Research Day Abstract

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Abstract Category:* Clinical Research
Principal Investigator:* Bonnie Spring, PhD
Department:* Preventive Medicine
Does this research involve women’s health?* No

Abstract Title:* Mixed Methods Evaluation of a Web-Based Portal for Assessing Anxiety, Depression, and Quality of Life

**Background:** Anxiety disorders are the most common mental illness in the US, affecting 40 million adults. Often co-morbid with depression, anxiety disorders are highly treatable, yet only about one-third of those suffering receive treatment or regular follow-up assessments. Regular assessments have been shown to independently enhance patient engagement and treatment outcomes. We developed a novel web-based portal with computer adaptive tests (CATs), extremely brief and precise instruments, to assess anxiety, depression, and quality of life. According to the Consolidated Framework for Implementation Research (CFIR), intervention-level and user-level constructs are associated with effective implementation (Damschroder et al., 2009). However, given the promise of CATs-based assessment, there is a need to expand implementation science to novel web-based assessment portals that utilize CATs.

**Methods:** A two-phase mixed-methods sequential explanatory design was used to conduct implementation-focused formative evaluations. Following completion of a quantitative questionnaire (Phase 1), semi-structured interviews (Phase 2) were administered. Both phases contained sections on demographics, usability, and two CFIR constructs (portal and clinician characteristics). Purposive samples of 41 clinicians completed Phase 1 and 10 clinicians completed Phase 2. Clinicians were recruited by email from the portal registry, as well as clinics and universities in a metropolitan area. Recruitment for Phase 2 continued until “theme saturation”, and a codebook was created, resulting in 110 codes.

**Results:** Univariate descriptive analyses indicated that usability, portal characteristics, and clinician characteristics may influence implementation of a web-based portal that uses CATs for assessing anxiety, depression, and quality of life. Frequent users of the portal (n=10), compared to infrequent users (n=8), reported more positive attitudes (t=2.53, p=.02) and greater self-efficacy (t=2.67, p=.01) for administering CATs, but reported lower usability (t=-2.71, p=.02). In thematic analyses, a total of 352 codes were applied, and initial (k=.84) and final (k=.80) inter-coder reliabilities were assessed. Five primary themes emerged, including (1) viability of alternative platforms (i.e., electronic health record and mobile) (n=106 excerpts), (2) knowledge, attitudes, and self-efficacy of patient assessment (n=79 excerpts), (3) portal training (n=48 excerpts), (4) positive usability (n=40 excerpts), and (5) CATs (n=32 excerpts).

**Conclusion:** Findings extend prior research on the CFIR to a novel web-based portal that uses CATs to assess anxiety, depression, and quality of life. These data may help clinicians implement web-based portals that use CATs for ongoing patient assessment. These data have implications for the development of web- and mobile-based portals that use CATs to facilitate assessment in day-to-day patient care to inform evidence-based treatment decisions.

*Abstracts longer than one page will not be accepted.*
A Conceptual Model for Understanding the Benefits of Mindfulness Training among Couples Affected by Prostate Cancer on Active Surveillance

PURPOSE: To develop a guiding conceptual model that illustrates the impact of mindfulness meditation training on couples affected by prostate cancer on active surveillance.

METHODS: As a part of a 6 and 12 month follow up to a Mindfulness Based Stress Reduction (MBSR) pilot study for men diagnosed with prostate cancer on active surveillance and their spouses, participants were asked to respond to open-ended questions about how mindfulness has affected them, and whether they have made any lifestyle changes as a result of participating in the study. Using qualitative research methods, we systematically coded these open-ended statements, followed by purposeful categorization into higher-order themes, which were subsequently organized into a guiding conceptual model.

