

Henry Ford Health System Publication List July 2008

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Biostatistics & Research Epidemiology

Johnson, C. C., B. Kessel, et al. (2008). "The epidemiology of CA-125 in women without evidence of ovarian cancer in the Prostate, Lung, Colorectal and Ovarian Cancer (PLCO) Screening Trial." *Gynecol Oncol*. Epub Ahead of Print. [PDF Full Text](#)

Josephine Ford Cancer Center, Henry Ford Hospital, Detroit, MI, USA.

OBJECTIVE: To determine the epidemiology of CA-125 in women without ovarian cancer. **METHODS:** We analyzed demographic, medical and lifestyle characteristics related to CA-125, measured using the Centocor CA-125II RIA assay, among 25,608 multi-ethnic U.S. women aged 55-74 years enrolled in a cancer screening trial and found to have no evidence of ovarian cancer. **RESULTS:** Mean CA-125 level was 11.9 U/ml (SD 8.3); median 10.0 U/ml, interquartile range 8.0-14.0. High levels, using the clinical cut point of ≥ 35 U/ml, were associated with increased age ($p < 0.001$) and former smoking ($p < 0.021$), while hysterectomy and obesity were protective ($p < 0.001$). Mean levels were higher with increasing age ($p < 0.001$), ever use of hormone therapy ($p < 0.001$), former smoking ($p < 0.017$) and history of breast cancer ($p < 0.002$), but lower ($p < 0.001$) with non-White status, previous hysterectomy, current smoking, and obesity. Current hormone therapy use was not associated with CA-125 in women without a uterus. **CONCLUSION:** In post-menopausal women without ovarian cancer, CA-125 level is influenced by a number of factors, including race/ethnicity, age, hysterectomy, smoking history and obesity.

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Bone & Joint Center

Dougherty, P. J., D. G. Kim, et al. (2008). "Biomechanical comparison of bicortical versus unicortical screw placement of proximal tibia locking plates: a cadaveric model." *J Orthop Trauma* **22**(6): 399-403. [PDF Full Text](#)

Department of Orthopaedic Surgery, Henry Ford Hospital, Detroit, Michigan 48202, USA. pauldoug@med.umich.edu

OBJECTIVE: The purpose of this study was to compare the biomechanical properties of bicortical with unicortical screws in a proximal tibial fracture cadaveric model. **SETTING:** Biomechanics laboratory at a Level 1 trauma center. **PATIENTS/PARTICIPANTS:** Eight pairs (4 male and 4 female) of elderly (average age, 79 years; range, 63 to 104 years) cadaveric tibiae. **INTERVENTION:** Osteotomies were performed in the proximal tibia to reproduce a 41-C2 bicondylar fracture pattern. The 4.5-mm proximal tibial periarticular locking plates (Smith-Nephew, Memphis, TN) were applied to the tibiae with 4 proximal bicortical or unicortical locking screws and 3 screws distal to the fracture site. The fixed tibiae were tested by using a materials testing machine (Instron, Canton, MA) with the axial load on the medial condyle. **OUTCOME MEASUREMENTS:** The bicortical and unicortical constructs were compared for stiffness, yield load and displacement, and maximum load and displacement to failure. **RESULTS:** Bicortical screw placement significantly outperformed unicortical screw placement

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in stiffness (53.1 +/- 6.7 N/mm versus 35.6 +/- 7.2 N/mm, $P < 0.002$) and maximum load (476.5 +/- 83.8 N versus 258.9 +/- 62.1 N, $P < 0.001$) but the yield properties and the ultimate displacement were not significantly different. CONCLUSION: Bicortical screw placement may provide a biomechanically superior construct than unicortical screw placement for the stabilization of unstable proximal tibia fractures.

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Cardiology

Al-Mallah, M., F. Alqaisi, et al. (2008). "Long Term Favorable Prognostic Value of Negative Treadmill Echocardiogram in the Setting of Abnormal Treadmill Electrocardiogram: A 95 Month Median Duration Follow-Up Study." *J Am Soc Echocardiogr*. Epub Ahead of Print. [PDF Full Text](#)

Henry Ford Hospital, Heart and Vascular Institute, Detroit, Michigan.

BACKGROUND: The aim of this retrospective study was to assess if negative treadmill echocardiographic (NTME) results retained their favorable prognosis over a long period of follow-up (median, 95 months) in the setting of ischemic stress electrocardiographic (ISECG) results. METHODS: Consecutive patients with NTME results were analyzed as 2 groups (those with ISECG results and those with normal stress electrocardiographic results). Patients were followed up for a median duration of 95 months to identify major adverse cardiac events (MACEs), including all-cause death, myocardial infarction, and coronary revascularization. RESULTS: Six hundred seventy-seven patients fulfilled the inclusion criteria. Fifty-eight patients had MACEs (8.6%). The annual event rate was 1%. There was an increased unadjusted rate of MACEs among patients with ISECG results (15% vs 8%; $P = .025$). After adjusting for clinical and stress variables, ISECG results were not independently predictive of MACEs ($P = .2$). Female gender, prior coronary artery disease, metabolic equivalents achieved, and chest pain at stress were the independent predictors of MACEs. CONCLUSIONS: Patients with NTME results had excellent long-term outcomes, regardless of ISECG results, over a median 95-month follow-up period. The findings of this study reaffirm the importance of benign long-term outcomes in the setting of good exercise capacity.

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Cardiology

Mao, J., K. Fang, et al. (2008). "Nonsustained polymorphic ventricular tachycardia during adenosine stress perfusion imaging in the setting of resting pre-excitation electrocardiographic pattern: should we be avoiding adenosine pharmacologic stress testing in pre-excitation syndromes?" *J Nucl Cardiol* **15**(3): 469-72. [PDF Full Text](#)

Department of Cardiovascular Medicine, Henry Ford Hospital, Heart & Vascular Institute, Detroit, Mich, USA.

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Cardiology

Patel, S. J., A. Srivastava, et al. (2008). "Prognostic significance of submaximal negative dobutamine stress echocardiography: a 3-year follow-up study." *Cardiol J* **15**(3): 237-44. [Click for Article Request Form](#)

Heart and Vascular Institute, Henry Ford Hospital, Heart and Vascular Institute, K-14, Detroit, MI 48202, USA.

BACKGROUND: To estimate the prognostic value of submaximal negative dobutamine stress echocardiography (NDSE) on major cardiac events. METHODS AND RESULTS: Patients with NDSE were analyzed in 2 cohorts based on predicted maximal heart rate (PMHR) ($< 85\%$ or $\geq 85\%$ PMHR) and were assessed for major adverse cardiac events over 3 years. Of 756 patients with NDSE, 415 achieved $\geq 85\%$ PMHR. Both groups had comparable ejection fractions (EF) $> 50\%$ (80.6% vs. 81.9%, $p = 0.66$). The NsubDSE group had higher rates of atrioventricular nodal blocker use (58.7% vs. 39.9%, $p < 0.0001$), and diabetes (38.7% vs. 27.6%, $p = 0.001$). Kaplan-Meier survival analysis showed no differences in freedom from cardiac death (98% vs. 98%, $p = 0.88$), nonfatal myocardial infarction (94% vs. 94%, $p = 0.85$), or combined major cardiac events (81% vs. 78%, $p = 0.24$). Diabetes and preserved ejection fraction were predictive of cardiac events in a multi-variate analysis ($p = 0.005$). CONCLUSIONS: In our study, NsubDSE carried a favorable prognosis. Diabetics were more likely to have an NsubDSE and suffer from a cardiac event despite a preserved ejection fraction. Hence further evaluation for coronary artery disease in this high risk cohort should be pursued.

