma Patients." Critical Care Medicine **37**(12): 172. [Article Request Form](#)

[Sen, Ayan; Rubinfeld, Ilan; Coba, Victor; Horst, Mathilda; Patton, Joe] Henry Ford Hosp, Detroit, MI USA. [Azuh, Ogochukwu; Brady, Paul; Khouradji, Iyad] Wayne State Univ, Sch Med, Detroit, MI 48202 USA.

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### **Emergency Medicine**

Suzuki, T., A. Distante, A. Zizza, S. Trimarchi, M. Villani, J. A. S. Uriarte, L. D. T. Schinosa, A. Renzulli, F. Sabino, R. Nowak, R. Birkhahn, J. E. Hollander, F. Counselman, R. Vijayendran, E. Bossone and K. Eagle (2010). "Response to Letter Regarding Article, "Diagnosis of Acute Aortic Dissection by D-Dimer: The International Registry of Acute Aortic Dissection Substudy on Biomarkers (IRAD-Bio) Experience"." Circulation **121**(4): E24-E24. [Article Request Form](#)

[Suzuki, Toru] Univ Tokyo, Tokyo, Japan. [Distante, Alessandro] Ist Sci Biomed Euro Mediterraneo, Brindisi, Italy. [Zizza, Antonella] CNR, Inst Clin Physiol, Lecce, Italy. [Trimarchi, Santi] Policlin San Donato, IRCCS, Milan, Italy. [Villani, Massimo] Vito Fazzi Hosp, Lecce, Italy. [Uriarte, Jorge Antonio Salerno] Univ Insubria, Osped Circolo, Varese, Italy. [Uriarte, Jorge Antonio Salerno] Fdn Macchi, Varese, Italy. [Schinosa, Luigi De Luca Tupputi] Policlin Hosp, Bari, Italy. [Renzulli, Attilio] UMG, Catanzaro, Italy. [Sabino, Federico] ALIV Healthcare R&D, Forte Dei Marmi, Italy. [Nowak, Richard] Henry Ford Hosp, Detroit, MI 48202 USA. [Birkhahn, Robert] New York Methodist Hosp, Brooklyn, NY USA. [Hollander, Judd E.] Univ Penn, Philadelphia, PA 19104 USA. [Counselman, Francis] Eastern Virginia Med Sch, Norfolk, VA 23501 USA. [Vijayendran, Ravi] Biosite, San Diego, CA USA. [Eagle, Kim] Univ Michigan, Ann Arbor, MI 48109 USA. Suzuki, T, Univ Tokyo, Tokyo, Japan.

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### **Endocrinology & Metabolism**

Odvin, C. V., S. Levy, S. Rao, J. E. Zerwekh and D. S. Rao (2010). "Unusual mid-shaft fractures during long-term bisphosphonate therapy." Clinical Endocrinology **72**(2): 161-168. [PDF Full-Text](#)

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Background Bisphosphonates are the most commonly prescribed medications for the treatment of osteoporosis. Although existing evidence supports a good safety profile, there is concern that chronic administration of these agents could result in severe suppression of bone turnover with increased risk of nonvertebral fractures. Objective The objective of this study was to report the clinical presentation, selected bone histomorphometry and X-ray images of patients who developed mid-shaft long bone fractures during bisphosphonate therapy, six of whom had bone biopsy for histomorphometry. Results Of the 13 patients who sustained atraumatic mid-shaft fractures, 10 were on alendronate and three were on risedronate therapy before the fractures. In addition to bisphosphonates, three patients were on oestrogen and two on tamoxifen concomitantly. Four patients with glucocorticoid-induced osteoporosis were on alendronate for 3-11 years along with glucocorticoid therapy. Bone histomorphometry showed severe suppression of bone turnover in five patients and low bone turnover in one patient. Conclusion Long-term bisphosphonate therapy may increase the risk of unusual long bone mid-shaft fractures. This is probably due to prolonged suppression of bone turnover, which could lead to accumulation of microdamage and development of hypermineralized bone. At present, the scope of this complication in the larger context of patients receiving bisphosphonate therapy remains unknown, but appears to be small.

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### **Gastroenterology**

Aggarwal, R., I. Hanschu and A. Silverman (2009). "Black Americans are More Likely to have Intermediate TPMT Enzyme Levels than White Americans." American Journal of Gastroenterology **104**: 1225. [PDF Full-Text](#) (Scroll down to abstract #1225)

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### **Gastroenterology**

Hammoud, I., O. Sharif, N. A. L. Hannat and A. Nawras (2009). "Co-incidence of Diverticulosis and Polyps in the Colon." American Journal of Gastroenterology **104**: 442. [PDF Full-Text](#) (Scroll down to abstract 442)

[Hammoud, Ihab; Sharif, Omar; Hannat, Nidal A. L.; Nawras, Ali] Henry Ford Hosp, Detroit, MI 48202 USA.

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Hsu, R. and G. Olds (2009). "An Analysis of Gastric Polyps at a Single Institution." American Journal of Gastroenterology **104**: 122. [PDF Full-Text](#) (Scroll down to abstract #122)

[Hsu, Richard; Olds, Gregory] Henry Ford Hosp, Detroit, MI 48202 USA.

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Khan, F., A. Zalawadia, M. Raoufi, C. Ma and A. Yudovich (2009). "Incidence of Autoimmune Pancreatitis in Patients Referred for Whipple's Resection for Presumed Malignancy 2009 Presidential Poster." American Journal of Gastroenterology **104**: 213. [PDF Full-Text](#) (Scroll down to abstract #213)

[Khan, Faisal; Zalawadia, Ashish; Raoufi, Mohammad; Ma, Chan; Yudovich, Allen] Henry Ford Hosp, Detroit, MI 48202 USA.

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Pai, C., M. Kazimi and D. Simmons (2009). "Bilious Ascites After Liver Transplantation Due to Duodenal Perforation from Biliary Stent." American Journal of Gastroenterology **104**: 669. [PDF Full-Text](#) (Scroll down to abstract #669)

[Pai, Chetan; Kazimi, Marwan; Simmons, Dia] Henry Ford Hosp, Detroit, MI 48202 USA.

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Patel, D., J. Kinzie, B. Lee, R. Peleman and S. Hoffman (2009). "Emergent Endoscopic Reduction of an Acute Gastric Volvulus with Double Percutaneous Endoscopic Gastrostomy Fixation." American Journal of Gastroenterology **104**: 1013. [PDF Full-Text](#) (Scroll down to abstract # 1013)

[Kinzie, Joseph; Lee, Byung; Peleman, Rene] Henry Ford Macomb Hosp, Clinton Township, MI USA. [Patel, Daksesh; Hoffman, Stephen] St John Macomb Oakland, Royal Oak, MI USA.

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Sharif, O., D. Alromaihi, M. AboulJoud and M. A. Huang (2009). "Focal Hepatic Steatosis Presenting as a Liver Mass." American Journal of Gastroenterology **104**: 347. [PDF Full-Text](#) (Scroll down to abstract #347)

[Sharif, Omar; Alromaihi, Dalal; AboulJoud, Marwan; Huang, Mary Ann] Henry Ford Hosp, Detroit, MI 48202 USA.

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Sharif, O., I. Hammoud and M. Ibrahim (2009). "Left-Sided Portal Hypertension Caused by an Accessory Spleen." American Journal of Gastroenterology **104**: 806. [PDF Full-Text](#) (Scroll down to page #806)

[Sharif, Omar; Hammoud, Ihab; Ibrahim, Mostafa] Henry Ford Hosp, Dearborn, MI USA.

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[Silverman, Ann; Gikas, Helen; Samuels, Qiana; Jacobsen, Gordon] Henry Ford Hlth Syst, Detroit, MI USA.

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### **Gastroenterology**

Tang, J., H. Gonzalez and A. Bhan (2009). "Is the Inflammatory Bowel Disease Serology 7 Panel a Useful Diagnostic Tool?" American Journal of Gastroenterology **104**: 1277. [PDF Full-Text](#) (Scroll down to abstract #1277)

[Tang, Jeffrey; Gonzalez, Humberto; Bhan, Amit] Henry Ford Hlth Syst, Gastroenterol, Detroit, MI USA.

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

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Thekdi, A., G. Divine and D. Moonka (2009). "Impact of Intraoperative Blood Transfusions on Survival and Severity of Recurrent Hepatitis C After Liver Transplantation." American Journal of Gastroenterology **104**: 364. [PDF Full-Text](#) (Scroll down to abstract #364)

[Thekdi, Ashish; Divine, George; Moonka, Dilip] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Gastroenterology**

Thekdi, A. and A. Nawras (2009). "EUS-FNA for the Diagnosis of Retroperitoneal Primitive Neuroectodermal Tumor." American Journal of Gastroenterology **104**: 1031. [PDF Full-Text](#) (Scroll down to abstract #1031)

[Thekdi, Ashish; Nawras, Ali] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Health Enhancement Center**

Horwich, T., E. S. Leifer, C. A. Brawner, M. B. Fitz-Gerald and G. C. Fonarow (2009). "The Relationship Between Body Mass Index and Cardiopulmonary Exercise Testing in Chronic Systolic Heart Failure." Circulation **120**(18): S757-S757. [Article Request Form](#)

[Horwich, Tamara; Fonarow, Gregg C.] Univ Calif Los Angeles, Med Ctr, Los Angeles, CA 90024 USA. [Leifer, Eric S.] Natl Heart Lung Blood Inst, Bethesda, MD USA. [Brawner, Clinton A.] Henry Ford Hosp, Detroit, MI 48202 USA. [Fitz-Gerald, Meredith B.] Univ Alabama, Birmingham, AL USA.

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

Calcul, L., W. D. Inman, A. A. Morris, K. Tenney, J. Ratnam, J. H. McKerrow, F. A. Valeriote and P. Crews (2010). "Additional Insights on the Bastadins: Isolation of Analogues from the Sponge lanthella cf. reticulata and Exploration of the Oxime Configurations (dagger)." J Nat Prod **EPub Ahead of Print**. [PDF Full-Text](#)

Department of Chemistry and Biochemistry, University of California, Santa Cruz, California 95064, Sandler Center for Basic Research in Parasitic Disease, University of California, San Francisco, San Francisco, California 94143, and Josephine Ford Cancer Center, Henry Ford Hospital, Detroit, Michigan 48202.

The focus of this study is on the bastadin class of bromotyrosine derivatives, commonly isolated from lanthella marine sponges, and is the first report on the secondary metabolites from lanthella cf. reticulata. Two new bastadins were isolated, (E,Z)-bastadin 19 (1b), a diastereoisomer of the known (E,E)-bastadin 19 (1a), and dioxepine bastadin 3 (2), an unusual dibenzo-1,3-dioxepine. A bastadin NMR database was created and assisted in the structure determination of 1b and 2 and the rapid dereplication of 10 other known compounds including bastadins 2-9 (3-10), 13 (11), and 19 (1a). The geometry of the 2-(hydroxyimino)-N-alkylamide chains, a chemical feature present in all bastadins, was further probed, and new insights regarding the natural oxime configuration are discussed. Bastadins possessing (E,Z)-, (Z,E)-, or (E,E)-dioxime configurations could be artifacts of isolation or storage in solution. Therefore, this point was explored by photochemical and thermal

isomerization studies, as well as molecular mechanics calculations. Bastadins 13 (11) and 19 (1a) exhibited moderate inhibition against *Trypanosoma brucei*, and bastadin 4 (5) was cytotoxic to HCT-116 colon cancer cells.