RESULTS: Data were available from 13 separate male/female couples. A total of 49 unique codes were created and applied to the data, including the following examples: appreciation of people’s goodness; awareness of breath; greater self-care; less emotionally reactive; more expressions of kindness to others; more tolerance for peoples’ quirks; and greater patience with oneself. We then grouped these codes into the following 9 themes: 1) Greater Awareness, 2) Greater Appreciation, 3) Increased Mindfulness Meditation Practice; 4) Reduced Stress/Increased Relaxation, 5) Improved Communication/Relationships with Others, 6) Greater Acceptance/Letting Go, 7) Greater Self-Regulation, 8) Greater Openness, 9) Positive Lifestyle Change. Next we created a guiding conceptual model whereby mindfulness training creates heightened internal and external awareness, greater appreciation, increased acceptance, and more openness to experience. This in turn leads to cognitive and emotional self-regulation. From this stems increases in positive health behaviors and lifestyle changes and enhanced communication and relationships with others.

CONCLUSION: This conceptual model helps organize and frame important contextual factors associated with mindfulness training for couples. These may go undetected from traditional patient reported outcomes assessments yet are particularly meaningful for couples faced with extreme stressors such as cancer.
Abstract Title: Management of Clinical Stage I Seminoma: headed in the right direction, but fast enough?

Introduction:
Patients with clinical stage I (CSI) seminoma of the testis have a high rate of cure with decades of survival. In recent years, a better understanding of the long-term morbidity associated with chemotherapy and radiation has changed the testis cancer treatment paradigm. Post-orchiectomy surveillance is now recommended by the NCCN guidelines as the preferred management option for CSI seminoma. We sought to determine factors associated with patients receiving treatment in a contemporary setting as a first step toward reducing the use of potentially unnecessary treatment.

Methods:
The National Cancer Data Base was queried for all patients with CSI seminoma from 1998 to 2012. Adjuvant treatment after orchiectomy was classified into three groups: surveillance, adjuvant radiotherapy (XRT), and adjuvant chemotherapy (chemo). Yearly trends in management are described. Specific sub-group analysis for the years 2010-2012 was completed using logistic regression to determine predictors of treatment.

Results:
Of the 80,385 patients with testicular cancer, 16,931 had CSI seminoma. There was a progressive decline in the use of post-orchiectomy treatment from 1998-2012. In the years 2010-2012 (5,816 patients total), 61.2% of patients chose surveillance compared to 24% receiving XRT and 14.8% chemo. Regression modeling demonstrated that patients aged 18-30 were 18% less likely to receive treatment than those aged 31-37. Increasing pathologic stage was associated with a greater likelihood of treatment [OR 1.76, 95% CI 1.51-2.05] while academic hospitals were less likely to deliver adjuvant therapy [OR 0.75, 95% CI 0.61-0.92].

Conclusion:
Despite a trend towards increased use of post-orchiectomy surveillance for CSI seminoma patients, a significant portion are still receiving treatment. Pathologic stage and treatment hospital type are the biggest predictors of management decisions.
Menthol cigarette smoking does not moderate the effect of fast nicotine metabolism on short-term smoking cessation during nicotine replacement therapy

**Background:** Faster nicotine metabolism ratio (NMR) and menthol cigarette use are each linked with difficulty quitting. However, basic animal and human research suggests that menthol slows NMR, which should attenuate its effect on abstinence.

**Objective:** This study tested whether menthol cigarette use influences the association between fast NMR and short-term abstinence after 8 weeks of treatment with 21 mg/day nicotine patch and behavior counseling. We hypothesized that cigarette type (menthol vs. non-menthol) would modify this association (i.e., menthol use would mitigate the adverse effect of fast NMR). An alternative prediction was that fast NMR and menthol cigarette use would serve as independent risk factors for continued smoking.

**Methods:** 525 smokers were enrolled in a randomized controlled trial of maintenance therapy for smoking cessation. Those missing NMR and race data or who reported using both menthol and non-menthol cigarettes were excluded from the current analyses. Participants (N=474, 49% Black, 50% female, 17±7.8 cigarettes/day) were categorized as menthol (64%) or non-menthol users based on self-report of usual cigarette type, and fast (23%) or slow metabolizers based on NMR determined from saliva 3’hydroxycotinine/cotinine (NMR≥.47). Self-reported abstinence at Week 8 was bioverified by expired carbon monoxide (≤10 parts per million). We used logistic regression analyses to test the interaction of cigarette type by NMR and main effects of NMR and cigarette type. Covariates included nicotine dependence, age, race, and gender.