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Cardiology

Rastogi, S., S. Mishra, et al. (2008). "Effects of chronic therapy with cardiac contractility modulation electrical signals on cytoskeletal proteins and matrix metalloproteinases in dogs with heart failure." *Cardiology* **110**(4): 230-7. [Click for Article Request Form](#)

Division of Cardiovascular Medicine, Henry Ford Heart and Vascular Institute, Detroit, Mich. 48202, USA.

OBJECTIVES: Therapy with cardiac contractility modulation (CCM) electrical signals delivered to left ventricular (LV) muscle during the absolute refractory period improves LV systolic and diastolic function in dogs with heart failure (HF). This study examined the effects of CCM therapy on mRNA and protein expression of cytoskeletal proteins, matrix metalloproteinases (MMPs) and tissue inhibitors of MMPs (TIMPs) in the LV myocardium of dogs with HF. METHODS: HF was produced in 14 dogs by coronary microembolizations. Dogs were randomized to 3 months of CCM therapy (n = 7) or to sham-operated controls (n = 7). LV tissue from 6 normal (NL) dogs was used for comparison. mRNA expression was measured using reverse-transcriptase polymerase chain reaction and protein expression using Western blots. RESULTS: Compared with NL dogs, controls showed upregulation of mRNA and protein expression of the cytoskeletal proteins tubulin and fibronectin and MMP-1, MMP-2 and MMP-9, and downregulation of the cytoskeletal protein titin. Normalized expression of all these genes and proteins was seen after CCM therapy. No differences in expression of TIMP-1 and TIMP-2 were observed among groups. CONCLUSIONS: CCM therapy normalizes expression of key cytoskeletal proteins and MMPs and may partly explain the improvement in LV function seen in HF following CCM therapy.

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Dermatology

Kouba, D. J., R. L. Moy, et al. (2008). "Dual Nasal Sidewall and Lip Defects Combined into a Single Arcuate Advancement Flap." *Dermatol Surg*. Epub Ahead of Print. [PDF Full Text](#)

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

The authors have indicated no significant interest with commercial supporters.

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Diagnostic Radiology

Williams, T. R., Blase, J.J. (2008). "Iliopsoas bursitis presenting as hip pain secondary to Crohn's fistula." *The Internet Journal of Gastroenterology* **7**(1). [PDF Full Text](#)

Department of Radiology, Henry Ford Hospital, Detroit, MI

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Endocrinology & Metabolism

Guardia, G., N. Parikh, et al. (2008). "Prevalence of vitamin D depletion among subjects seeking advice on osteoporosis: a five-year cross-sectional study with public health implications." *Osteoporos Int* **19**(1): 13-9. [PDF Full Text](#)

Bone & Mineral Research Laboratory, Henry Ford Hospital, Detroit, MI, USA.

We assessed vitamin D nutritional status in unselected consecutive patients seeking advice on osteoporosis. The prevalence of vitamin D depletion ranged from 15-72% depending upon the cut-off levels used for serum 25-hydroxyvitamin D, and the prevalence did not change over the 5 years of the study. INTRODUCTION: Vitamin D depletion is a significant public health problem and has been studied in different populations using different cut-off levels, but the optimal level is yet to be established. METHODS: In a cross-sectional study of 2,924 patients seen for osteoporosis advice we determined the prevalence of vitamin D depletion, as assessed by 25-hydroxyvitamin D (25-OHD), using three different cut-off levels stratified by gender, race and the year of the study over 5 years. RESULTS: Mean age was 68.3 +/- 10.0 years; 90% women and 88% white. Mean 25-OHD level was 24.6 +/- 10 ng/ml and mean PTH was 48.4 +/- 32 pg/ml. The prevalence of vitamin

D depletion was 15% with a cut-off level of <15 ng/ml, and rose to 32% and 72% with cut-off levels <20 ng/ml and <30 ng/ml, respectively. The prevalence was higher in men and blacks and remained constant over 5 years, regardless of the cut-off level. The expected inverse relationship between 25-OHD and PTH was observed irrespective of gender or ethnicity. CONCLUSIONS: The prevalence of vitamin D depletion in patients seeking advice for osteoporosis is high and did not change over the 5 years of the study.

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Endocrinology & Metabolism

Kruger, D. F. (2008). "Exploring the pharmacotherapeutic options for treating type 2 diabetes." *Diabetes Educ* **34 Suppl 3**: 60S-65S. [Click for Article Request Form](#)

Division of Endocrinology, Diabetes, Bone and Mineral Disorders, Henry Ford Medical Center, Detroit, MI 48202, USA. Dkruger1@HFHS.org

There has been a dramatic increase in the prevalence of the most common form of diabetes, with approximately 14.6 million diagnosed and 6.2 million undiagnosed cases of type 2 (non-insulin-dependent) diabetes in the United States since 2005. If diabetes is not diagnosed early and managed properly, patients are at greater risk for microvascular and macrovascular complications, such as nerve damage, heart disease, blindness, and kidney damage. The pathogenesis of type 2 diabetes includes impaired insulin secretion, increased hepatic and muscle/fat insulin resistance, and increased glucagon secretion. Problems commonly associated with type 2 diabetes and consequent hyperglycemia are weight gain, hypertension, and dyslipidemia. The natural progression of type 2 diabetes involves increased insulin deficiency as a result of decreased beta cell function over time, which can raise glycosylated hemoglobin to dangerous levels and consequently increase the risk of death. Lifestyle modifications (eg, diet changes and increased physical activity) remain the cornerstone of early treatment, but glycemic control may worsen despite behavior changes and treatment with oral hypoglycemic agents. Historically, upon failure to maintain glucose levels with exercise and oral medication, insulin was the second-line treatment option. Current treatment algorithms include a new class of agents, incretin mimetics, such as the glucagon-like peptide-1 (GLP-1) receptor agonist exenatide. Exenatide mimics the actions of the hormone GLP-1 that occurs naturally in the gastrointestinal tract and has emerged as an efficacious therapy adjunct to 1 or more oral hypoglycemic agent(s).

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Hematology, Medical Oncology & Josephine Ford Cancer Center

Guo, A. M., J. Sheng, et al. (2008). "Expression of CYP4A1 in U251 Human Glioma Cell Induces Hyperproliferative Phenotype in vitro and Rapidly Growing Tumors in vivo." *J Pharmacol Exp Ther*. Epub Ahead of Print. [PDF Full Text](#)

Henry Ford Hospital.