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### **Hypertension & Vascular Research**

Peng, H., O. A. Carretero, E. L. Peterson and N. E. Rhaleb (2010). "AC-SDKP INHIBITS TRANSFORMING GROWTH FACTOR- $\beta$  1-INDUCED DIFFERENTIATION OF HUMAN CARDIAC FIBROBLASTS INTO MYOFIBROBLASTS." [Am J Physiol Heart Circ Physiol EPub Ahead of Print.](#) [PDF Full-Text](#)

Henry Ford Hospital.

N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) inhibits collagen production and cell proliferation in cultured rat cardiac fibroblasts, but its effect on differentiation of fibroblasts into myofibroblasts is not known. High amounts of transforming growth factor- $\beta$ 1 (TGF- $\beta$ 1) have been found in fibrotic cardiac tissue. TGF- $\beta$ 1 converts fibroblasts into myofibroblasts, which produce more extracellular matrix proteins than fibroblasts. We hypothesized that 1) Ac-SDKP inhibits TGF- $\beta$ 1-induced differentiation of fibroblasts into myofibroblasts; and 2) this effect is mediated in part by blocking phosphorylation of Smad2 and ERK1/2. For this study, we used human fetal cardiac fibroblasts (HCFs), which do not spontaneously become myofibroblasts when cultured at low passages. We investigated the effect of Ac-SDKP on TGF- $\beta$ 1-induced HCF transformation into myofibroblasts, Smad2 and ERK1/2 phosphorylation, Smad7 expression, cell proliferation and collagen production. We also investigated TGF- $\beta$ 1 production by HCFs stimulated with endothelin 1 (ET-1). As expected, HCFs treated with TGF- $\beta$ 1 transformed into myofibroblasts as indicated by increased expression of alpha-smooth muscle actin and a higher proportion of the embryonic isoform of smooth muscle myosin compared to untreated cells. TGF- $\beta$ 1 also increased Smad2 and ERK1/2 phosphorylation but did not affect Smad7 expression. In addition, TGF- $\beta$ 1 stimulated HCF proliferation as indicated by an increase in mitochondrial dehydrogenase activity and collagen production on hydroxyproline assay. Ac-SDKP significantly inhibited all of the effects of TGF- $\beta$ 1. It also inhibited ET-1-stimulated TGF- $\beta$ 1 production. We concluded that Ac-SDKP markedly suppresses differentiation of human cardiac fibroblasts into myofibroblasts, probably by inhibiting the TGF- $\beta$ /Smad/ERK1/2 signaling pathway, and thus mediating its anti-fibrotic effects. Key words: transforming growth factor- $\beta$  1, human cardiac myofibroblasts, fibroblast differentiation, Ac-SDKP.

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### **Hypertension & Vascular Research**

Perez-Rojas, J. M., K. M. Kassem, W. H. Beierwaltes, J. L. Garvin and M. Herrera (2010). "NO produced by endothelial NO synthase (NOS 3) promotes diuresis." [Am J Physiol Regul Integr Comp Physiol EPub Ahead of Print.](#) [PDF Full-Text](#)

Henry Ford Hospital.

Extracellular fluid volume is highly regulated, at least in part, by peripheral resistance and renal function. Nitric oxide (NO) produced by NO synthase type 3 (NOS 3) in the non-renal vasculature may promote fluid retention by reducing systemic vascular resistance and arterial pressure. In contrast, NO produced by renal NOS 3 promotes water excretion by reducing renal vascular resistance, increasing glomerular filtration and inhibiting reabsorption along the nephron. Thus, the net effect of NO from NOS 3 on urinary volume (UV) is unclear. We hypothesized that NO produced by NOS 3 promotes water excretion primarily due to renal tubular effects. We gave conscious wild-type and NOS 3  $-/-$  mice an acute volume load and measured UV, blood pressure, plasma renin concentration (PRC), Na(+), vasopressin and urinary Na(+) and creatinine concentration. To give the acute volume load, we trained mice to drink a large volume of water while in metabolic cages. On the day of the experiment water was replaced with 1% sucrose, and mice had access to it for 1hr. Volume intake was similar in both groups. Over 3 hrs wild-type excreted 62  $\pm$  10% of the volume load, but NOS 3  $-/-$  excreted only 42  $\pm$  5% (  $p < 0.05$ ). Blood pressure in NOS 3  $-/-$  was 118  $\pm$  3 compared to 110  $\pm$  2 mmHg in wild-types (  $p < 0.05$ ) but it did not change following volume load in either strain. PRC, vasopressin and creatinine excretion rates were similar between groups. UNaV was 49.3  $\pm$  7.0 in wild-type vs. 37.8  $\pm$  6.4  $\mu$ moles/3 hrs in NOS 3  $-/-$  (  $p < 0.05$ ). We conclude that: 1) NO produced by NOS 3 promotes water and Na(+) excretion; 2) the renal epithelial actions of NO produced by NOS 3 supersede the systemic and renal vascular actions. Key words: nitric oxide, NOS 3, Na excretion, transport.

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## Infectious Diseases

Aguilar, J., A. S. Hingwe and J. A. Vazquez (2010). "A 25-year-old woman with an ulcerative earlobe lesion." Clin Infect Dis **50**(4): 552-3, 613-5. [PDF Full-Text](#)

Division of Infectious Diseases, Henry Ford Hospital, Detroit, Michigan, USA.

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## Infectious Diseases

Martinez-Capolino, C., K. Reyes, L. Johnson, J. Sullivan, L. Samuel, B. Digiovine, M. Eichenhorn, H. M. Horst, P. Varelas, M. A. Mickey, R. Washburn and M. Zervos (2010). "Impact of active surveillance on meticillin-resistant Staphylococcus aureus transmission and hospital resource utilisation." J Hosp Infect **Epub Ahead of Print**. [PDF Full-Text](#)

Division of Infectious Diseases, and Infection Prevention, Henry Ford Hospital, Detroit, Michigan, USA.

The utility of active surveillance cultures (ASCs) for meticillin-resistant Staphylococcus aureus (MRSA) has been a controversial aspect of infection prevention. This prospective cohort study analyses the effect of ASCs for MRSA on hospital-acquired infections in a tertiary care hospital (hospital 1) and a community-based hospital (hospital 2). Both hospitals have high MRSA prevalence and are part of a large healthcare system in southeastern Michigan. Hospital-acquired infections in the intensive care unit (ICU) and in the rest of the hospital were compared before and after the implementation of ASCs in the ICUs. Patients in hospital 1 with evidence of MRSA colonisation from ASCs were placed in contact isolation during their stay in the ICU; patients from hospital 2 remained in contact isolation throughout their hospital stay. Prevalence of MRSA colonisation on admission to the ICU was 23% and 13% in hospitals 1 and 2, respectively. Average incidence of new colonisation during the study period was 1.85 per 1000 patient-days and 3.47 per 1000 patient-days in hospitals 1 and 2, respectively. A decrease in ventilator-associated pneumonia (VAP) occurred in both hospitals, whereas decrease in hospital-wide nosocomial MRSA infection was demonstrated only in hospital 2. We conclude that, in addition to standard infection prevention initiatives, ASC with contact precautions can be effective in reducing the incidence of VAP and nosocomial MRSA infection in healthcare communities with endemic MRSA.

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## Infectious Diseases

Vazquez, J. A. (2010). "Invasive Fungal Infections in the Intensive Care Unit." Seminars in Respiratory and Critical Care Medicine **31**(1): 79-86. [PDF Full-Text](#)

[Vazquez, Jose A.] Henry Ford Hosp, Div Infect Dis, Dept Med, Detroit, MI 48202 USA. [Vazquez, Jose A.] Wayne State Univ, Sch Med, Detroit, MI USA.

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Invasive fungal infections, especially candidemia and systemic candidiasis, have become a major cause of morbidity and mortality in the last few decades. This comes in parallel with the major advances made in intensive care. Patients who are critically ill, in medical or surgical ICUs are especially at risk for Candida infections. Invasive candidiasis accounts for up to 15 to 30% of all nosocomial infections in critically ill patients. Management of these severe infections has been challenging due to a lack of rapid and reliable diagnostic methods, leading to delays in initiating appropriate antifungal therapy. However, some notable improvements have been made in diagnostics with improved culturing methods, rapid species identification, and detection of fungemia with newer antigen assays. Newer classes of antifungals have recently become available with broader antifungal activity, fewer drug-drug interactions, and improved tolerability when compared with the older antifungal agents. Despite these advancements, the mortality rates associated with candidiasis remain excessively high, with an overall mortality in the range of 30 to 50% and an attributable mortality of similar to 30%. In addition to this high case-fatality rate, candidemia is also associated with a substantial economic burden, primarily due to an extended length of stay. Strategies to evaluate either the prevention, early diagnosis, or initiation of appropriate therapy should yield both clinical and socioeconomic benefits.

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### **Internal Medicine**

Arnaout, K., M. Khalife, M. Younes and A. Hanbali (2009). "HER-2 Status May Change in Recurrent Breast Cancer." Cancer Research **69**(24): 802S-802S. [PDF Full-Text](#)

[Arnaout, K.; Khalife, M.; Younes, M.; Hanbali, A.] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Internal Medicine**

Gonzalez, H., R. Sharma and M. A. Huang (2009). "Does Midodrine and Octreotide Truly Improve Survival in Cirrhotic Patients with Hepatorenal Syndrome?" American Journal of Gastroenterology **104**: 414. [PDF Full-Text](#) (Scroll down to abstract #414)

[Gonzalez, Humberto; Sharma, Rishi; Huang, Mary Ann] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Internal Medicine**

Kaatz, S., C. Cooper, K. Morgan, Z. Muhammad, D. Ferrans and D. Paje (2010). "Improving the Rate of Prescribed Subtherapeutic INR Ranges: A Quality Improvement Project." Journal of Thrombosis and Thrombolysis **29**(2): 254-255. [PDF Full-Text](#) (Scroll down to page 254)

[Kaatz, S.; Cooper, C.; Morgan, K.; Muhammad, Z.; Ferrans, D.; Paje, D.] Henry Ford Hosp, Detroit, MI 48202 USA.

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### **Internal Medicine**

Kaatz, S., J. D. Douketis, H. Zhou, B. F. Gage and R. H. White (2010). "Risk of stroke after surgery in patients with and without chronic atrial fibrillation." J Thromb Haemost **EPub Ahead of Print**. [PDF Full-Text](#)

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

Background: The extent to which chronic atrial fibrillation affects the risk of postoperative stroke is largely unknown. Objectives: We sought to determine the 30 day rate of stroke among patients with and without chronic AF who underwent 10 different types of surgery. Patients/Methods: The crude incidence of stroke was retrospectively determined using a population-based linked administrative database of hospitalized patients who underwent specified operations between January 1, 1996 and November 30, 2005. The risk of stroke in patients with AF was adjusted for age, race, sex, presence of diabetes, heart failure, hypertension and prior stroke. Results: The overall 30-day rate of stroke in 69,202 patients with chronic AF was 1.8% (95% CI: 1.7%-1.9%) versus 0.6% (CI: 0.58%-0.62%) in 2,470,649 patients without AF. The risk-adjusted odds of a postoperative stroke in patients with chronic AF was 2.1 (CI: 2.0-2.3). The highest incremental difference in the crude rate of stroke was observed in patients undergoing neurologic or vascular surgery, with a difference of approximately 2%. Conclusion: Patients with chronic AF had twice the risk of post-operative stroke. Randomized trials are needed to determine if aggressive perioperative anticoagulation can reduce the incidence of postoperative stroke in patients with AF.