**Results:** Results revealed that NMR did not interact with cigarette type to predict abstinence (OR=.91, p=.86). Omitting the interaction term, there was a significant main effect of faster metabolism (OR=.58, p=.049), but no main effect of cigarette type (OR=1.11, p=.61).

**Conclusion:** Our findings replicate prior research showing that fast metabolism is an important risk factor for continued smoking during treatment. Menthol cigarette use neither moderated the effect of fast NMR nor predicted short-term abstinence. Future research should address the mixed findings in the literature regarding the association between menthol cigarette use and smoking cessation treatment outcome.
**Research Day Abstract**

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Does this research involve women’s health? No

**Abstract Title:** Surgical Learning Curve of Posterior Urethroplasty for Radiation-Induced Bulbomembranous Urethral Strictures

**Introduction and Objective:** Recent reports show a long surgical learning curve for optimal success rates after anterior urethroplasty. We have found excision and primary anastomosis (EPA) for radiation-induced bulbomembranous strictures to be a uniquely challenging procedure, having previously reported a 72% success rate, but we continue to receive a steady volume of referred cases. We evaluate our experience with posterior urethroplasty in the setting of obliterative radiation-induced bulbomembranous strictures to analyze whether outcomes have improved over time.

**Methods:** Retrospective review was performed of patients undergoing reconstruction of radiation-induced posterior urethral strictures by a single surgeon at a tertiary academic referral center. Cases were divided into 2 cohorts, 2007-2012 and 2013-2015. Only patients with 4 months of follow-up were included. Median follow-up was 50.0 months (17-97 mo) for the initial cohort and 22.0 months (4-34 mo) for the later cohort.

**Results:** Overall 72 patients were included, 37 men in the initial cohort (2007-2012) and 35 in the subsequent cohort (2013-2015). Despite strictures treated in the second cohort being significantly longer than in the first (median 3.0 cm (range 1-6 cm) vs 2.0 cm (1-3 cm), p=0.001), we observed a decrease in recurrence rate from 32.4% (12/37) in the first to 14.3% (5/35) in the second cohort (p=0.07, Fig. 1). Recurrences also occurred later in the second cohort (median 10.0 months (2.2–21 mo) vs 3.6 months (0.3 – 57 mo), p=0.15) and tended to be thin and amenable to endoscopic treatment. With increased follow-up time of our first cohort from 2.7 to 4.2 years, only one delayed recurrence was observed. Although single dilation was successful in 50% (6/12) of initial and 40% (2/5) of later patients with recurrence, multiple recurrences occurred in 6/12 (50%) patients in the initial and only 1/5 (20%) in the subsequent cohort. Stricture location, radiation type, time from radiation exposure to surgery, and artificial urinary sphincter rate did not vary significantly among cohorts.

**Conclusions:** Increasing experience over time has resulted in improved outcomes of EPA for radiation-induced bulbomembranous urethral strictures despite increased stricture length. Longer follow-up confirms our success rate of EPA in nearly three-quarters of patients.

**Figure 1.** Probability of Remaining Stricture-Recurrence Free After Urethroplasty for Radiation-Induced Stricture Based on Surgical Year. Black line represents patients undergoing surgery between 2007 and 2012. Light gray line represents patients undergoing surgery between 2013 and 2015.
Research Day Abstract

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Does this research involve women’s health?* No
Abstract Title:* Resilience and Psychological Morbidity in Parents of Critically-Ill Children

1. Introduction
Research has shown elevated rates of depression, anxiety and post-traumatic stress among parents following their child’s pediatric intensive care unit (PICU) stay. Resilience, one’s propensity to thrive in the face of adversity, is correlated with depression, anxiety and post-traumatic stress (PTS) in several contexts. Parents with low resilience may be at increased risk for psychological morbidity following their child’s PICU course. This study assesses the correlation between parental resilience at PICU admission with psychological outcomes at PICU discharge.

2. Methods
We gave surveys to parents of patients anticipated to be in the PICU at least 24 hours at admission and discharge. Admission surveys included the Connor-Davidson Resilience Scale (CD-RISC), scored from 0 (lowest) to 100 (highest). Discharge surveys included the PROMIS Short Forms (8a) for depression and anxiety and Impact of Event Scale-Revised (IES-R). We performed Spearman correlations to compare resilience with depression, anxiety and PTS symptoms.