Exogenous 20-HETE increases the growth of human glioma cells in vitro. However, glioma cells in culture show negligible 20-HETE synthesis. We examined whether inducing the expression of a 20-HETE synthase in a human glioma U251 cell line would increase proliferation. U251 cells transfected with CYP4A1 cDNA (termed U251 O) increased the formation of 20-HETE from less than 1 to over 60 pmol/min/mg proteins and increased their proliferation rate by two fold ($p < 0.01$). Compared to control U251, U251 O cells were rounded, smaller, showed a disorganized cytoskeleton, exhibited reduced vinculin staining, and were easily detached from the growing surface. They showed a marked increase in dihydroethidium staining suggesting increased oxidative stress. The expression of phosphorylated ERK1/2, cyclin D1/2 and VEGF was markedly elevated in U251 O. The hyperproliferative and signaling effects seen in U251 O cells are abolished by selective CYP4A inhibition of 20-HETE formation with HET0016 (N-hydroxy-N'-(4-butyl-2-methylphenyl)-formamidine) as well as by siRNA against the enzyme, and by the putative 20-HETE antagonist, 20-hydroxyeicosa-6(Z),15(Z)-dienoic acid (20-HEDE). In vivo, implantation of U251O cells in the brain of nude rats resulted in a ~10 fold larger tumor volume (10 days post implantation) as compared with animals receiving mock-transfected U251 cells. These data show that elevations in 20-HETE synthesis in U251 cells lead to an increased growth both in vitro and in vivo. This suggests that 20-HETE may have proto-oncogenic properties in U251 human gliomas and contributes to the regulation of the growth of some human gliomas.

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Hypertension & Vascular Research

Haurani, M. J., M. E. Cifuentes, et al. (2008). "Nox4 oxidase overexpression specifically decreases endogenous Nox4 mRNA and inhibits angiotensin II-induced adventitial myofibroblast migration." *Hypertension* **52**(1): 143-9. [PDF Full Text](#)

Department of General Surgery, Hypertension and Vascular Research Division, Room 7044, E&R Building, Henry Ford Hospital, 2799 West Grand Blvd, Detroit, MI 48202-2689, USA.

The vascular adventitia is emerging as an important modulator of vessel remodeling. Adventitial myofibroblasts migrate to the neointima after balloon angioplasty, contributing to restenosis. We postulated that angiotensin II (Ang II) enhances adventitial myofibroblast migration in vitro via reduced nicotinamide-adenine dinucleotide phosphate oxidase-derived H(2)O(2) and that Nox4-based oxidase promotes migration. Ang II increased myofibroblast migration in a concentration-dependent manner, with a peak increase of 1023±83%. Rat adventitial myofibroblasts were cotransfected with human Nox4 and human p22-phox plasmids or an empty vector. PCR showed an 8-fold increase in human Nox4 and human p22-phox plasmid expression. Using RT-PCR with primers specifically designed for rat reduced nicotinamide-adenine dinucleotide phosphate oxidases, endogenous Nox levels were determined. Ang II decreased endogenous Nox4 and Nox1 mRNA to 41% and 27% of control, respectively, but had no effect on Nox2. Cotransfection with human Nox4 and human p22-phox plasmids combined with Ang II reduced endogenous Nox4 mRNA levels (37±5% of control; P<0.05), whereas it had no significant effect on Nox1 or Nox2. In empty vector-transfected cells, Ang II increased myofibroblast migration by 192±32% versus vehicle (P<0.01) while increasing H(2)O(2) (473±22% versus control; P<0.001). Cotransfection with human Nox4 and human p22-phox plasmids decreased Ang II-induced migration (46±6%; P<0.001) in parallel with attenuation of H(2)O(2) production (23±8% versus empty vector; P<0.05). Our data suggest that Nox4 promotes Ang II-induced myofibroblast migration via an H(2)O(2)-dependent pathway. The data also suggest that Nox4 causes feedback inhibition of its own expression in adventitial myofibroblasts.

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Hypertension & Vascular Research

Lin, C. X., N. E. Rhaleb, et al. (2008). "Prevention of Aortic Fibrosis by N-acetyl-Seryl-Aspartyl-Lysyl-Proline in Angiotensin II-Induced hypertension." *Am J Physiol Heart Circ Physiol*. Epub Ahead of Print. [PDF Full Text](#)

Henry Ford Hospital.

Fibrosis is an important component of large conduit artery disease in hypertension. The endogenous tetrapeptide N-acetyl-seryl-aspartyl-lysyl-proline (Ac-SDKP) has anti-inflammatory and anti-fibrotic effects in the heart and kidney. However, it is not known whether Ac-SDKP has an anti-inflammatory and anti-fibrotic effect on conduit arteries such as the aorta. We hypothesize that in Ang II-induced hypertension Ac-SDKP prevents aortic fibrosis and that this effect is associated with decreased protein kinase C (PKC) activation, leading to reduced oxidative stress and inflammation and a decrease in the pro-fibrotic cytokine, transforming growth factor-beta1 (TGF-beta1), and phosphorylation of its second messenger Smad2. To test this hypothesis we used rats with Ang II-induced hypertension and treated with either vehicle or Ac-SDKP. In this hypertensive model we found an increased collagen deposition and collagen type I and III mRNA expression in the aorta. These changes were associated with increased PKC activation, oxidative stress, intracellular adhesion molecules-1 (ICAM-1) mRNA expression, and macrophage infiltration. TGF-beta1 expression and Smad2 phosphorylation also increased. Ac-SDKP prevented these effects without decreasing blood pressure or aortic hypertrophy. Ac-SDKP also enhanced expression of the inhibitory Smad7. These data indicate that in Ang II-induced hypertension, Ac-SDKP has an aortic anti-fibrotic effect. This effect may be due in part to inhibition of PKC activation, which in turn could reduce oxidative stress, ICAM-1 expression and macrophage infiltration. Part of the effect of Ac-SDKP could also be due to reduced expression of the pro-fibrotic cytokine TGF-beta1 and inhibition of Smad-2 phosphorylation. Key words: Angiotensin II, Hypertension, Ac-SDKP, inflammation.

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Infectious Diseases

Vazquez, J. A., J. A. Schranz, et al. (2008). "A phase 2, open-label study of the safety and efficacy of intravenous anidulafungin as a treatment for azole-refractory mucosal candidiasis." *J Acquir Immune Defic Syndr* **48**(3): 304-9. [PDF Full Text](#)

Division of Infectious Diseases, Henry Ford Hospital and Wayne State University School of Medicine, Detroit, MI 48202, USA. jvazque@hfhs.org

BACKGROUND: Azole-refractory mucosal candidiasis is a debilitating disease frequently seen in patients who are immunosuppressed as a result of HIV, malignancy, posttransplant immunosuppressive therapy, persistent neutropenia, steroid use, or diabetes. Anidulafungin has potent activity against a broad spectrum of *Candida* species, including strains resistant to azoles and amphotericin B. We performed an open-label, noncomparative study to examine efficacy and safety of anidulafungin in patients with azole-refractory oropharyngeal and esophageal candidiasis. **METHODS:** Patients enrolled met diagnostic criteria for azole-refractory mucosal candidiasis. They received intravenous anidulafungin 100 mg on day 1 followed by daily 50-mg doses on day 2 through day 14 or for a maximum of 21 days. Primary efficacy variables were clinical response (for oropharyngeal candidiasis) and endoscopic and clinical response (for esophageal candidiasis) at the end of therapy. **RESULTS:** Nineteen patients were enrolled; 89% had advanced HIV infection. Clinical success was observed in 95% of patients at end of therapy, and endoscopic success was observed in 92% of patients with esophageal candidiasis. At follow-up, clinical success was maintained in 47% of patients. The most common adverse event, experienced by 4 patients, was nausea and/or vomiting. **CONCLUSIONS:** Anidulafungin was well tolerated and efficacious in the treatment of patients with azole-refractory esophageal and oropharyngeal candidiasis.