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### **Internal Medicine**

Nieuwlaat, R., Y. K. Kim, S. J. Connolly, S. Schulman, J. Hirsh, K. Meijer, N. Raju, S. Kaatz and J. W. Eikelboom (2009). "Impact of the Modified Henry Ford Warfarin Maintenance Dosing Algorithm on Quality of Anticoagulation at a Specialist Anticoagulation Clinic." Circulation **120**(18): S1150-S1150. [Article Request Form](#)

[Nieuwlaat, Robby; Connolly, Stuart J.; Eikelboom, John W.] McMaster Univ, PHRI, Hamilton, ON, Canada.  
[Kaatz, Scott] Henry Ford Hosp, Detroit, MI 48202 USA.

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## Medical Genetics

Wolf, B. (2010). "Clinical issues and frequent questions about biotinidase deficiency." Mol Genet Metab **EPub Ahead of Print**. [Article Request Form](#)

Department of Medical Genetics, Henry Ford Hospital, 3031 West Grand Blvd., Suite 700, Detroit, MI 48202, USA; Center for Molecular Medicine and Genetics, Wayne State University School of Medicine, Detroit, MI, USA.

Biotinidase deficiency is a biotin-responsive, inherited neurocutaneous disorder. The disorder is readily treatable and is screened for in the newborn period. Over the years since the discovery of the disorder, many practical questions and issues have been raised as to the diagnosis, management, treatment, and newborn screening of the disorder. In this paper, many of these issues are addressed using evidence-based medicine and anecdotal experiences. If adequate answers are not known, the answers to these queries will require future investigations.

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## Miscellaneous

Bhattacharjee, H., J. Sheng, A. A. Ajees, R. Mukhopadhyay and B. P. Rosen (2010). "Adventitious Arsenate Reductase Activity of the Catalytic Domain of the Human Cdc25B and Cdc25C Phosphatases." Biochemistry **49(4)**: 802-809. [PDF Full-Text](#)

[Bhattacharjee, Hiranmoy; Ajees, A. Abdul; Rosen, Barry P.] Florida Int Univ, Herbert Wertheim Coll Med, Dept Cellular Biol & Pharmacol, Miami, FL 33199 USA. [Mukhopadhyay, Rita] Florida Int Univ, Herbert Wertheim Coll Med, Dept Mol Microbiol & Infect Dis, Miami, FL 33199 USA. [Sheng, Ju] Henry Ford Hosp, Detroit, MI 48202 USA.

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A number of eukaryotic enzymes that function as arsenate reductases are homologues of the catalytic domain of the human Cdc25 phosphatase. For example, the Leishmania major enzyme LmACR2 is both it phosphatase and an arsenate reductase, and its Structure bears similarity to the structure of the catalytic domain of human Cdc25 phosphatase. These reductases contain an active site C-X-5-R signature motif, where C is the catalytic cysteine, the five X residues form a phosphate binding loop, and R is a highly conserved arginine, which is also present in human Cdc25 phosphatases. We therefore investigated the possibility that the three human Cdc25 isoforms might have adventitious arsenate reductase activity. The sequences for the catalytic domains of Cdc25A, -B, and -C were cloned individually into a prokaryotic expression vector, and their gene products were purified from a bacterial host using nickel affinity chromatography. While each of the three Cdc25 catalytic domain exhibited phosphatase activity, arsenate reductase activity was observed only with Cdc25B and -C. These two enzymes reduced inorganic arsenate but not methylated pentavalent arsenicals. Alteration of either the cysteine and arginine residues of the Cys-X-5-Arg motif led to the loss of both reductase and phosphatase activities. Our observations suggest that Cdc25B and -C may adventitiously reduce arsenate to the more toxic arsenite and may also provide a framework for identifying other human protein tyrosine phosphatases containing the active site Cys-X-5-Arg loop that might moonlight as arsenate reductases.

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## Nephrology

Parasuraman, R. and K. K. Venkat (2010). "Crystal-Induced Kidney Disease in 2 Kidney Transplant Recipients." American Journal of Kidney Diseases **55(1)**: 192-197. [PDF Full-Text](#)

[Parasuraman, Ravi] William Beaumont Hosp, Div Nephrol & Transplantat, Kidney Transplant Outreach Program, Royal Oak, MI 48703 USA. [Venkat, K. K.] Henry Ford Hosp, Div Nephrol & Hypertens, Detroit, MI 48202 USA.

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## Neurology

Kressler, B., L. de Rochefort, T. Liu, P. Spincemaille, Q. Jiang and Y. Wang (2010). "Nonlinear Regularization for Per Voxel Estimation of Magnetic Susceptibility Distributions From MRI Field Maps." IEEE Transactions on Medical Imaging **29**(2): 273-281. [Article Request Form](#)

[Kressler, Bryan; Liu, Tian; Wang, Yi] Cornell Univ, Dept Biomed Engr, Ithaca, NY 14853 USA. [Kressler, Bryan; de Rochefort, Ludovic; Liu, Tian; Spincemaille, Pascal; Wang, Yi] Weill Cornell Med Coll, Dept Radiol, New York, NY 10021 USA. [Jiang, Quan] Henry Ford Hosp, Dept Neurol, Detroit, MI 48202 USA. Kressler, B, Cornell Univ, Dept Biomed Engr, Ithaca, NY 14853 USA. [bmk22@cornell.edu](mailto:bmk22@cornell.edu)

Magnetic susceptibility is an important physical property of tissues, and can be used as a contrast mechanism in magnetic resonance imaging (MRI). Recently, targeting contrast agents by conjugation with signaling molecules and labeling stem cells with contrast agents have become feasible. These contrast agents are strongly paramagnetic, and the ability to quantify magnetic susceptibility could allow accurate measurement of signaling and cell localization. Presented here is a technique to estimate arbitrary magnetic susceptibility distributions by solving an ill-posed inversion problem from field maps obtained in an MRI scanner. Two regularization strategies are considered: conventional Tikhonov regularization and a sparsity promoting nonlinear regularization using the norm. Proof of concept is demonstrated using numerical simulations, phantoms, and in a stroke model in a rat. Initial experience indicates that the nonlinear regularization better suppresses noise and streaking artifacts common in susceptibility estimation.

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## Neurology

Kumar, G., M. K. Goyal, P. K. Sahota and R. Jain (2010). "Penumbra, the basis of neuroimaging in acute stroke treatment: Current evidence." Journal of the Neurological Sciences **288**(1-2): 13-24. [PDF Full-Text](#)

[Kumar, Gyanendra; Goyal, Munish Kumar; Sahota, Pradeep Kumar] Univ Missouri Healthcare Columbia, Dept Neurol, Columbia, MO 65212 USA. [Jain, Rajan] Henry Ford Hosp, Dept Radiol, Div Neuroradiol, Detroit, MI 48202 USA.

Kumar, G, Univ Missouri Healthcare Columbia, Dept Neurol, CE 507 5 Hosp Dr, Columbia, MO 65212 USA. [kumargy@health.missouri.edu](mailto:kumargy@health.missouri.edu)

In modern medicine brain imaging is an essential prerequisite not only to acute stroke triage but also to determining the specific therapy indicated. This article reviews the need for imaging the brain in acute stroke, penumbral pathophysiology, penumbral imaging techniques, as well as current status of various imaging modalities that are being employed to select patients for specific therapeutic approaches. (C) 2009 Elsevier B.V. All rights reserved.

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## Neurology

Liu, Z., Y. Li, Z. G. Zhang, X. Cui, Y. Cui, M. Lu, S. Savant-Bhonsale and M. Chopp (2010). "Bone marrow stromal cells enhance inter- and intracortical axonal connections after ischemic stroke in adult rats." J Cereb Blood Flow Metab **EPub Ahead of Print**. [PDF Full-Text](#)

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

We investigated axonal plasticity in the bilateral motor cortices in rats after unilateral stroke and bone marrow stromal cell (BMSC) treatment. Rats were subjected to permanent right middle cerebral artery occlusion followed by intravenous administration of phosphate-buffered saline or BMSCs 1 day later. Adhesive-removal test and modified neurologic severity score were performed weekly to monitor limb functional deficit and recovery. Anterograde tracing with biotinylated dextran amine injected into the right motor cortex was used to assess axonal sprouting in the contralateral motor cortex and ipsilateral rostral forelimb area. Animals were killed 28 days after stroke. Progressive functional recovery was significantly enhanced by BMSCs. Compared

with normal animals, axonal density in both contralateral motor cortex and ipsilateral rostral forelimb area significantly increased after stroke. Bone marrow stromal cells markedly enhanced such interhemispheric and intracortical connections. However, labeled transcallosal axons in the corpus callosum were not altered with either stroke or treatment. Both interhemispheric and intracortical axonal sprouting were significantly and highly correlated with behavioral outcome after stroke. This study suggests that, after stroke, cortical neurons surviving in the peri-infarct motor cortex undergo axonal sprouting to restore connections between different cerebral areas. Bone marrow stromal cells enhance axonal plasticity, which may underlie neurologic functional improvement.

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## Neurology

Smith, B. J. (2010). "Management of Epilepsy in Drug-Resistant Patients." Cns Spectrums 15(1): 3-+. [Article Request Form](#)

[Smith, Brien J.] Henry Ford Hosp, Comprehens Epilepsy Program, Detroit, MI 48202 USA. [Smith, Brien J.] Wayne State Univ, Dept Neurol, Detroit, MI 48202 USA.

Smith, BJ, Henry Ford Hosp, Comprehens Epilepsy Program, Detroit, MI 48202 USA.

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

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## Neurology

Xin, H., Y. Li, L. H. Shen, X. Liu, X. Wang, J. Zhang, D. S. Pourabdollah-Nejad, C. Zhang, L. Zhang, H. Jiang, Z. G. Zhang and M. Chopp (2010). "Increasing tPA activity in astrocytes induced by multipotent mesenchymal stromal cells facilitate neurite outgrowth after stroke in the mouse." PLoS One 5(2): e9027. 2815778. [PDF Full-Text](#)

Department of Neurology, Henry Ford Health System, Detroit, Michigan, United States of America.

We demonstrate that tissue plasminogen activator (tPA) and its inhibitors contribute to neurite outgrowth in the central nervous system (CNS) after treatment of stroke with multipotent mesenchymal stromal cells (MSCs). In vivo, administration of MSCs to mice subjected to middle cerebral artery occlusion (MCAo) significantly increased activation of tPA and downregulated PAI-1 levels in the ischemic boundary zone (IBZ) compared with control PBS treated mice, concurrently with increases of myelinated axons and synaptophysin. In vitro, MSCs significantly increased tPA levels and concomitantly reduced plasminogen activator inhibitor 1 (PAI-1) expression in astrocytes under normal and oxygen and glucose deprivation (OGD) conditions. ELISA analysis of conditioned medium revealed that MSCs stimulated astrocytes to secrete tPA. When primary cortical neurons were cultured in the conditioned medium from MSC co-cultured astrocytes, these neurons exhibited a significant increase in neurite outgrowth compared to conditioned medium from astrocytes alone. Blockage of tPA with a neutralizing antibody or knock-down of tPA with siRNA significantly attenuated the effect of the conditioned medium on neurite outgrowth. Addition of recombinant human tPA into cortical neuronal cultures also substantially enhanced neurite outgrowth. Collectively, these in vivo and in vitro data suggest that the MSC mediated increased activation of tPA in astrocytes promotes neurite outgrowth after stroke.