3. Results
We obtained admission and discharge surveys from 31 parents. The mean resilience score was 78.5 (SD=12.9, range 40–100), comparable to the general population. Resilience was negatively correlated with depression (r=-0.41, p=0.02) and anxiety (r=-0.28, p=0.11), though only depression met the threshold for statistical significance. No significant correlation was found with PTS (r=-0.12, p=0.53).

4. Conclusions
We found a statistically significant correlation between parents’ resilience at PICU admission and symptoms of depression at PICU discharge. Symptoms of anxiety and PTS did not reach a statistically significant threshold. This work is limited by the small sample size and timing of the surveys—post-traumatic stress is better assessed further removed from the acute stressor. Further study about the relationship between resilience and psychological morbidity in parents of critically ill children could elucidate how these factors relate over time, and whether interventions targeted at resilience-building could mitigate these adverse psychological outcomes.
**Research Day Abstract**

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**Principal Investigator:** James Carr, MD

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Does this research involve women’s health? No

**Abstract Title:** Pro-B-Type Natriuretic Peptide is associated with regional left ventricular function and dyssynchrony measured by MRI: The Multi-Ethnic Study of Atherosclerosis (MESA)

**Introduction:** Pro-B-Type Natriuretic Peptide (BNP) is a regulator of cardiovascular function, and is elevated in acute myocardial infarction (MI) and heart failure. Cardiac magnetic resonance imaging (MRI) can determine peak systolic circumferential strain (Ecc) as a measure of regional systolic function and difference in time to peak systolic circumferential strain (TPS) as a measure of regional myocardial dysfunction. We aimed to examine the association between BNP levels with Ecc and TPS among asymptomatic participants of the Multi-Ethnic Study of Atherosclerosis (MESA).

**Methods:** A total of 868 participants (mean age 66, 44% women) with Pro-BNP measures and Ecc calculated from tagged MRI were included. Ecc and TPS was analyzed by harmonic phase imaging separately in mid LV anterior wall, septum, lateral wall, and inferior wall. Global Ecc was calculated as the average of Ecc in all myocardial segments. Linear regression models were used to investigate the association of BNP levels with Ecc and LV dyssynchrony, adjusting for traditional risk factors (TRF): age, sex, race, education, physical activity, cigarette smoking, diabetes, BMI, systolic blood pressure, anti-hypertensive medication use, HDL cholesterol, total cholesterol, statin use, and prevalence of CAC>10.

**Results:** The median BNP level (interquartile range) was 64.0 (28.6 – 130.4) pg/mL. Individuals with elevated levels of BNP were more likely to be older, have higher blood pressure and higher prevalence of Coronary Artery Calcium (CAC)>10. In multivariable models adjusted for TRF, there was significant reduction of global Ecc (P=0.030) and systolic function in the anterior wall (P=0.007) with 1 SD increases in log-transformed BNP (Table 1), and higher BNP levels were associated with greater TPS for all regions of analysis (Table 2).

**Conclusion:** Among asymptomatic individuals without documented cardiovascular disease, elevated BNP levels were associated with reduced regional LV systolic function and greater extent of myocardial dysfunction. These associations implicate BNP is a strong and independent prognostic marker in the pathogenesis of cardiovascular disease and heart failure. However, the observed associations and findings warrant further investigation.

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**Table 1. Relations of Plasma BNP to Systolic Circumferential Strains**

<table>
<thead>
<tr>
<th>Systolic circumferential strain (%)</th>
<th>Regression Coefficients* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>0.44 (0.12 to 0.76)</td>
<td>0.007</td>
</tr>
<tr>
<td>Lateral</td>
<td>0.24 (-0.07 to 0.55)</td>
<td>0.133</td>
</tr>
<tr>
<td>Posterior</td>
<td>0.25 (-0.12 to 0.58)</td>
<td>0.201</td>
</tr>
<tr>
<td>Septal</td>
<td>-0.02 (-0.32 to 0.28)</td>
<td>0.899</td>
</tr>
<tr>
<td>Global</td>
<td>0.23 (0.02 to 0.42)</td>
<td>0.030</td>
</tr>
</tbody>
</table>