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Internal Medicine

Caverzagie, K. J., J. A. Shea, et al. (2008). "Resident identification of learning objectives after performing self-assessment based upon the ACGME core competencies." *J Gen Intern Med* **23**(7): 1024-7. [PDF Full Text](#)

Division of Hospitalist Medicine, Henry Ford Hospital, Detroit, MI, USA. kcaverz1@hfhs.org

BACKGROUND: Self-assessment is increasingly being incorporated into competency evaluation in residency training. Little research has investigated the characteristics of residents' learning objectives and action plans after self-assessment. **OBJECTIVE:** To explore the frequency and specificity of residents' learning objectives and action plans after completing either a highly or minimally structured self-assessment. **DESIGN:** Internal Medicine residents (N = 90) were randomized to complete a highly or minimally structured self-assessment instrument based on the Accreditation Council for Graduate Medical Education Core Competencies. All residents then identified learning objectives and action plans. **MEASUREMENTS:** Learning objectives and action plans were analyzed for content. Differences in specificity and content related to form, gender, and training level were assessed. **RESULTS:** Seventy-six residents (84% response rate) identified 178 learning objectives. Objectives were general (79%), most often focused on medical knowledge (40%), and were not related to the type of form completed ($p > 0.01$). "Reading more" was the most common action plan. **CONCLUSIONS:** Residents commonly identify general learning objectives focusing on medical knowledge regardless of the structure of the self-assessment form. Tools and processes that further facilitate self-assessment should be identified.

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Internal Medicine

Meza, J. P. and G. F. Fahoome (2008). "The development of an instrument for measuring healing." *Ann Fam Med* **6**(4): 355-60. [PDF Full Text](#)

Henry Ford Hospital, Department of Family Medicine, Detroit, Michigan, USA. jmeza1@hfhs.org

PURPOSE: Our lack of ability to measure healing attributes impairs our ability to research the topic. The specific aim of this project is to describe the psychological and social construct of healing and to create a valid and reliable measurement scale for attributes of healing. **METHODS:** A content expert conducted a domain analysis examining the existing literature of midrange theories of healing. Theme saturation of content sampling was ensured by brainstorming more than 220 potential items. Selection of items was sequential: pile sorting and data reduction, with factor analysis of a mailed 54-item questionnaire. Criterion validity (convergent and divergent) and temporal reliability were established using a second mailing of the development version of the instrument. Construct validity was judged with structural equation modeling for goodness of fit. **RESULTS:** Cronbach's alpha of the original questionnaire was .869 and the final scale was .862. The test-retest reliability was .849. Eigenvalues for the 2 factors were 8 and 4, respectively. Divergent and convergent validity using the Spann-Fischer Codependency Scale and SF-36 mental health and emotional subscales were consistent with predictions.

The root mean square error of approximation was 0.066 and Bentler's Comparative Fit Index was 0.871. Root mean square residual was 0.102. CONCLUSIONS: We developed a valid and reliable measurement scale for attributes of healing, which we named the Self-Integration Scale v 2.1. By creating a new variable, new areas of research in humanistic health care are possible.

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Neurology

Knight, R. A., Y. Han, et al. (2008). "Temporal MRI Assessment of Intracerebral Hemorrhage in Rats." *Stroke*. [Click for Article Request Form](#)

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

BACKGROUND AND PURPOSE: MRI was used to evaluate the effects of experimental intracerebral hemorrhage (ICH) on brain tissue injury and recovery. METHODS: Primary ICH was induced in rats (n=6) by direct infusion of autologous blood into the striatum. The evolution of ICH damage was assessed by MRI estimates of T2 and T1sat relaxation times, cerebral blood flow, vascular permeability, and susceptibility-weighted imaging before surgery (baseline) and at 2 hours and 1, 7, and 14 days post-ICH. Behavioral testing was done before and at 1, 7, and 14 days post-ICH. Animals were euthanized for histology at 14 days. RESULTS: The MRI appearance of the hemorrhage and surrounding regions changed in a consistent manner over time. Two primary regions of interest were identified based on T2 values. These included a core, corresponding to the bulk of the hemorrhage, and an adjacent rim; both varied with time. The core was associated with significantly lower cerebral blood flow values at all post-ICH time points, whereas cerebral blood flow varied in the rim. Increases in vascular permeability were noted at 1, 7, and 14 days. Changes in T1sat were similar to those of T2. MRI and histological estimates of tissue loss were well correlated and showed approximately 9% hemispheric tissue loss. CONCLUSIONS: Although the cerebral blood flow changes observed with this ICH model may not exactly mimic the clinical situation, our results suggest that the evolution of ICH injury can be accurately characterized with MRI. These methods may be useful to evaluate therapeutic interventions after experimental ICH and eventually in humans.

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Neurology

Liu, X. S., M. Chopp, et al. (2008). "Functional response to SDF1alpha through over-expression of CXCR4 on adult subventricular zone progenitor cells." *Brain Res*. Epub Ahead of Print. [PDF Full Text](#)

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

The chemokine receptor CXCR4 and its ligand, stromal cell derived factor-1alpha (SDF1alpha) regulate neuroblast migration towards the ischemic boundary after stroke. Using loss- and gain-function, we investigated the biological effect of CXCR4/SDF1alpha on neural progenitor cells. Neural progenitor cells, from the subventricular zone (SVZ) of the adult rat, were transfected with rat CXCR4-pLEGFP-C1 and pSIREN-RetroQ-CXCR4-siRNA retroviral vectors. Migration assay analysis showed that inhibition of CXCR4 by siRNA significantly reduced cell migration compared to the empty vector, indicating that CXCR4 mediated neural progenitor cell motility. When neural progenitor cells were cultured in growth medium containing bFGF (20 ng/ml), over-expression of CXCR4 significantly reduced the cell proliferation as measured by the number of bromodeoxyuridine+ (BrdU+) cells (26.4%) compared with the number in the control group (54.0%). Addition of a high concentration of SDF1alpha (500 ng/ml) into the progenitor cells with over-expression of CXCR4 reversed the cell proliferation back to the control levels (57.6%). Immunostaining analysis showed that neither over-expression nor inhibition of CXCR4 altered the population of neurons and astrocytes, when neural progenitor cells were cultured in differentiation medium. These in vitro results suggest that CXCR4/SDF1alpha primarily regulates adult neural progenitor cell motility but not differentiation, while over-expression of CXCR4 in the absence of SDF1alpha decreases neural progenitor cell proliferation.