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## Neurology

Zuniga, R. M., R. Torcuator, R. Jain, J. Anderson, T. Doyle, L. Schultz and T. Mikkelsen (2010). "Rebound tumour progression after the cessation of bevacizumab therapy in patients with recurrent high-grade glioma." J Neurooncol **Epub Ahead of Print**. [PDF Full-Text](#)

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After withdrawal of bevacizumab in patients with recurrent high-grade glioma, we have observed a rapid tumour re-growth or "rebound" radiographic phenomenon with accelerated clinical decline. We retrospectively reviewed 11 patients treated at the Henry Ford Hermelin Brain Tumor Center with recurrent high-grade glioma who demonstrated a rebound progression pattern after the discontinuation of bevacizumab. The original tumour area-of-enhancement increased by a mean of 158%, when compared to the rebound magnetic resonance imaging. After rebound, no patients (0/8) showed a response to next-line treatments that did not include bevacizumab. The median survival of those re-treated with bevacizumab was 149 and 32 days for those who received other regimens. Abrupt discontinuation of bevacizumab after recurrence often leads to a dramatic rebound phenomenon and rapid clinical decline. Slow tapering of the bevacizumab dose after tumour progression may prevent this from occurring and improve responsiveness to next-line therapies.

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## Neurosurgery

Ammirati, M., C. S. Cobbs, M. E. Linskey, N. A. Paleologos, T. C. Ryken, S. H. Burri, A. L. Asher, J. S. Loeffler, P. D. Robinson, D. W. Andrews, L. E. Gaspar, D. Kondziolka, M. McDermott, M. P. Mehta, T. Mikkelsen, J. J. Olson, R. A. Patchell and S. N. Kalkanis (2010). "The role of retreatment in the management of recurrent/progressive brain metastases: a systematic review and evidence-based clinical practice guideline." Journal of Neuro-Oncology **96**(1): 85-96. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Neurosurg, Detroit, MI 48202 USA. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. [Burri, Stuart H.] Carolinas Med Ctr, Dept Radiat Oncol, Charlotte, NC 28203 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [Robinson, Paula D.] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Gaspar, Laurie E.] Univ Colorado, Dept Radiat Oncol, Denver, CO 80202 USA. [Kondziolka, Douglas] Univ Pittsburgh, Dept Neurol Surg, Med Ctr, Pittsburgh, PA 15260 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. Kalkanis, SN, Henry Ford Hlth Syst, Hermelin Brain Tumor Ctr, Dept Neurosurg, 2799 W Grand Blvd, K-11, Detroit, MI 48202 USA. [kalkanis@neuro.hfh.edu](mailto:kalkanis@neuro.hfh.edu)

What evidence is available regarding the use of whole brain radiation therapy (WBRT), stereotactic radiosurgery (SRS), surgical resection or chemotherapy for the treatment of recurrent/progressive brain metastases? Target population This recommendation applies to adults with recurrent/progressive brain metastases who have previously been treated with WBRT, surgical resection and/or radiosurgery. Recurrent/progressive brain metastases are defined as metastases that recur/progress anywhere in the brain (original and/or non-original sites) after initial therapy. Recommendation Level 3 Since there is insufficient evidence to make definitive treatment recommendations in patients with recurrent/progressive brain metastases, treatment should be individualized based on a patient's functional status, extent of disease, volume/number of metastases, recurrence or progression at original versus non-original site, previous treatment and type of primary cancer, and enrollment in clinical trials is encouraged. In this context, the following can be recommended depending on a patient's specific condition: no further treatment (supportive care), re-irradiation (either WBRT and/or SRS), surgical excision or, to a lesser extent, chemotherapy. Question If WBRT is used in the setting of recurrent/progressive brain metastases, what impact does tumor

histopathology have on treatment outcomes? No studies were identified that met the eligibility criteria for this question.

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### Neurosurgery

Awaad, Y. A. S. and N. O. R. Roosen (2009). "Analysis of surgical intrathecal [i.t.] baclofen [ITB] implant results emphasizing revision surgery in a mixed pediatric/adult population." Journal of the Neurological Sciences **285**: S181-S181. [PDF Full-Text](#)

[Awaad, Y. A. S.] KFMC, Riyadh, Saudi Arabia. [Roosen, N. O. R.] Henry Ford Hlth Syst, Detroit, MI USA.

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### Neurosurgery

Awaad, Y. S. E., N. O. R. Roosen and T. Rizk (2009). "Vagus nerve stimulation (VNS) in a pediatric population - surgical technique considerations in young children." Journal of the Neurological Sciences **285**: S107-S107. [PDF Full-Text](#)

[Awaad, Y. S. E.; Rizk, T.] KFMC, Riyadh, Saudi Arabia. [Roosen, N. O. R.] Henry Ford Hosp, Detroit, MI 48202 USA.

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### Neurosurgery

Gaspar, L. E., M. P. Mehta, R. A. Patchell, S. H. Burri, P. D. Robinson, R. E. Morris, M. Ammirati, D. W. Andrews, A. L. Asher, C. S. Cobbs, D. Kondziolka, M. E. Linskey, J. S. Loeffler, M. McDermott, T. Mikkelsen, J. J. Olson, N. A. Paleologos, T. C. Ryken and S. N. Kalkanis (2010). "The role of whole brain radiation therapy in the management of newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline." Journal of Neuro-Oncology **96**(1): 17-32. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. [Gaspar, Laurie E.] Univ Colorado, Dept Radiat Oncol, Denver, CO 80202 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. [Burri, Stuart H.] Carolinas Med Ctr, Dept Radiat Oncol, Charlotte, NC 28203 USA. [Robinson, Paula D.; Morris, Rachel E.] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Kondziolka, Douglas] Univ Pittsburgh, Dept Neurol Surg, Med Ctr, Pittsburgh, PA 15260 USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. Kalkanis, SN, Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, 2799 W Grand Blvd, K-11, Detroit, MI 48202 USA. [kalkanis@neuro.hfh.edu](mailto:kalkanis@neuro.hfh.edu)

Target population This recommendation applies to adults with newly diagnosed single brain metastases amenable to surgical resection; however, the recommendation does not apply to relatively radiosensitive tumors histologies (i.e., small cell lung cancer, leukemia, lymphoma, germ cell tumors and multiple myeloma). Recommendation Surgical resection plus WBRT versus WBRT alone Level 1 Class I evidence supports the use of surgical resection plus post-operative WBRT, as compared to WBRT alone, in patients with good performance status (functionally independent and spending less than 50% of time in bed) and limited extra-cranial disease. There is insufficient evidence to make a recommendation for patients with poor performance scores, advanced systemic disease, or multiple brain metastases. If WBRT is used, is there an optimal dosing/fractionation schedule? Target population This recommendation applies to adults with newly diagnosed brain metastases. Recommendation Level 1 Class I evidence suggests that altered dose/fractionation

schedules of WBRT do not result in significant differences in median survival, local control or neurocognitive outcomes when compared with "standard" WBRT dose/fractionation. (i.e., 30 Gy in 10 fractions or a biologically effective dose (BED) of 39 Gy10). If WBRT is used, what impact does tumor histopathology have on treatment outcomes? Target population This recommendation applies to adults with newly diagnosed brain metastases. Recommendation Given the extremely limited data available, there is insufficient evidence to support the choice of any particular dose/fractionation regimen based on histopathology. The following question is fully addressed in the surgery guideline paper within this series by Kalkanis et al. Given that the recommendation resulting from the systematic review of the literature on this topic is also highly relevant to the discussion of the role of WBRT in the management of brain metastases, this recommendation has been included below. Does the addition of WBRT after surgical resection improve outcomes when compared with surgical resection alone? Target population This recommendation applies to adults with newly diagnosed single brain metastases amenable to surgical resection. Recommendation Surgical resection plus WBRT versus surgical resection alone Level 1 Surgical resection followed by WBRT represents a superior treatment modality, in terms of improving tumor control at the original site of the metastasis and in the brain overall, when compared to surgical resection alone.

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## Neurosurgery

Jenrow, K. A., S. L. Brown, J. Liu, A. Kolozsvary, K. Lapanowski and J. H. Kim (2010). "Ramipril mitigates radiation-induced impairment of neurogenesis in the rat dentate gyrus." Radiat Oncol **5**: 6. 2825515. [PDF Full-Text](#)

Henry Ford Hospital, Department of Neurosurgery, 3074 E&R Building, 2799 W Grand Boulevard, Detroit, Michigan 48202, USA. [nskje@neuro.hfh.edu](mailto:nskje@neuro.hfh.edu)

ABSTRACT: BACKGROUND: Sublethal doses of whole brain irradiation (WBI) are commonly administered therapeutically and frequently result in late delayed radiation injuries, manifesting as severe and irreversible cognitive impairment. Neural progenitors within the subgranular zone (SGZ) of the dentate gyrus are among the most radiosensitive cell types in the adult brain and are known to participate in hippocampal plasticity and normal cognitive function. These progenitors and the specialized SZG microenvironment required for neuronal differentiation are the source of neurogenic potential in the adult dentate gyrus, and provide a continuous supply of immature neurons which may then migrate into the adjacent granule cell layer to become mature granule cell neurons. The extreme radiosensitivity of these progenitors and the SGZ microenvironment suggests the hippocampus as a prime target for radiation-induced cognitive impairment. The brain renin-angiotensin system (RAS) has previously been implicated as a potent modulator of neurogenesis within the SGZ and selective RAS inhibitors have been implicated as mitigators of radiation brain injury. Here we investigate the angiotensin converting enzyme (ACE) inhibitor, ramipril, as a mitigator of radiation injury in this context. METHODS: Adult male Fisher 344 rats received WBI at doses of 10 Gy and 15 Gy. Ramipril was administered beginning 24 hours post-WBI and maintained continuously for 12 weeks. RESULTS: Ramipril produced small but significant reductions in the deleterious effects of radiation on progenitor proliferation and neuronal differentiation in the rat dentate gyrus following 10 Gy-WBI, but was not effective following 15 Gy-WBI. Ramipril also reduced the basal rate of neurogenesis within the SGZ in unirradiated control rats. CONCLUSIONS: Our results indicate that chronic ACE inhibition with ramipril, initiated 24 hours post-irradiation, may reduce apoptosis among SGZ progenitors and/or inflammatory disruption of neurogenic signaling within SGZ microenvironment, and suggest that angiotensin II may participate in maintaining the basal rate of granule cell neurogenesis.