CI indicates confidence interval. Model adjusted for age, sex, race, education, physical activity, cigarette smoking, diabetes, BMI, systolic blood pressure, anti-hypertensive medication use, HDL cholesterol, total cholesterol, statin use, and prevalence of CAC>10. *Linear regression coefficient represents changes in systolic strain (%) per 1-SD (1.18 pg/ml) increment in log-transformed BNP, adjusting for all other covariates in the model. Systolic circumferential strains are negative values, positive regression coefficients indicate less/worse systolic function.

**Table 2. Relations of Plasma BNP to Time-to-Peak Systolic Circumferential Strains**

<table>
<thead>
<tr>
<th>Time-to-Peak Systolic circumferential strain (ms)</th>
<th>Regression Coefficients* (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anterior</td>
<td>1.32 (1.09 to 1.55)</td>
<td>0.006</td>
</tr>
<tr>
<td>Lateral</td>
<td>1.16 (0.88 to 1.44)</td>
<td>0.002</td>
</tr>
<tr>
<td>Posterior</td>
<td>1.31 (1.09 to 1.53)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Septal</td>
<td>0.92 (0.61 to 1.23)</td>
<td>0.050</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; ms, millisecond. Model adjusted for age, sex, race, education, physical activity, cigarette smoking, diabetes, BMI, systolic blood pressure, anti-hypertensive medication use, HDL cholesterol, total cholesterol, statin use, and prevalence of CAC>10. *Linear regression coefficient represents changes in time-to-peak systolic circumferential strain (ms) per 1-SD (1.18 pg/ml) increment in log-transformed BNP, adjusting for all other covariates in the model.
Abstract Title: *A Systematic Review of Vigorous Physical Activity in Eczema*

Summary/Objective:
The hallmark of atopic dermatitis (AD or eczema) is intense itch that can disturb all aspects of patients’ lives. Excess heat and sweat are the most commonly reported exacerbants of itch in eczema.1,2 Thus, patients with AD may avoid exercise or other physical activity accompanied by sweating, in order to avoid worsening itch. We conducted a systematic review of the literature and meta-analysis to explore the relationship between AD and physical activity levels.

Methods:
We searched PubMed (1946 to present), EMBASE (1947 to present), Scopus (1823 to present), Global Resource for Eczema Trials (all years) and the Cochrane Library (1992 to present) up to March 11, 2015. The search strategy was based on a previous Cochrane review3 (Table S1). Both reviewers, A.K. and J.I.S., independently performed data extraction from these studies, and differences were resolved by discussion. The exposure was the level of physical activity and the outcome was AD. The Newcastle-Ottawa Scale (NOS) was used to assess study quality based on selection criteria, between-group comparability and study outcome using a nine-star scoring system.9,10 We included only studies with NOS ≥ 7 in the meta-analysis. Statistical analyses were performed using SAS version 9.4 (SAS Institute Inc, Cary, NC, U.S.A.). Forest plots were constructed for studies included in the meta-analysis. Pooled OR and 95% confidence interval were estimated using both fixed- and random-effects models that accounted for variability between studies. Egger regression, Begg rank correlation and funnel plot regression were used to assess publication bias. A two-sided P-value of 0.05 was considered significant.

Results:
The literature search yielded 4993 non-duplicate articles that underwent titles and abstract review; 229 full-text articles were reviewed; 7 manuscripts including eight studies were included in the final analysis.4–6,11–14 Of these, five manuscripts had sufficient data for inclusion in a meta-analysis.6,11–14 Three studies found a positive association between eczema and physical activity,4,11,12 three found an inverse association5,6,14 and one found no association.13 No published studies of the association between physical activity and eczema severity were found. None of the self-reported assessments of physical activity were previously validated. There were four studies with NOS ≥ 7 included in the meta-analysis encompassing 61974 patients, including 3065 children and 58909 adults. Overall, 3298 (8.7%, range 7.5–47.3%) of patients with less than once-weekly exercise, 2136 (8.8%, range 6.8–51.0%) with at least once-weekly exercise and 147 (23.8%, range 14.9–47.9) with at least thrice-weekly exercise or other vigorous physical had a history of AD. Vigorous physical activity or exercise at least once weekly (odds ratio: 1.04, 95% CI: 0.92–1.17) or thrice weekly (1.11, 95% CI 0.88–1.40, P=0.40) were not associated with AD in random-effects models. Publication bias was not detected.