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Neurology

Liu, Z., Y. Li, et al. (2008). "Contralesional Axonal Remodeling of the Corticospinal System in Adult Rats After Stroke and Bone Marrow Stromal Cell Treatment." *Stroke*. [Click for Article Request Form](#)

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

BACKGROUND AND PURPOSE: Motor recovery after stroke is associated with neuronal reorganization in bilateral hemispheres. We investigated contralesional corticospinal tract remodeling in the brain and spinal cord in rats after stroke and treatment of bone marrow stromal cells. **METHODS:** Adult male Wistar rats were subjected to permanent right middle cerebral artery occlusion. Phosphate-buffered saline or bone marrow stromal cells were injected into a tail vein 1 day postischemia. An adhesive removal test was performed weekly to monitor functional recovery. Threshold currents of intracortical microstimulation on the left motor cortex for evoking bilateral forelimb movements were measured 6 weeks after stroke. When intracortical microstimulation was completed, biotinylated dextran amine was injected into the left motor cortex to anterogradely label the corticospinal tract. At 4 days before euthanization, pseudorabies virus-152-EGFP and 614-mRFP were injected into left or right forelimb extensor muscles, respectively. All animals were euthanized 8 weeks after stroke. **RESULTS:** In normal rats (n=5), the corticospinal tract showed a unilateral innervation pattern. In middle cerebral artery occlusion rats (n=8), our data demonstrated that: 1) stroke reduced the stimulation threshold evoking ipsilateral forelimb movement; 2) EGFP-positive pyramidal neurons were increased in the left intact cortex, which were labeled from the left stroke-impaired forelimb; and 3) biotinylated dextran amine-labeled contralesional axons sprouted into the denervated spinal cord. Bone marrow stromal cells significantly enhanced all 3 responses (n=8, P<0.05). **CONCLUSIONS:** Our data demonstrated that corticospinal tract fibers originating from the contralesional motor cortex sprout into the denervated spinal cord after stroke and bone marrow stromal cells treatment, which may contribute to functional recovery.

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Neurology

Shen, L. H., Y. Li, et al. (2008). "Down-regulation of neurocan expression in reactive astrocytes promotes axonal regeneration and facilitates the neurorestorative effects of bone marrow stromal cells in the ischemic rat brain." *Glia*. Epub Ahead of Print. [PDF Full Text](#)

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

The glial scar, a primarily astrocytic structure bordering the infarct tissue inhibits axonal regeneration after stroke. Neurocan, an axonal extension inhibitory molecule, is up-regulated in the scar region after stroke. Bone marrow stromal cells (BMSCs) reduce the thickness of glial scar wall and facilitate axonal remodeling in the ischemic boundary zone. To further clarify the role of BMSCs in axonal regeneration and its underlying mechanism, the current study focused on the effect of BMSCs on neurocan expression in the ischemic brain. Thirty-one adult male Wistar rats were subjected to 2 h of middle cerebral artery occlusion followed by an injection of 3×10^6 rat BMSCs (n = 16) or phosphate-buffered saline (n = 15) into the tail vein 24 h later. Animals were sacrificed at 8 days after stroke. Immunostaining analysis showed that reactive astrocytes were the primary source of neurocan, and BMSC-treated animals had significantly lower neurocan and higher growth associated protein 43 expression in the penumbral region compared with control rats, which was confirmed by Western blot analysis of the brain tissue. To further investigate the effects of BMSCs on astrocyte neurocan expression, single reactive astrocytes were collected from the ischemic boundary zone using laser capture microdissection. Neurocan gene expression was significantly down-regulated in rats receiving BMSC transplantation (n = 4/group). Primary cultured astrocytes showed similar alterations; BMSC coculture during reoxygenation abolished the up-regulation of neurocan gene in astrocytes undergoing oxygen-glucose deprivation (n = 3/group). Our data suggest that BMSCs promote axonal regeneration by reducing neurocan expression in peri-infarct astrocytes. (c) 2008 Wiley-Liss, Inc.

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Neurology

Varelas, P. N., M. Rehman, et al. (2008). "Vancomycin-resistant enterococcal meningitis treated with intrathecal streptomycin." *Clin Neurol Neurosurg* **110**(4): 376-80. [PDF Full Text](#)

Department of Neurology, Henry Ford Hospital, Detroit, MI 48202, United States. varelas@neuro.hfh.edu

Enterococcal meningitis is a rare complication of neurosurgical procedures. We present a patient who developed vancomycin-resistant enterococcal ventriculitis - meningitis after a brain tumor resection and ventriculoperitoneal shunt

placement, treated successfully with intrathecal streptomycin through bilateral cerebrospinal fluid drainage catheters in addition to systemic antibiotics. This is the first report of such treatment for this resistant organism.

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Neurology

Weiland, B. J., N. N. Boutros, et al. (2008). "Evidence for a frontal cortex role in both auditory and somatosensory habituation: AMEG study." *Neuroimage* **42**(2): 827-35. [Click for Article Request Form](#)

Department of Neurology, Henry Ford Health System, Neuromagnetism Laboratory, 2799 West Grand Blvd., CFP 75, Detroit, MI 48202, USA.

Auditory and somatosensory responses to paired stimuli were investigated for commonality of frontal activation that may be associated with gating using magnetoencephalography (MEG). A paired stimulus paradigm for each sensory evoked study tested right and left hemispheres independently in ten normal controls. MR-FOCUSS, a current density technique, imaged simultaneously active cortical sources. Each subject showed source localization, in the primary auditory or somatosensory cortex, for the respective stimuli following both the first (S1) and second (S2) impulses. Gating ratios for the auditory M50 response, equivalent to the P50 in EEG, were 0.54 ± 0.24 and 0.63 ± 0.52 for the right and left hemispheres. Somatosensory gating ratios were evaluated for early and late latencies as the pulse duration elicits extended response. Early gating ratios for right and left hemispheres were 0.69 ± 0.21 and 0.69 ± 0.41 while late ratios were 0.81 ± 0.41 and 0.80 ± 0.48 . Regions of activation in the frontal cortex, beyond the primary auditory or somatosensory cortex, were mapped within 25ms of peak S1 latencies in 9/10 subjects during auditory stimulus and in 10/10 subjects for somatosensory stimulus. Similar frontal activations were mapped within 25ms of peak S2 latencies for 75% of auditory responses and for 100% of somatosensory responses. Comparison between modalities showed similar frontal region activations for 17/20 S1 responses and for 13/20 S2 responses. MEG offers a technique for evaluating cross modality gating. The results suggest similar frontal sources are simultaneously active during auditory and somatosensory habituation.