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## Neurosurgery

Kalkanis, S. N., D. Kondziolka, L. E. Gaspar, S. H. Burri, A. L. Asher, C. S. Cobbs, M. Ammirati, P. D. Robinson, D. W. Andrews, J. S. Loeffler, M. McDermott, M. P. Mehta, T. Mikkelsen, J. J. Olson, N. A. Paleologos, R. A. Patchell, T. C. Ryken and M. E. Linskey (2010). "The role of surgical resection in the management of newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline." Journal of Neuro-Oncology **96**(1): 33-43. [PDF Full-Text](#)

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Charlotte, NC 28203 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Robinson, Paula D.] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. Kalkanis, SN, Henry Ford Hlth Syst, Dept Neurosurg, 2799 W Grand Blvd,K-11, Detroit, MI 48202 USA. [kalkanis@neuro.hfh.edu](mailto:kalkanis@neuro.hfh.edu)

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

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## Neurosurgery

Linskey, M. E., D. W. Andrews, A. L. Asher, S. H. Burri, D. Kondziolka, P. D. Robinson, M. Ammirati, C. S. Cobbs, L. E. Gaspar, J. S. Loeffler, M. McDermott, M. P. Mehta, T. Mikkelsen, J. J. Olson, N. A. Paleologos, R. A. Patchell, T. C. Ryken and S. N. Kalkanis (2010). "The role of stereotactic radiosurgery in the management of patients with newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline." *Journal of Neuro-Oncology* **96**(1): 45-68. [PDF Full-Text](#)

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Boston, MA 02114 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. Kalkanis, SN, Henry Ford Hlth Syst, Dept Neurosurg, 2799 W Grand Blvd, K-11, Detroit, MI 48202 USA. [kalkanis@neuro.hfh.edu](mailto:kalkanis@neuro.hfh.edu)

Should patients with newly-diagnosed metastatic brain tumors undergo stereotactic radiosurgery (SRS) compared with other treatment modalities? Target population These recommendations apply to adults with newly diagnosed solid brain metastases amenable to SRS; lesions amenable to SRS are typically defined as measuring less than 3 cm in maximum diameter and producing minimal (less than 1 cm of midline shift) mass effect. Recommendations SRS plus WBRT vs. WBRT alone Level 1 Single-dose SRS along with WBRT leads to significantly longer patient survival compared with WBRT alone for patients with single metastatic brain tumors who have a KPS a parts per thousand yen 70. Level 2 Single-dose SRS along with WBRT is superior in terms of local tumor control and maintaining functional status when compared to WBRT alone for patients with 1-4 metastatic brain tumors who have a KPS a parts per thousand yen 70. Level 3 Single-dose SRS along with WBRT may lead to significantly longer patient survival than WBRT alone for patients with 2-3 metastatic brain tumors. Level 4 There is class III evidence demonstrating that single-dose SRS along with WBRT is superior to WBRT alone for improving patient survival for patients with single or multiple brain metastases and a KPS < 70. SRS plus WBRT vs. SRS alone Level 2 Single-dose SRS alone may provide an equivalent survival advantage for patients with brain metastases compared with WBRT + single-dose SRS. There is conflicting class I and II evidence regarding the risk of both local and distant recurrence when SRS is used in isolation, and class I evidence demonstrates a lower risk of distant recurrence with WBRT; thus, regular careful surveillance is warranted for patients treated with SRS alone in order to provide early identification of local and distant recurrences so that salvage therapy can be initiated at the soonest possible time. Surgical Resection plus WBRT vs. SRS +/- WBRT Level 2 Surgical resection plus WBRT, vs. SRS plus WBRT, both represent effective treatment strategies, resulting in relatively equal survival rates. SRS has not been assessed from an evidence-based standpoint for larger lesions (> 3 cm) or for those causing significant mass effect (> 1 cm midline shift). Level 3: Underpowered class I evidence along with the preponderance of conflicting class II evidence suggests that SRS alone may provide equivalent functional and survival outcomes compared with resection + WBRT for patients with single brain metastases, so long as ready detection of distant site failure and salvage SRS are possible. SRS alone vs. WBRT alone Level 3 While both single-dose SRS and WBRT are effective for treating patients with brain metastases, single-dose SRS alone appears to be superior to WBRT alone for patients with up to three metastatic brain tumors in terms of patient survival advantage.

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## Neurosurgery

Linskey, M. E. and S. N. Kalkanis (2010). "Evidence-linked, clinical practice guidelines-getting serious; getting professional." Journal of Neuro-Oncology **96**(1): 1-5. [PDF Full-Text](#)

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## Neurosurgery

Mehta, M. P., N. A. Paleologos, T. Mikkelsen, P. D. Robinson, M. Ammirati, D. W. Andrews, A. L. Asher, S. H. Burri, C. S. Cobbs, L. E. Gaspar, D. Kondziolka, M. E. Linskey, J. S. Loeffler, M. McDermott, J. J. Olson, R. A. Patchell, T. C. Ryken and S. N. Kalkanis (2010). "The role of chemotherapy in the management of newly diagnosed brain metastases: a systematic review and evidence-based clinical practice guideline." Journal of Neuro-Oncology **96**(1): 71-83. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Robinson, Paula D.] McMaster Univ, Evidence Based Practice

Ctr, Hamilton, ON, Canada. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Burri, Stuart H.] Carolinas Med Ctr, Dept Radiat Oncol, Charlotte, NC 28203 USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Gaspar, Laurie E.] Univ Colorado, Dept Radiat Oncol, Denver, CO 80202 USA. [Kondziolka, Douglas] Univ Pittsburgh, Dept Neurol Surg, Med Ctr, Pittsburgh, PA 15260 USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. Kalkanis, SN, Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, 2799 W Grand Blvd, K-11, Detroit, MI 48202 USA. [skalkan1@hfhs.org](mailto:skalkan1@hfhs.org)

This recommendation applies to adults with newly diagnosed brain metastases; however, the recommendation below does not apply to the exquisitely chemosensitive tumors, such as germinomas metastatic to the brain. Should patients with brain metastases receive chemotherapy in addition to whole brain radiotherapy (WBRT)? Level 1 Routine use of chemotherapy following WBRT for brain metastases has not been shown to increase survival and is not recommended. Four class I studies examined the role of carboplatin, chloroethylnitrosoureas, tegafur and temozolomide, and all resulted in no survival benefit. Two caveats are provided in order to allow the treating physician to individualize decision-making: First, the majority of the data are limited to non small cell lung (NSCLC) and breast cancer; therefore, in other tumor histologies, the possibility of clinical benefit cannot be absolutely ruled out. Second, the addition of chemotherapy to WBRT improved response rates in some, but not all trials; response rate was not the primary endpoint in most of these trials and end-point assessment was non-centralized, non-blinded, and post-hoc. Enrollment in chemotherapy-related clinical trials is encouraged.

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## Neurosurgery

Olson, J. J., N. A. Paleologos, L. E. Gaspar, P. D. Robinson, R. E. Morris, M. Ammirati, D. W. Andrews, A. L. Asher, S. H. Burri, C. S. Cobbs, D. Kondziolka, M. E. Linskey, J. S. Loeffler, M. McDermott, M. P. Mehta, T. Mikkelsen, R. A. Patchell, T. C. Ryken and S. N. Kalkanis (2010). "The role of emerging and investigational therapies for metastatic brain tumors: a systematic review and evidence-based clinical practice guideline of selected topics." *Journal of Neuro-Oncology* **96**(1): 115-142. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Gaspar, Laurie E.] Univ Colorado, Dept Radiat Oncol, Denver, CO 80202 USA. [Robinson, Paula D.; Morris, Rachel E.] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Burri, Stuart H.] Carolinas Med Ctr, Dept Radiat Oncol, Charlotte, NC 28203 USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Kondziolka, Douglas] Univ Pittsburgh, Dept Neurol Surg, Med Ctr, Pittsburgh, PA 15260 USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. Kalkanis, SN, Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, 2799 W Grand Blvd, K-11, Detroit, MI 48202 USA. [kalkanis@neuro.hfh.edu](mailto:kalkanis@neuro.hfh.edu)

What evidence is available regarding the emerging and investigational therapies for the treatment of metastatic brain tumors? Target population These recommendations apply to adults with brain metastases. Recommendations New radiation sensitizers Level 2 A subgroup analysis of a large prospective randomized controlled trial (RCT) suggested a prolongation of time to neurological progression with the early use of motexafin-gadolinium (MGd). Nonetheless this was not borne out in the overall study population and therefore an unequivocal recommendation to use the currently available radiation sensitizers, motexafin-gadolinium and

efaproxiral (RSR 13) cannot be provided. Interstitial modalities There is no evidence to support the routine use of new or existing interstitial radiation, interstitial chemotherapy and or other interstitial modalities outside of approved clinical trials. New chemotherapeutic agents Level 2 Treatment of melanoma brain metastases with whole brain radiation therapy and temozolomide is reasonable based on one class II study. Level 3 Depending on individual circumstances there may be patients who benefit from the use of temozolomide or fotemustine in the therapy of their brain metastases. Molecular targeted agents Level 3 The use of epidermal growth factor receptor inhibitors may be of use in the management of brain metastases from non-small cell lung carcinoma.

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## Neurosurgery

Robinson, P. D., S. N. Kalkanis, M. E. Linskey and P. L. Santaguida (2010). "Methodology used to develop the AANS/CNS management of brain metastases evidence-based clinical practice parameter guidelines." Journal of Neuro-Oncology **96**(1): 11-16. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI 48202 USA. [Robinson, Paula D.; Santaguida, P. Lina] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA.

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## Neurosurgery

Ryken, T. C., M. McDermott, P. D. Robinson, M. Ammirati, D. W. Andrews, A. L. Asher, S. H. Burri, C. S. Cobbs, L. E. Gaspar, D. Kondziolka, M. E. Linskey, J. S. Loeffler, M. P. Mehta, T. Mikkelsen, J. J. Olson, N. A. Paleologos, R. A. Patchell and S. N. Kalkanis (2010). "The role of steroids in the management of brain metastases: a systematic review and evidence-based clinical practice guideline." Journal of Neuro-Oncology **96**(1): 103-114. [PDF Full-Text](#)

[Kalkanis, Steven N.] Henry Ford Hlth Syst, Dept Neurosurg, Hermelin Brain Tumor Ctr, Detroit, MI 48202 USA. [Ryken, Timothy C.] Iowa Spine & Brain Inst, Dept Neurosurg, Iowa City, IA USA. [McDermott, Michael] Univ Calif San Francisco, Dept Neurosurg, San Francisco, CA 94143 USA. [Robinson, Paula D.] McMaster Univ, Evidence Based Practice Ctr, Hamilton, ON, Canada. [Ammirati, Mario] Ohio State Univ, Med Ctr, Dept Neurosurg, Columbus, OH 43210 USA. [Andrews, David W.] Thomas Jefferson Univ, Dept Neurosurg, Philadelphia, PA 19107 USA. [Asher, Anthony L.] Carolina Neurosurg & Spine Associates, Dept Neurosurg, Charlotte, NC USA. [Burri, Stuart H.] Carolinas Med Ctr, Dept Radiat Oncol, Charlotte, NC 28203 USA. [Cobbs, Charles S.] Calif Pacific Med Ctr, Dept Neurosci, San Francisco, CA USA. [Gaspar, Laurie E.] Univ Colorado, Dept Radiat Oncol, Denver, CO 80202 USA. [Kondziolka, Douglas] Univ Pittsburgh, Dept Neurol Surg, Med Ctr, Pittsburgh, PA 15260 USA. [Linskey, Mark E.] Univ Calif Irvine, Med Ctr, Dept Neurosurg, Orange, CA USA. [Loeffler, Jay S.] Massachusetts Gen Hosp, Dept Radiat Oncol, Boston, MA 02114 USA. [Mehta, Minesh P.] Univ Wisconsin, Dept Human Oncol, Sch Publ Hlth & Med, Madison, WI USA. [Mikkelsen, Tom] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Olson, Jeffrey J.] Emory Univ, Sch Med, Dept Neurosurg, Atlanta, GA USA. [Paleologos, Nina A.] Northshore Univ Hlth Syst, Dept Neurol, Evanston, IL USA. [Patchell, Roy A.] Barrow Neurol Inst, Dept Neurol, Phoenix, AZ 85013 USA.