Conclusions:
This systematic review revealed few high-quality studies, with varying definitions of exercise and vigorous physical activity. Future studies are needed to address the knowledge gaps about the association of eczema and physical activity.
Research Day Abstract

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Does this research involve women’s health?* Yes

Abstract Title:* Understanding Differences in Men and Women Receiving Acute Care Treatment for Eating Disorders

**Background:** Often mistaken as only affecting women, men are more likely to face stigma and dismissal when seeking treatment for eating disorders (Vogel, Wester, Hammer, & Downing-Matibag, 2014). Indeed, men are expected to suppress their worries regarding body image, depression, or other traditionally feminine issues (Strother, Lemberg, Stanford, & Turberville, 2012). The tendency to overlook eating disorders in men may, in part, be due to different manifestation of symptoms. For instance, there is a growing body of research examining men who control their diet and exercise for the purposes of growing larger muscle mass, not for decreasing weight (Strother et al., 2012). Despite their low numbers, men in studies of eating disorders have consistently reported greater impairment and decreased quality of life when compared to men without eating disorders (Mitchinson, Mond, Slewana-Younan, & Hay, 2013; Mond & Hay, 2007). Yet, studies examining differences between men and women with eating disorders are lacking. Mitchinson et al. (2013) compared health related quality of life in 3034 men and women (48.75% male) and found that binge eating had a greater impact on quality of life in males. This and other studies (Streigel, Bedrosian, Wang, & Schwartz, 2012), however, were conducted on community samples and may not generalize to clinical populations. One of the few studies examining clinical populations found significant differences between men and women on the EDI-3 (Stanford & Lemberg, 2012). The current study adds to the literature by examining gender differences in a clinical sample with regard to eating disordered characteristics, quality of life, functional impairment and treatment outcomes.

**Method:** Data were collected from a large behavioral health hospital providing inpatient, partial hospitalization (PHP), and intensive outpatient (IOP) treatment for eating disorders. Data were collected as part of routine clinical assessment and de-identified prior to analyses. The sample consisted of 1002 patients (449 inpatients, 553 PHP/IOP) composed mostly of patients of non-Hispanic white (89%) and Hispanic (7%) backgrounds, with a mean age of 23.2 years (SD=11.4, range=11-66) and 79 males. The sample included diagnoses of anorexia nervosa (29%), bulimia nervosa (14%), binge eating disorder (4%), or eating disorder not-otherwise-specified (53%). Data were collected from the following measures: Eating Disorder Examination Questionnaire (EDE-Q), Patient Health Questionnaire – 9 (PHQ-9), Quality of Life Enjoyment and Satisfaction Questionnaire (QLESQ), and Work and Social Impairment Scales (WSAS).

**Preliminary Results:** At admission, males evidenced significantly lower scores on the EDE-Q than women, including on the restraint ($t_{995}=3.23$, $p<.001$), eating ($t_{995}=4.00$, $p<.001$), shape ($t_{995}=4.90$, $p<.001$), and weight ($t_{995}=4.69$, $p<.001$) subscales. Males also had significantly higher quality of life ($t_{957}=1.98$, $p=.048$) and less depression ($t_{785}=3.01$, $p=.003$), but no significant difference was found for functional impairment or global assessment of functioning. Despite lower pathology on many of the measures, males evidenced no significant difference in length of stay in treatment, nor in treatment outcome, when compared to females.