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Neurology

Zhang, J., Y. Li, et al. (2008). "Bone marrow stromal cells protect oligodendrocytes from oxygen-glucose deprivation injury." *J Neurosci Res* **86**(7): 1501-10. [PDF Full Text](#)

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

Oligodendrocyte (OLG) damage leads to demyelination, which is frequently observed in ischemic cerebrovascular diseases. In this study, we investigated the effect of bone marrow stromal cells (BMSCs) on OLGs subjected to oxygen-glucose deprivation (OGD). N20.1 cells (mouse OLG cell line) were transferred into an anaerobic chamber for 3 hr in glucose-free and serum-free medium. After OGD incubation, OLG cultures were divided into the following groups: 1) OGD alone, 2) OLG cocultured with BMSCs, 3) treatment with the phosphoinositide 3-kinase (PI3k) inhibitor LY294002, 4) LY294002-treated OLGs with BMSC cocultured, and 5) anti-p75 antibody-treated OLGs. After an additional 3 hr of reoxygenation incubation, OLG viability and apoptosis were measured. The mRNA expression in the BMSCs and OLGs was analyzed using quantitative real-time PCR (RT-PCR). Serine/threonine-specific protein kinase (Akt), phosphorylated Akt (p-Akt), p75, and caspase 3 protein expressions in OLGs were measured by Western blot. Our results suggest that BMSCs produce growth factors, activate the Akt pathway, and increase the survival of OLGs. BMSCs also reduce p75 and caspase 3 expressions in the OGD-OLGs, which leads to decreased OLG apoptosis. BMSCs participate in OLG protection that may occur with promoting growth factors/PI3K/Akt and inhibiting the p75/caspase pathways. Our study provides insight into white matter damage and the therapeutic benefits of BMSC-based remyelinating therapy after stroke and demyelinating diseases.

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Neurology

Zhang, R. L., Z. G. Zhang, et al. (2008). "Ischemic stroke and neurogenesis in the subventricular zone." *Neuropharmacology*. [Click for Article Request Form](#)

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

The subventricular zone (SVZ) of the lateral ventricle contains neural stem and progenitor cells that generate neuroblasts, which migrate to the olfactory bulb where they differentiate into interneurons. Ischemic stroke induces neurogenesis in the SVZ and these cells migrate to the boundary of the ischemic lesion. This article reviews current data on cytokinetics, signaling pathways and vascular niche that are involved in processes of proliferation, differentiation, and migration of neural progenitor cells after stroke.

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Neurosurgery

Lomonaco, S. L., S. Kahana, et al. (2008). "Phosphorylation of protein kinase Cdelta on distinct tyrosine residues induces sustained activation of Erk1/2 via down-regulation of MKP-1: role in the apoptotic effect of etoposide." J Biol Chem **283**(25): 17731-9. [PDF Full Text](#)

William and Karen Davidson Laboratory of Cell Signaling and Tumorigenesis, Hermelin Brain Tumor Center, Department of Neurosurgery, Henry Ford Hospital, Detroit, Michigan 48202, USA.

The mechanism underlying the important role of protein kinase Cdelta (PKCdelta) in the apoptotic effect of etoposide in glioma cells is incompletely understood. Here, we examined the role of PKCdelta in the activation of Erk1/2 by etoposide. We found that etoposide induced persistent activation of Erk1/2 and nuclear translocation of phospho-Erk1/2. MEK1 inhibitors decreased the apoptotic effect of etoposide, whereas inhibitors of p38 and JNK did not. The activation of Erk1/2 by etoposide was downstream of PKCdelta since the phosphorylation of Erk1/2 was inhibited by a PKCdelta-KD mutant and PKCdelta small interfering RNA. We recently reported that phosphorylation of PKCdelta on tyrosines 64 and 187 was essential for the apoptotic effect of etoposide. Using PKCdelta tyrosine mutants, we found that the phosphorylation of PKCdelta on these tyrosine residues, but not on tyrosine 155, was also essential for the activation of Erk1/2 by etoposide. In contrast, nuclear translocation of PKCdelta was independent of its tyrosine phosphorylation and not necessary for the phosphorylation of Erk1/2. Etoposide induced down-regulation of kinase phosphatase-1 (MKP-1), which correlated with persistent phosphorylation of Erk1/2 and was dependent on the tyrosine phosphorylation of PKCdelta. Moreover, silencing of MKP-1 increased the phosphorylation of Erk1/2 and the apoptotic effect of etoposide. Etoposide induced polyubiquitylation and degradation of MKP-1 that was dependent on PKCdelta and on its tyrosine phosphorylation. These results indicate that distinct phosphorylation of PKCdelta on tyrosines 64 and 187 specifically activates the Erk1/2 pathway by the down-regulation of MKP-1, resulting in the persistent phosphorylation of Erk1/2 and cell apoptosis.

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Other

Mani, N. S. (2008). "Library-on-the-go": utilizing technology to provide educational programming." J Med Libr Assoc **96**(3): 230-2. [PDF Full Text](#)

Sladen Library, Henry Ford Hospital, K-17, 2799 West Grand Boulevard, Detroit, MI 48331, USA. nmani1@sladen.hfhs.org

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Other

Mani, N. S. (2008). "Improving scholarly communication via manuscript preparation services." Journal of Hospital Librarianship **8**(1): 113-8. [Click for Article Request Form](#)

Henry Ford Hospital, Sladen Library, Detroit, MI, nmani1@hfhs.org

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Otolaryngology

Somers, M. L. and D. L. Suskind (2008). "Near-complete tracheal ring deformity: A case report." Ear Nose Throat J **87**(7): 405-7. [PDF Full Text](#)

Department of Otolaryngology-Head and Neck Surgery, Henry Ford Health System, Detroit, MI, USA.

Long-segment near-complete tracheal ring deformity is a rare condition with few documented cases. We present the case of a 7-week-old male with total anomalous pulmonary venous return and long-segment near-complete tracheal rings. We discuss the presentation, evaluation, and management of near-complete and complete tracheal rings.

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Pathology

Meier, F. A., R. J. Zarbo, et al. (2008). "Amended reports: development and validation of a taxonomy of defects." *Am J Clin Pathol* **130**(2): 238-46. [PDF Full Text](#)

Department of Pathology and Laboratory Medicine, Henry Ford Hospital, Detroit, MI.

Amended pathology reports produce rework, confusion, and distrust. To develop a reproducible amendment taxonomy we derived a classification from 141 amended reports, then validated it with 130 new cases before 4 observers independently reviewed 430 cases measuring agreement (k). Next, agreement in classifying 30 other amended reports in 7 institutions was measured. We further tracked amendment rates, defect categories, defect discoverers, and discovery mechanisms. In the 430-case validation set agreement was excellent ($k = 0.8780$ [range, 0.8416-0.9144]). Among the 7 institutions, agreement was good ($k = 0.6235$ [range, 0.3105-0.8975]). Amendment rates ranged from 2.6 to 4.8 per 1,000 reports. Misinterpretation fractions varied least (23%-29%). Misidentification fractions ranged more widely (20%-38%). Specimen defects were least frequent (4%-10%) and report defects most frequent (29%-48%). Misidentifications and report defects inversely correlated. Pathologists discovered most misinterpretations, and clinicians found most misidentifications. Conference review revealed 40% to 80% of misinterpretations. This taxonomy produced excellent reproducibility and good agreement across institutions.