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Do steroids improve neurologic symptoms in patients with metastatic brain tumors compared to no treatment? If steroids are given, what dose should be used? Comparisons include: (1) steroid therapy versus none. (2) comparison of different doses of steroid therapy. Target population These recommendations apply to adults diagnosed with brain metastases. Recommendations Steroid therapy versus no steroid therapy Asymptomatic brain metastases patients without mass effect Insufficient evidence exists to make a treatment recommendation for this clinical scenario. Brain metastases patients with mild symptoms related to mass effect Level 3 Corticosteroids are recommended to provide temporary symptomatic relief of symptoms related to increased intracranial pressure and edema secondary to brain metastases. It is recommended for patients who are symptomatic from metastatic disease to the brain that a starting dose of 4-8 mg/day of dexamethasone be considered. Brain metastases patients with moderate to severe symptoms related to mass effect Level 3 Corticosteroids are recommended to provide temporary symptomatic relief of symptoms related to increased intracranial pressure and edema secondary to brain metastases. If patients exhibit severe symptoms

consistent with increased intracranial pressure, it is recommended that higher doses such as 16 mg/day or more be considered. Choice of Steroid Level 3 If corticosteroids are given, dexamethasone is the best drug choice given the available evidence. Duration of Corticosteroid Administration Level 3 Corticosteroids, if given, should be tapered slowly over a 2 week time period, or longer in symptomatic patients, based upon an individualized treatment regimen and a full understanding of the long-term sequelae of corticosteroid therapy. Given the very limited number of studies (two) which met the eligibility criteria for the systematic review, these are the only recommendations that can be offered based on this methodology. Please see "Discussion" and "Summary" section for additional details.

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## **Neurosurgery**

Seyfried, D. M., Y. X. Han, D. M. Yang, J. Ding, L. H. Shen, S. Savant-Bhonsale and M. Chopp (2010). "Localization of bone marrow stromal cells to the injury site after intracerebral hemorrhage in rats Laboratory investigation." Journal of Neurosurgery **112**(2): 329-335.

[PDF Full-Text](#)

[Seyfried, Donald M.; Han, Yuxia; Yang, Dongmei; Ding, Jennifer] Henry Ford Hlth Syst, Dept Neurosurg, Detroit, MI 48202 USA. [Shen, Li Hong; Chopp, Michael] Henry Ford Hlth Syst, Dept Neurol, Detroit, MI 48202 USA. [Savant-Bhonsale, Smita] Theradigm Inc, Dept Neurobiol, Baltimore, MD USA.

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Object. Previous studies demonstrated that intravascular injection of bone marrow stromal cells (BMSCs) significantly improved neurological functional recovery in a rat model of intracerebral hemorrhage (ICH). To further investigate the fate of transplanted cells, we examined the effect of male rat BMSCs administered to female rats after ICH. Methods. Twenty-seven female Wistar rats were subjected to ICH surgery. At 24 hours after ICH, these rats were randomly divided into 3 groups and injected intravenously with 1 ml phosphate-buffered saline or 0.5 million or 1 million male rat BMSCs in phosphate-buffered saline. To evaluate the neurological functional Outcome, each rat was subjected to a series of behavioral tests (modified neurological severity score and corner turn test) at 1, 7, and 14 days after ICH. The rats were anesthetized intraperitoneally and killed, and the brain tissues were processed at Day 14 after ICH. Immunohistochemistry and in situ hybridization were used to identify cell-specific markers. Results. The male rat BMSCs significantly improved the neurological functional outcome and also significantly diminished tissue loss when intravenously transplanted into the rats after ICH. Immunoassay for bromodeoxyuridine (BrdU) and neuronal markers demonstrated a significant increase in the number of BrdU-positive cells, which indicated endogenous neurogenesis, and a significant increase in the number of cells positive for immature neuronal markers. In situ hybridization showed that more BMSCs resided around the hematoma of the rats treated with the 1-million-cell dose compared with the 0.5-million-cell-dose group. In addition, a subfraction of Y chromosome-positive cells were co-immunostained with the neuronal marker microtubule-associated protein-2 or the astrocytic marker glial fibrillary acidic protein. Conclusions. Male rat BMSCs improve neurological outcome and increase histochemical parameters of neurogenesis when administered to female rats after ICH. This study has shown that the intravenously administered male rat BMSCs enter the brain, migrate to the perihematoma area, and express parenchymal markers. (DOI: 10.3171/2009.2.JNS08907)

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## **Obstetrics & Gynecology**

Yerge-Cole, G. (2010). "Collecting Every Drop." Journal of Human Lactation **26**(1): 10-10.

[Article Request Form](#)

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Yerge-Cole, G, Henry Ford W Bloomfield Hosp, Birthing Unit, W Bloomfield, MI USA.

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## **Ophthalmology**

Shah, S. A. and W. J. Stark (2010). "Mechanical penetration of a femtosecond laser-created laser-assisted in situ keratomileusis flap." Cornea **29**(3): 336-8. [PDF Full-Text](#)

From the Henry Ford Health System, Detroit, MI; and the Wilmer Ophthalmological Institute, Johns Hopkins University School of Medicine, Baltimore, MD.

**PURPOSE::** We report a case of mechanical flap penetration during LASIK using the Intralase femtosecond laser. **METHODS::** Case Report. **RESULTS::** A 50-year-old hyperope planned to have LASIK using the Intralase femtosecond laser. During the creation of the flap, a gas bubble formed anterior to the flap. This area was noted to be adherent to the cornea. Attempts to lift the flap resulted in flap penetration. The case was aborted, and the flap was repositioned. At postoperative week one, the patient's visual acuity was restored to preoperative levels. **CONCLUSIONS::** When a gas bubble appears during the creation of a LASIK flap with the Intralase femtosecond laser, we recommend waiting for the bubble to disperse. If significant resistance is encountered during the lifting of the flap, we suggest aborting the case.

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## **Pathology**

Lee, H., R. T. Stapp, A. H. Ormsby and V. V. Shah (2010). "The usefulness of IgG and IgM immunostaining of periportal inflammatory cells (plasma cells and lymphocytes) for the distinction of autoimmune hepatitis and primary biliary cirrhosis and their staining pattern in autoimmune hepatitis-primary biliary cirrhosis overlap syndrome." *Am J Clin Pathol* **133**(3): 430-7. [PDF Full-Text](#)

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, 2799 West Grand Blvd., Detroit, MI 48202, USA.

Autoimmune hepatitis (AIH)-primary biliary cirrhosis (PBC) overlap syndrome (OS) is a vaguely defined entity demonstrating features of AIH and PBC. We investigated the usefulness of IgG and IgM immunostaining for the distinction of AIH and PBC and their staining pattern in cases of possible OS. The approximate quantity of IgG+ and IgM+ periportal inflammatory cells in immunohistochemical analysis were compared in cases of AIH, PBC, and OS. AIH cases showed predominant IgG immunostaining of periportal inflammatory cells. A significant number of PBC cases also demonstrated IgG predominance rather than IgM. Six OS cases had IgG predominance, 4 had IgM predominance, and 1 was equivocal. The usefulness of IgG and IgM immunostaining is limited in PBC cases with IgM predominance for excluding AIH. IgG predominance is not specific for AIH. OS does not demonstrate either IgG or IgM predominance ( $P > .2$ ) and does not help classify OS into either category.

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## **Pharmacy**

Fichuk, S., R. Chambers, S. Davis, A. Michael, M. Peters and M. Mlynarck (2009). "Prediction Model to Identify Risk Factors for Multidrug Resistant Gram-Negative Bacilli in Patients with Sepsis." *Critical Care Medicine* **37**(12): 478. [Article Request Form](#)

[Fichuk, Sarah; Chambers, Rachel; Davis, Susan; Michael, Angela; Peters, Michael; Mlynarck, Mark] Henry Ford Hosp, Detroit, MI USA.

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## **Pharmacy**

Lasak-Myall, T., M. Peters, M. Mylnarek and J. Moody (2009). "The Opportunity for Pharmacy Intervention on an Urban Teaching Hospital Rapid Response Team." *Critical Care Medicine* **37**(12): 958. [Article Request Form](#)

[Lasak-Myall, Tracey; Peters, Michael; Mylnarek, Mark; Moody, Jeffery] Henry Ford Hosp, Detroit, MI USA.

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## **Pulmonary & Critical Care Medicine**

Parodi, O., R. Patel, M. Chiha, H. Kanneh, I. Obeid, H. Rana and R. Kattoo (2009). "I Ate Something Bad: A Rare Case of Multiple Brain Abscesses Secondary to *Listeria Monocytogenes*." *Critical Care Medicine* **37**(12): 1039. [Article Request Form](#)

[Parodi, Oscar; Patel, Ruchir; Chiha, Maguy; Kanneh, Haitham; Obeid, Imad; Rana, Haris; Kattoo, Ron] Henry Ford Hosp, Detroit, MI USA.

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## **Radiation Oncology**

Potters, L., B. Kavanagh, J. M. Galvin, J. M. Hevezi, N. A. Janjan, D. A. Larson, M. P. Mehta, S. Ryu, M. Steinberg, R. Timmerman, J. S. Welsh and S. A. Rosenthal (2010). "American Society for Therapeutic Radiology and Oncology (Astro) and American College of Radiology (Acr) Practice Guideline for the Performance of Stereotactic Body Radiation Therapy." International Journal of Radiation Oncology Biology Physics **76**(2): 326-332. [PDF Full-Text](#)

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These guidelines are an educational tool designed to assist practitioners in providing appropriate radiologic care for patients. They are not inflexible rules or requirements of practice and are not intended, nor should they be used, to establish a legal standard of care. For these reasons and those set forth below, the American College of Radiology cautions against the use of these guidelines in litigation in which the clinical decisions of a practitioner are called into question. The ultimate judgment regarding the propriety of any specific procedure or course of action must be made by the physician or medical physicist in light of all the circumstances presented. Thus, an approach that differs from the guidelines, standing alone, does not necessarily imply that the approach was below the standard of care. To the contrary, a conscientious practitioner may responsibly adopt a course of action different from that set forth in the guidelines when, in the reasonable judgment of the practitioner, such course of action is indicated by the condition of the patient, limitations of available resources, or advances in knowledge or technology subsequent to publication of the guidelines. However, a practitioner who employs an approach substantially different from these guidelines is advised to document in the patient record information sufficient to explain the approach taken. The practice of medicine involves not only the science, but also the art of dealing with the prevention, diagnosis, alleviation, and treatment of disease. The variety and complexity of human conditions make it impossible to always reach the most appropriate diagnosis or to predict with certainty a particular response to treatment. Therefore, it should be recognized that adherence to these guidelines will not assure an accurate diagnosis or a successful outcome. All that should be expected is that the practitioner will follow a reasonable course of action based on current knowledge, available resources, and the needs of the patient to deliver effective and safe medical care. The sole purpose of these guidelines is to assist practitioners in achieving this objective.