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Pulmonary & Critical Care Medicine

Betensley, A. D., I. Khalid, et al. (2008). "Patient comfort during pressure support and volume controlled-continuous mandatory ventilation." *Respir Care* **53**(7): 897-902. [Click for Article Request Form](#)

Division of Pulmonary and Critical Care Medicine, Henry Ford Hospital, 2799 W Grand Boulevard, K-17, Detroit MI 48202, USA. abetens1@hfhs.org

BACKGROUND: Pressure-support ventilation (PSV) is more comfortable than volume controlled-continuous mandatory ventilation (VC-CMV) in acute hypercapnic respiratory failure, in patients undergoing noninvasive ventilation. Physiologic measurements of patient status have been compared in PSV and VC-CMV in endotracheally intubated patients, but patient perception of comfort has not been measured in this population. **OBJECTIVE:** To determine if PSV is more comfortable than VC-CMV (volume-cycled, flow-limited) in intubated mechanically ventilated patients. **METHODS:** In a randomized prospective trial, patients underwent PSV and VC-CMV for 30 min each, separated by a 30 min washout with the baseline ventilation mode (pressure-regulated volume-control ventilation [PRVC]). The level of pressure support was set as the plateau pressure on VC-CMV with a tidal volume of 8 mL/kg minus the end-expiratory pressure. After each mode the patient was asked to mark his or her comfort level on a visual analog scale. **RESULTS:** Eleven of the 14 patients were more comfortable during PSV. The baseline mean comfort score (during PRVC) was 62 +/- 18 (95% confidence interval 51.7-72.5). The mean comfort score for PSV was 83 +/- 11 (95% confidence interval 76.9-89.6). The mean comfort score for VC-CMV was 70 +/- 18 (95% confidence interval 59.4-79.9). PSV was significantly more comfortable than VC-CMV ($p = 0.02$) or PRVC ($p = 0.009$), whereas the comfort scores for VC-CMV and PRVC were not significantly different ($p = 0.278$). Respiratory rate, blood pressure, heart rate, minute ventilation, and blood oxygen saturation showed no difference between PRVC, VC-CMV, and PSV. **CONCLUSIONS:** On average the patients felt more comfortable during PSV than during VC-CMV or PRVC, so PSV may be the preferred mode for awake intubated patients.

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Radiation Oncology

Kumar, S., S. L. Brown, et al. (2008). "Efficacy of suicide gene therapy in hypoxic rat 9L glioma cells." *J Neurooncol*. EPub Ahead of Print. [PDF Full Text](#)

Department of Radiation Oncology, Henry Ford Health System, Detroit, MI, 48202, USA, skumar4@hfhs.org.

Viral vector mediated suicide gene therapy (SGT) involving thymidine kinase (TK) or cytosine deaminase (CD) have considerable promise in the treatment of malignant brain tumors. An unresolved issue is to what extent tumor hypoxia influences the outcome of SGT since brain tumors characterized by regions of hypoxia have potentially reduced cellular metabolism and SGT's cytotoxicity is manifest through cellular metabolism. We studied in vitro and in vivo, the effect of hypoxia on the cytotoxicity of SGT in rat 9L glioma cells. Neither acute nor chronic hypoxia affected the cell killing of SGT by TK or CD. In vivo confirmation that SGT efficacy was not adversely affected by tumor hypoxia using the hypoxic cell marker pimonidazole was shown by the absence of a change in tumor hypoxia by SGT. These studies support the use of SGT utilizing either TK or CD gene strategies even when tumors are characterized by a hypoxic microenvironment.

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Radiation Oncology

Yan, S., S. L. Brown, et al. (2008). "Mitigation of radiation-induced skin injury by AAV2-mediated MnSOD gene therapy." *J Gene Med*. [Click for Article Request Form](#)

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

BACKGROUND: Radiation-induced, long-lived free radicals, reactive oxygen species and pro-inflammatory cytokines have been implicated in the resultant tissue injury after exposure to ionizing radiation. METHODS: An approach designed to reduce the damaging effects of reactive oxidants employs metalloenzymes of superoxide dismutase (SOD), such as MnSOD. Recombinant adeno-associated virus 2 (AAV2) provides safe and long-term expression in humans. We tested the effectiveness of AAV2-MnSOD-hrGFP, a vector expressing MnSOD and green fluorescent protein (GFP) in preclinical models. RESULTS: Infection of cultured cells with AAV2-MnSOD-hrGFP showed enhanced expression of MnSOD and GFP. Sustained expression of GFP was achieved for at least 1 month in vivo following administration of AAV2-MnSOD-hrGFP to subcutaneous tissue of C57BL/6J mice. A single subcutaneous injection of AAV2-MnSOD-hrGFP significantly mitigated acute skin injury following single dose of irradiation of either 30 or 35 Gy. CONCLUSIONS: The proof-of-concept demonstrated in the present study together with the known safety profile in humans indicate that AAV-mediated MnSOD expression has potential countermeasure utility against normal tissue injury following radiation therapy or radiological accident. Copyright (c) 2008 John Wiley & Sons, Ltd.

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Surgery

Gao, X., D. Deeb, et al. (2008). "Immunomodulatory activity of synthetic triterpenoids: inhibition of lymphocyte proliferation, cell-mediated cytotoxicity, and cytokine gene expression through suppression of NF-kappaB." *Immunopharmacol Immunotoxicol* **30**(3): 581-600. [Click for Article Request Form](#)

Division of Surgical Research, Department of Surgery, Henry Ford Health System, Detroit, Michigan, USA.

Synthetic oleanane triterpenoids (CDDO, CDDO-Im and CDDO-Me) are potent anti-inflammatory agents, but have not been investigated for effects on T cell-mediated immune responses. Here we demonstrate that CDDOs have profound immunosuppressive effects on T cell proliferation, development of IL-2 activated LAK cells and cytotoxic T lymphocytes (CTLs), and expression of cytokines at concentrations of 1.25 microM to 0.078 microM. Treatment with CDDO-Me also inhibited the generation of allo-reactive T cell responses in vivo. The suppression of these cell-mediated immune responses by CDDO-Me was associated with the inhibition of NF-kappaB transcription factor.

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Surgery

Kakkos, S. K., G. K. Haddad, et al. (2008). "Secondary Patency of Thrombosed Prosthetic Vascular Access Grafts with Aggressive Surveillance, Monitoring and Endovascular Management." *Eur J Vasc Endovasc Surg*. [Click for Article Request Form](#)

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

BACKGROUND: To study the long-term patency of thrombosed prosthetic vascular access grafts treated with percutaneous mechanical thrombectomy (PMT) followed by aggressive surveillance and monitoring and repeated endovascular interventions. STUDY DESIGN: Two hundred seven vascular access grafts presented with first-time thrombosis were treated with PMT using the AngioJet device (n=185) or the Arrow-Trerotola percutaneous thrombolytic device (n=22) followed by angioplasty (+/- stenting) of the anatomical lesion responsible for the thrombotic event. Clinical success was considered at least one successful subsequent hemodialysis session. Graft surveillance/monitoring included clinical and hemodialysis parameters to detect a failing or thrombosed graft. RESULTS: PMT was technically successful in 202 cases (97.6%) and clinically successful in 193 cases (93.2%). During follow-up, 149 got thrombosed and either abandoned (n=33) or underwent at least once repeat thrombectomy (n=116); finally 100 grafts were abandoned (n=90), ligated (n=5) or removed (n=5). Endovascular management (0.54 procedures per 100 graft-days, thrombectomy, n=307 sessions and angioplasty, n=162 sessions) increased significantly functional assisted-primary patency rates from 29% and 14% at 1 and 2 years to a secondary patency of 62% and 47%, respectively. Secondary patency was worse in loop grafts (P=.02) and intermediate graft thrombosis (occurred between 31-182 days after graft placement, P<.001) and better when renal failure was due to hypertension or diabetes (compared to other or cryptogenic causes, P=.048) or isolated angioplasty for graft dysfunction during follow-up had been performed (P<.001). Multivariate analysis identified intermediate graft thrombosis and isolated angioplasty as independent predictors of secondary patency (P<.001, relative risk 2.77 and P<.001, relative risk 0.28, respectively). CONCLUSIONS: PMT is a highly successful procedure with acceptable long-term secondary patency results, provided that aggressive endovascular management of subsequent thrombotic or dysfunction episode is performed. Further research to identify the causes of intermediate graft thrombosis is justified.

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Surgery

Kakkos, S. K., G. K. Haddad, et al. (2008). "Effectiveness of a new tunneled catheter in preventing catheter malfunction: a comparative study." *J Vasc Interv Radiol* **19**(7): 1018-26. [Click for Article Request Form](#)

Division of Vascular Surgery, Department of Surgery, Henry Ford Hospital, 2799 W Grand Boulevard, Detroit, MI 48202, USA.

PURPOSE: To compare infection and malfunction rates of two different types of antimicrobial-eluting tunneled cuffed catheters (TCCs) for hemodialysis. MATERIALS AND METHODS: The HemoSplit TCC with BioBloc (silver sulfadiazine) coating (n = 100, control group) and the Tal Palindrome Ruby TCC, which has a novel silver antimicrobial sleeve and a spiral-z tip design (n = 100, study group), were compared in this case-controlled study. The main endpoints were TCC infection and malfunction. RESULTS: Primary-assisted TCC patency was significantly reduced with the BioBloc TCC (71% and 61% at 90 and 180 days, respectively) compared with the Palindrome Ruby TCC (94% at 90 and 180 days, P < .0001). Multivariate analysis identified only the BioBloc TCC and common femoral access site as independent predictors of worse patency. The unadjusted relative risk (95% confidence interval) for TCC dysfunction with the BioBloc compared with the Palindrome Ruby was 6.0 (2.33-15.53, P < .001), and the relative risk adjusted for access site was 3.2 (1.71-11.96, P = .002). The infection-free rates of the two TCC types were similar (P = .36). The reintervention-free rate for infection or malfunction was significantly better with the Palindrome Ruby TCC (76% and 58% at 90 and 180 days, respectively) than with the BioBloc TCC (60% and 45% at 90 and 180 days, respectively; P = .03). CONCLUSIONS: The results support the use of the Palindrome Ruby TCC on the basis of the significantly lower thrombosis and reintervention rate; randomized trials are justified to confirm this finding and to evaluate its role in the prevention of TCC infection.

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Surgery

Kwon, D. S., X. Gao, et al. (2008). "Treatment with bone marrow-derived stromal cells accelerates wound healing in diabetic rats." *Int Wound J* 5(3): 453-63. [Click for Article Request Form](#)

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

Bone marrow stem cells participate in tissue repair processes and may have a role in wound healing. Diabetes is characterised by delayed and poor wound healing. We investigated the potential of bone marrow-derived mesenchymal stromal cells (BMSCs) to promote healing of fascial wounds in diabetic rats. After manifestation of streptozotocin (STZ)-induced diabetic state for 5 weeks in male adult Sprague-Dawley rats, healing of fascial wounds was severely compromised. Compromised wound healing in diabetic rats was characterised by excessive polymorphonuclear cell infiltration, lack of granulation tissue formation, deficit of collagen and growth factor [transforming growth factor (TGF-beta), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), platelet-derived growth factor PDGF-BB and keratinocyte growth factor (KGF)] expression in the wound tissue and significant decrease in biomechanical strength of wounds. Treatment with BMSC systemically or locally at the wound site improved the wound-breaking strength (WBS) of fascial wounds. The improvement in WBS was associated with an immediate and significant increase in collagen levels (types I-V) in the wound bed. In addition, treatment with BMSCs increased the expression of growth factors critical to proper repair and regeneration of the damaged tissue moderately (TGF-beta, KGF) to markedly (EGF, VEGF, PDGF-BB). These data suggest that cell therapy with BMSCs has the potential to augment healing of the diabetic wounds.

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Urology

Menon, M., F. Muhletaler, et al. (2008). "Assessment of Early Continence After Reconstruction of the Periprostatic Tissues in Patients Undergoing Computer Assisted (Robotic) Prostatectomy: Results of a 2 Group Parallel Randomized Controlled Trial." *J Urol*. Epub Ahead of Print. [PDF Full Text](#)

Vattikuti Urology Institute, Henry Ford Hospital, Detroit, Michigan (MM, FM, JOP); Case School of Medicine, Cleveland, Ohio (MM); New York University School of Medicine, New York, New York (MM).

PURPOSE: Several case series have shown that reconstruction of the anterior or posterior periprostatic tissues facilitates early return of urinary continence after radical prostatectomy. We conducted a randomized clinical trial comparing early continence rates in patients undergoing urethrovesical anastomosis with or without periprostatic reconstruction. **MATERIALS AND METHODS:** A total of 116 consecutive patients undergoing computer assisted (robotic) prostatectomy performed by 1 of 2 experienced surgeons were randomized to single (without periprostatic reconstruction) or double layer (with periprostatic tissue reconstruction) urethrovesical anastomosis. Urinary loss was measured by pad weight at 1, 2, 7 and 30 days after catheter removal. Patients and data gatherers were blinded to treatment allocation. **RESULTS:** There were 57 patients randomized to the single and 59 to the double layer anastomosis group. All patients completed the study and followup. Using the conventional definition of urinary continence (0 to 1 pads daily) 26% and 34%, 49% and 46%, 51% and 54%, and 74% and 80% of patients undergoing single layer or double layer anastomoses were continent at 1, 2, 7 and 30 days, respectively ($p > 0.1$). Of the patients in the 2 groups 7% and 15%, 14% and 14%, 16% and 20%, and 47% and 42% had no urinary leakage (0 gm or 0 pads daily) at these intervals, respectively ($p > 0.1$). In each group 1 patient required prolonged catheterization because of cystographic evidence of anastomotic leakage. There were no other complications. **CONCLUSIONS:** Early urinary continence rates were high in patients undergoing single or double layer urethrovesical anastomosis. We found no improvement in early continence rates with reconstruction of the periprostatic tissues.

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