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## **Radiation Oncology**

Vlachaki, M. T. and S. Kumar (2010). "Helical tomotherapy in the radiotherapy treatment of Hodgkin's disease - a feasibility study." Journal of Applied Clinical Medical Physics **11**(1): 77-87. [Article Request Form](#)

[Vlachaki, Maria T.] British Columbia Canc Agcy, Vancouver Isl Ctr, Dept Radiat Oncol, Victoria, BC V8R 6V5, Canada. [Kumar, Sanath] Henry Ford Hosp, Dept Radiat Oncol, Detroit, MI 48202 USA. Vlachaki, MT, British Columbia Canc Agcy, Vancouver Isl Ctr, Dept Radiat Oncol, 2410 Lee Ave, Victoria, BC V8R 6V5, Canada. [mvlachaki@bccancer.bc.ca](mailto:mvlachaki@bccancer.bc.ca)

Radiation therapy for advanced Hodgkin's disease often requires large fields and may result in significant exposure of normal tissues to ionizing radiation. In longterm survivors, this may increase the risk for late toxicity including secondary malignancies. 3D CRT has been successfully used to treat this disease but treatment delivery is often complex requiring matching of photon with electron beams, and utilization of field-in-field techniques and of partial transmission blocks. HT is an arc-rotational intensity modulated radiation therapy technique proven to achieve superior target dose conformality and sharp dose gradients around critical normal tissues. HT, however, has also been associated with higher volumes of low-dose regions in normal tissues and, therefore, higher integral dose. The present study was undertaken to compare the dosimetry of 3D CRT to HT in a pediatric patient with advanced HD. Clinical target volume (CTV) included bilateral lower cervical and supraclavicular areas, mediastinum, bilateral hili, left axilla and bilateral diaphragmatic lymph nodes. The planning target volume (PTV) was derived by circumferentially expanding the CTV by 1 cm. Whole lung and heart irradiation was also planned due to bilateral pleural and pericardial effusions. The prescribed radiation dose was 21 Gy to the PTV and 10.5 Gy to the whole lung and heart. Target coverage was comparable for both plans. The minimum, maximum, and mean PTV doses were 18.61 Gy, 22.45 Gy and 21.52 Gy with 3D CRT and 19.85 Gy, 22.36 Gy and 21.39 Gy with HT, respectively. HT decreased mean normal tissue dose by 21.6% and 20.07% for right and left breast, 20.40% for lung, 30.78% for heart, and 22.74% for the thyroid gland. Integral dose also decreased with HT by 46.50%. HT results in significant dosimetric gain related to normal tissue sparing compared to 3D CRT. Further studies are warranted to evaluate clinical applications of HT in patients with HD.

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### **Sleep Medicine**

Ancoli-Israel, S., A. D. Krystal, W. V. McCall, K. Schaefer, A. Wilson, R. Claus, R. Rubens and T. Roth (2010). "A 12-Week, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Effect of Eszopiclone 2 mg on Sleep/Wake Function in Older Adults with Primary and Comorbid Insomnia." *Sleep* **33**(2): 225-234. [PDF Full-Text](#)

[Ancoli-Israel, Sonia] Univ Calif San Diego, San Diego, CA 92103 USA. [Krystal, Andrew D.] Duke Univ, Med Ctr, Durham, NC USA. [McCall, W. Vaughn] Wake Forest Univ Hlth Sci, Winston Salem, NC USA. [Schaefer, Kendyl; Wilson, Amy; Claus, Raymond; Rubens, Robert] Sepracor Inc, Marlborough, MA USA. [Roth, Thomas] Henry Ford Sleep Disorders Ctr, Detroit, MI USA.

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Background: Longer-term pharmacologic studies for insomnia in older individuals are sparse. Objective: To evaluate the efficacy and safety of 12 weeks of nightly eszopiclone in elderly outpatients with insomnia. Methods: Participants (65-85 years) met DSM-IV-TR criteria for insomnia with total sleep times (TST)  $\leq$  6 h, and wake time after sleep onset (WASO)  $\geq$  45 min. Participants were randomized to 12 weeks of eszopiclone 2 mg (n = 194) or placebo (n = 194), followed by a 2-week single-blind placebo run-out. Subject-reported measures of sleep (sTST, sleep latency [sSL], sWASO) and daytime function (alertness, concentration, wellbeing, ability to function) were assessed. AEs were monitored. Results: Subjects treated with 2 mg eszopiclone slept longer at night on average and at every individual time point compared to baseline than placebo subjects, as measured by TST over the 12-week double-blind period (P < 0.0001). Mean sTST over the double-blind period for eszopiclone-treated subjects was 360.08 min compared to 297.86 min at baseline, a mean change of 63.24 min. Over the double-blind period, eszopiclone-treated subjects also experienced a significantly greater improvement in sSL compared to placebo, with a mean decrease of 24.62 min versus a mean decrease of 19.92 min, respectively (P = 0.0014). Eszopiclone subjects also experienced a significantly greater decrease in WASO (mean decrease of 36.4 min) compared to placebo subjects (decrease of 14.8 min) (P < 0.0001). Post-discontinuation, sleep parameters were statistically improved versus baseline for eszopiclone (P-values  $\leq$  0.01), indicating no rebound. The most common AEs ( $\geq$  5%) were headache (eszopiclone 13.9%, placebo 12.4%), unpleasant taste (112.4%, 1.5%), and nasopharyngitis (5.7%, 6.2%). Conclusion: In this Phase IV trial of older adults with insomnia, eszopiclone significantly improved patient-reported sleep and daytime function relative to placebo. Improvements occurred within the first week and were maintained for 3 months, with no evidence of rebound insomnia following discontinuation. The 12 weeks of treatment were well tolerated.

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### **Sleep Medicine**

Budhiraja, R., S. F. Quan, N. M. Punjabi, C. L. Drake, R. Dickman and R. Fass (2010). "Power Spectral Analysis of the Sleep Electroencephalogram in Heartburn Patients With or

Without Gastroesophageal Reflux Disease A Feasibility Study." Journal of Clinical Gastroenterology **44**(2): 91-96. [Article Request Form](#)

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Goals: Determine the feasibility of using power spectrum of the sleep electroencephalogram (EEG) as a more sensitive tool than sleep architecture to evaluate the relationship between gastroesophageal reflux disease (GERD) and sleep. Background: GERD has been shown to adversely affect subjective sleep reports but not necessarily objective sleep parameters. Study: Data were prospectively collected from symptomatic patients with heartburn. All symptomatic patients underwent upper endoscopy. Patients without erosive esophagitis underwent pH testing. Sleep was polygraphically recorded in the laboratory. Spectral analysis was performed to determine the power spectrum in 4 bandwidths: delta (0.8 to 4.0 Hz), theta (4.1 to 8.0 Hz), alpha (8.1 to 13.0 Hz), and beta (13.1 to 20.0 Hz). Results: Eleven heartburn patients were included in the GERD group (erosive esophagitis) and 6 heartburn patients in the functional heartburn group (negative endoscopy, pH test, response to proton pump inhibitors). The GERD patients had evidence of lower average delta-power than functional heartburn patients. Patients with GERD had greater overall a-power in the latter half of the night (3 hours after sleep onset) than functional heartburn patients. No significant differences were noted in conventional sleep stage between the 2 groups. Conclusions: Among heartburn patients with GERD, EEG spectral power during sleep is shifted towards higher frequencies compared with heartburn patients without GERD despite similar sleep architecture. This feasibility study demonstrated that EEG spectral power during sleep might be the preferred tool to provide an objective analysis about the effect of GERD on sleep.

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## **Sleep Medicine**

Culpepper, L. and T. Roth (2009). "Recognizing and managing obstructive sleep apnea in primary care." Prim Care Companion J Clin Psychiatry **11**(6): 330-8. 2805569. [Article Request Form](#)

Department of Family Medicine, Boston Medical Center, Massachusetts and the Sleep Disorders and Research Center, Henry Ford Hospital, Detroit, Michigan.

OBJECTIVE: This review aims to impart information regarding recognition of obstructive sleep apnea (OSA) and associated excessive sleepiness (ES) in the primary care setting in order to provide optimal care to patients with this common but serious condition. This review will also discuss the prevalence and treatment of depression in patients with OSA. DATA SOURCES: A MEDLINE search of articles published between 1990 and 2008 was conducted using the search terms obstructive sleep apnea AND excessive sleepiness, obstructive sleep apnea AND depression, and obstructive sleep apnea AND primary care. Searches were limited to articles in English concerned with adult patients. STUDY SELECTION: In total, 239 articles were identified. Articles concerning other sleep disorders and forms of apnea were excluded. The reference lists of identified articles were searched manually to find additional articles of interest. DATA SYNTHESIS: Primary care physicians can aid in the diagnosis of OSA and associated ES by being vigilant for lifestyle and physical risk factors associated with this condition. In addition, primary care physicians should maintain a high level of clinical suspicion when presented with illnesses that are commonly comorbid with OSA, such as psychiatric disorders and depression, in particular. Conversely, assessment of patients with OSA for common comorbidities may also improve a patient's prognosis and quality of life. CONCLUSIONS: Primary care physicians play a vital role in recognizing OSA and ES. These clinicians are crucial in supporting their patients during treatment by ensuring that they have clear, concise information regarding available therapies and the correct application and maintenance of prescribed devices.

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## **Sleep Medicine**

Drake, C. L. (2010). "The characterization and pathology of circadian rhythm sleep disorders." J Fam Pract **59**(1 Suppl): S12-7. [PDF Full-Text](#)

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Being alert to excessive sleepiness and/or insomnia in shift workers may prevent comorbidities and accidents that can occur as a consequence of shift-worker disorder (SWD). Not all shift workers develop SWD. Thus, identification of sensitivity to shift work may be facilitated by asking patients whether they find it difficult to function in the absence of consolidated sleep, prefer to be active early in the day, or have previously experienced insomnia due to sleep challenges.

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### **Sleep Medicine**

Roehrs, T. A. (2009). "Does Effective Management of Sleep Disorders Improve Pain Symptoms?" Drugs **69**: 5-11. [PDF Full-Text](#)

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Co-morbid insomnia is a much more frequent problem than primary insomnia. In co-morbid insomnia, management of the underlying disease can improve sleep difficulty. Conversely, treating the sleep disorder may also improve the co-morbid condition. For example, patients with painful chronic illnesses are more likely to experience sleep disturbance than patients with non-painful illnesses. Moreover, there is evidence that insomnia further exacerbates pain in these illnesses. This suggests that a reciprocal relationship exists between pain and sleep, and that intervention targeted primarily at insomnia may improve pain. Treatment options for sleep disorders in the context of pain that have been assessed include cognitive behavioural therapy for insomnia and various pharmacological therapies. In randomized clinical trials, cognitive behavioural therapy significantly improved insomnia secondary to chronic pain compared with control therapy, but pain was only improved in patients in whom it was associated with pain disorders other than fibromyalgia. Of the pharmacological agents studied (zopiclone, zolpidem and triazolam), only triazolam improved both sleep and pain to a greater extent than placebo. Overall, clinical data supporting a cause-effect relationship between insomnia and pain are preliminary and are limited to several small trials. Further investigation is required to clarify the extent of the link between insomnia and pain and whether Successfully managing insomnia secondary to pain improves pain symptoms. Areas of particular interest include investigation of the effect of sleep agents on analgesia and the effect of analgesics on sleep.

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### **Sleep Medicine**

Roth, T. (2009). "Does Effective Management of Sleep Disorders Reduce Substance Dependence?" Drugs **69**: 65-75. [PDF Full-Text](#)

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Insomnia is often associated with substance dependence, with evidence suggesting that individuals seeking medical attention for sleep complaints are more likely to have drug or alcohol abuse problems than the general population. Disturbed sleep is associated with the abuse of a variety of drugs, with patients dependent on nicotine, alcohol and illicit drugs all reporting poor sleep. In addition, withdrawal from nicotine, alcohol and drugs of abuse is also associated with insomnia, and this may result in an increased risk of relapse if the sleep problems remain unresolved. Although studies suggest that the majority of pharmacological and behavioural interventions for insomnia are effective in treating sleep disturbances in dependent patients undergoing short-term drug withdrawal and short and long-term alcohol withdrawal, several questions remain unanswered. For example, little is known about the risk of relapse in abstinent drug-dependent patients experiencing withdrawal-related insomnia, the effect of insomnia treatment on nicotine withdrawal, or whether insomnia interventions prevent relapse. Participants of a workshop, held at the 6th annual meeting of The International Sleep

Disorders Forum: The Art of Good Sleep in 2008, evaluated whether the effective management of sleep disorders could reduce substance dependence and the risk of relapse. Following the workshop a targeted literature review was conducted addressing this question. Data from this review that either pharmacological or cognitive behavioural treatment of insomnia could reduce the risk of relapse in substance dependence were substantially lacking. Further research is therefore required to increase our understanding of the impact of insomnia on patients with substance dependence.

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### **Sleep Medicine**

Roth, T., J. M. Price, D. A. Amato, R. P. Rubens, J. M. Roach and T. J. Schnitzer (2009). "The effect of eszopiclone in patients with insomnia and coexisting rheumatoid arthritis: a pilot study." Prim Care Companion J Clin Psychiatry **11**(6): 292-301. 2805564. [Article Request Form](#)

Henry Ford Sleep Disorders Clinic, Detroit, Michigan ; Sepracor Inc, Marlborough, Massachusetts ; and Northwestern University Feinberg School of Medicine, Chicago, Illinois.

**OBJECTIVE:** To evaluate the efficacy and safety of eszopiclone 3 mg, a nonbenzodiazepine medication/hypnotic indicated for the treatment of insomnia with comorbid rheumatoid arthritis (RA). **METHOD:** This multicenter, double-blind, placebo-controlled pilot study was conducted in 153 patients aged 25-64 years with American College of Rheumatology-defined RA who met DSM-IV criteria for insomnia. The data were collected from February to November of 2004. Patients were randomly assigned to either eszopiclone or placebo nightly for 4 weeks, followed by a 2-week placebo run out. Efficacy was evaluated using patient reports of sleep (wake time after sleep onset [WASO], sleep latency [SL], and total sleep time [TST]), daytime function, pain, and RA assessments. Insomnia severity was evaluated using the Insomnia Severity Index. Safety was also evaluated. **RESULTS:** Eszopiclone significantly improved all patient-reported sleep measures (WASO, SL, and TST), sleep quality, depth of sleep, and daytime function ( $P < .05$  vs placebo). At week 4, 48% of eszopiclone-treated patients had no clinically meaningful insomnia as assessed by ISI score (versus 30% of placebo-treated patients,  $P = .03$ ). Eszopiclone was significantly better than placebo on some RA-associated pain measures: (1) overall ( $P = .05$ ), pain ( $P = .006$ ), and pain and other symptoms ( $P = .02$ ) scores of the Arthritis Self-Efficacy Scale, (2) tender joint counts ( $P = .03$ ) and pain severity scores ( $P = .023$ ), (3) the activities domain of the Health Assessment Questionnaire-Disability Index ( $P = .04$ ), and (4) the role physical ( $P = .03$ ) and bodily pain ( $P = .01$ ) scales of the 36-item Medical Outcomes Study Short-Form General Health Survey. The most commonly reported adverse events with eszopiclone were unpleasant taste and transient increases in RA symptoms. **CONCLUSIONS:** In this pilot study of patients with insomnia comorbid with RA, eszopiclone 3 mg improved all assessed sleep and daytime function measures over the treatment period, as well as some measures of RA-associated pain, disability, and quality of life. **TRIAL REGISTRATION:** clinicaltrials.gov Identifier: NCT00367965.

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### **Surgery**

Andrzejewski, T., Y. Huang, L. Combs, I. Rubinfeld, J. Jordan and M. Horst (2009). "Peg Tubes: Useful Adjunct or Dangerous Intervention?" Critical Care Medicine **37**(12): 275. [Article Request Form](#)

[Andrzejewski, Tanja; Huang, Yung; Combs, Lesley; Rubinfeld, Ilan; Jordan, Jack; Horst, Mathilda] Henry Ford Hosp, Detroit, MI USA.

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### **Surgery**

Combs, L., I. Rubinfeld, T. Andrzejewski, J. Jordon, H. Yung and M. Horst (2009). "Post Operative Hemorrhage: Where's the Harm." Critical Care Medicine **37**(12): 137. [Article Request Form](#)

[Combs, Lesley; Rubinfeld, Ilan; Andrzejewski, Tanja; Jordon, Jack; Yung, Huang; Horst, Mathilda] Henry Ford Hosp, Detroit, MI USA.

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## **Surgery**

Grossman, P. M., C. Kasapis, K. Munir, D. Share, S. J. Chetcuti, T. J. Nypaver, P. Bove, H. D. Aronow and H. S. Gurm (2009). "Contemporary Below-the-Knee and Femoral-Popliteal Percutaneous Arterial Intervention: A Comparison of Procedural Outcomes and Predictors of Success - Insights From the Blue Cross Blue Shield of Michigan Cardiovascular Consortium (BMC2-PVI)." Circulation **120**(18): S956-S957. [Article Request Form](#)

[Grossman, Paul M.; Kasapis, Christos; Munir, Khan; Share, David; Chetcuti, Stanley J.; Gurm, Hitinder S.] Univ Michigan Hosps & Hlth Cntr, Ann Arbor, MI USA. [Nypaver, Timothy J.] Henry Ford Hosp & Hlth Syst, Detroit, MI USA. [Bove, Paul] William Beaumont Hosps & Hlth Syst, Royal Oak, MI USA. [Aronow, Herbert D.] St Joseph Mercy Hosp, Ypsilanti, MI USA.

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## **Surgery**

Kakkos, S. K., J. A. Haddad and G. K. Haddad (2010). "A novel fluoroscopic-assisted balloon thrombectomy: technique for thrombosed hemodialysis prosthetic grafts." J Vasc Access **EPub Ahead of Print**. [Article Request Form](#)

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

Background: Previous studies have shown that stenosis of the arterial anastomosis of thrombosed hemodialysis (HD) grafts, unmasked after conventional thrombectomy, very often necessitate subsequent arterial angioplasty. The aim of this study was to describe a novel fluoroscopic-assisted balloon thrombectomy technique which permits simultaneous arterial angioplasty (should this is required) for thrombosed HD grafts. Methods: Thirty patients with 36 thrombotic episodes of their prosthetic HD grafts participated in this study. A balloon angioplasty catheter is placed beyond the arterial anastomosis, over a guidewire; the balloon is inflated with contrast solution under fluoroscopy and pulled back to remove the arterial thrombus from the anastomosis. Any coexisting stenosis revealed by balloon indentation is completely dilated at that time, rather than after the thrombectomy. Mechanical thrombolysis of the graft and venous outflow is then performed with the AngioJet catheter (Possis Medical, Inc). Results: Technical and clinical success rates (the latter defined as one subsequent HD session) of the procedure were 100% and 94%, respectively. No complications, including arterial embolism, vessel rupture or pulmonary embolism, were encountered. Primary assisted patency at 3 and 6 months was 51% and 32%, respectively, while functional secondary patency at the same follow-up points was 78%. Conclusions: Our technique is safe and also effective in both short- and long-term follow-up. Because it offers convenience, since the treatment of arterial anastomotic stenoses is accomplished in one (rather than two) steps, this method deserves further investigation.

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## **Surgery**

Kunkel, P., C. J. Thomas, C. Seguin, D. Dereczyk, C. Rajda and M. M. Brandt (2010). "A Hospital-Based Violence Prevention Tour: A Collaborative Approach to Empower Youth." Journal of Trauma-Injury Infection and Critical Care **68**(2): 289-293. [Article Request Form](#)

[Kunkel, Patti; Thomas, Casey J.; Seguin, Cara; Dereczyk, Darlene; Rajda, Carol] Henry Ford Hosp, Div Acute Care Surg, Detroit, MI 48202 USA. [Brandt, Mary-Margaret] St Joseph Mercy Hosp, Dept Surg, Adm Off, Ann Arbor, MI 48104 USA.

Kunkel, P, Henry Ford Hosp, Div Acute Care Surg, 2799 W Grand Blvd, 1st Floor Clara Ford Pavil, Detroit, MI 48202 USA. [pkunkel1@HFHS.org](mailto:pkunkel1@HFHS.org)

Background: Youth violence is a significant problem in the United States with high recidivism rates. Considering these high recidivism rates ill Youths after an initial injury, we hypothesized a hospital-based violence prevention program aimed at increasing awareness, empowering positive conflict resolution, and promoting future vocational goals would benefit at-risk youth before they are injured. Methods: A feasibility study was completed on our Violence and Injury Prevention (VIP) tour program at our urban Level 1 trauma center. Participants were at-risk youth, aged 11 years to 17 years. Anonymous data were collected using an Audience Response System. Results: One hundred eighty-five students participated from January 2007 to August 2008. Sixty-three percent were 6th to 8th graders, 70% were boys. Seventy-nine percent stated that

they knew someone who had been injured or killed because of violence, with significantly more boys than girls ( $p = 0.05$ ). More boys than girls stated that they have access to a gun ( $p < 0.05$ ). Almost 60% of the participants stated that they had engaged in violence within the past 6 months, with no difference by gender ( $p = 0.085$ ). Of the respondents, 84.2% reported an increase in their awareness on the consequences of violence. This was more significant for girls than boys ( $P < 0.05$ ). Of the participants, 86.3% reported increased understanding of hospital care for a trauma patient. Participants stated that they would recommend VIP to others. Conclusion: VIP educated local urban youth about violence and increased their awareness of the injuries resulting from violence. In addition, at-risk youths were exposed to career opportunities in health care.

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## Urology

Kim, S. H., M. Richardson, K. Chinnakannu, V. U. Bai, M. Menon, E. R. Barrack and G. P. Reddy (2010). "Androgen receptor interacts with telomeric proteins in prostate cancer cells." J Biol Chem **EPub Ahead of Print**. [PDF Full-Text](#)

Henry Ford Health System, United States.

The telomeric complex, shelterin, plays a critical role in protecting chromosome ends from erosion, and disruption of these complexes can lead to chromosomal instability culminating in cell death or malignant transformation. We reported previously that dominant-negative mutants of one of the telomeric proteins called TIN2 causes death of androgen receptor (AR)-negative, but not AR-positive prostate cancer cells, raising the question of a possible role of AR in the structural stability of telomeric complexes. Consistent with this possibility, in the present study we observed that the AR-antagonist Casodex (bicalutamide) disrupted telomeric complexes in AR-positive LNCaP cells, but not in AR-negative PC-3 cells. Immunofluorescent studies revealed colocalization of TIN2 and AR. Reciprocal immunoprecipitation studies showed association of AR with telomeric proteins. Furthermore, telomeric proteins were overexpressed in prostate cancer cells compared to normal prostate epithelial cells, and sucrose-density gradient analysis showed co-sedimentation of AR with telomeric proteins in a shelterin-like mega complex. Together, these observations suggest an allosteric role of AR in telomere complex stability in prostate cancer cells, and suggest that AR-antagonist Casodex-mediated cell death may be due to telomere complex disruption.

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## Urology

Patel, M. N., M. Menon and C. G. Rogers (2010). "Robotic partial nephrectomy: a comparison to current techniques." Urol Oncol **28**(1): 74-6. [PDF Full-Text](#)

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, MI 48202, USA.

The bar has been set high for nephron sparing surgery by experts in both open and laparoscopic approaches. Robotic partial nephrectomy has emerged as an option for minimally invasive nephron sparing surgery. We discuss the current literature for robotic partial nephrectomy in the context of reported outcomes for open and laparoscopic partial nephrectomy.

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