*Abstracts longer than one page will not be accepted.
Research Day Abstract

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Does this research involve women’s health?* No

Abstract Title:* Moderate Sedation Shortens Total Electrophysiology Lab Time Compared to General Anesthesia for Cryoballoon Ablation

Introduction. Cryoballoon ablation (CBA) for paroxysmal atrial fibrillation (pAF) can be performed under general anesthesia (GA) or moderate sedation (MS). Our objective was to compare the effectiveness, safety, procedure duration, and time spent in the electrophysiology (EP) laboratory for CBA performed under GA and MS.

Methods. Patients undergoing a first CBA for pAF were identified. Patients received either GA administered by an anesthesiologist or MS with midazolam and fentanyl administered by EP laboratory staff. Total time in laboratory (sum of procedure and non-procedure time), fluoroscopy time, freedom from AF (FFAF), acute pulmonary vein isolation (PVI) rate and 30-day complication rate were assessed.

Results. 55 patients received GA and 119 patients received MS. PVI success rate was 100% in GA and 98.1% in MS (p=0.04). Total laboratory time was longer for GA (280.4 ± 54.1 min vs. 245.5 ± 54.7 min; p<0.001), related to longer non-procedure time (92.2 ± 28.8 min GA vs. 71.0 ± 30.0 min MS; p < 0.001), but not procedure time (188.3 ± 49.3 min GA vs. 174.5 ± 50.2 min MS; p=0.09). Fluoroscopy time was greater with GA (49.0 ± 26.9 min vs. 37.9 ± 21.5 min; p=0.004). FFAF was not significantly different over a mean follow up duration of 1.2 ± 0.9 years (61.8% GA vs. 63.0% MS; log-rank p=0.90). There was no significant difference in complication rate.

Conclusion. Compared to GA, MS during CBA for pAF was associated with shorter total EP laboratory time and fluoroscopy exposure time without compromising FFAF or complication rates.
Research Day Abstract

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Department:* Anesthesiology
Does this research involve women’s health?* No
Abstract Title: * Outcomes of High-Risk Pediatric Patients Undergoing Low-Risk Surgery

Background: The accurate risk stratification of pediatric patients presenting for low-risk surgery is limited by a paucity of data. We sought to determine the incidence and independent predictors of postoperative complications and unplanned 30-day readmission in a cohort of pediatric patients who underwent low-risk surgery. We hypothesized that patients with greater illness severity would have an increased incidence of postoperative complications and 30-day readmission.

Methods: The study included pediatric patients who underwent minor procedures of the skin and soft tissue at a continuously enrolled American College of Surgeons National Surgical Quality Improvement Program Pediatric hospital over a three-year period. The primary outcome was a composite of 24 postoperative complications. Secondary outcomes included unplanned 30-day readmission. Univariable analyses were performed to identify associations with preoperative characteristics and postoperative complications and readmission. Multivariable logistic regression models were created to identify independent predictors for postoperative complications and readmission.

Results: The final analysis included 6,851 patients. There were a total of 169 postoperative complications among 152 patients (2.22%) with the majority of complications being either wound-related or postoperative mechanical ventilation. The independent predictors for postoperative complications were American Society of Anesthesiologists physical status classification ≥ 3 and nutritional deficiency. There were 41 unplanned readmissions (0.6%). The presence of a postoperative wound complication or a postoperative pulmonary complication was an independent risk factor for unplanned 30-day readmission.

Conclusions: Certain patients undergoing even low-risk surgery are still at risk for the development of postoperative complications and unplanned 30-day readmission. Identification of these higher risk patients allows the anesthesiologist to implement targeted therapies to minimize the likelihood of occurrence of these complications.
Research Day Abstract

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Abstract Category:* Clinical Research
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Department:* Radiology

Does this research involve women’s health?* No

Abstract Title:* The Use of Cardiac Magnetic Resonance Imaging in Diagnosing and Characterizing Hypertrophic Cardiomyopathy

Background: In Hypertrophic Cardiomyopathy (HCM), measurements of maximal myocardial thickness serve a critical role in diagnosis and risk stratification. CMR plays an increasingly significant clinical role. The purpose of this study is to examine the influence of slice obliquity on CMR-measured maximum myocardial thickness in the basal anteroseptum comparing 3-Chamber long-axis with short-axis CMR imaging and further, to assess the degree of agreement between long-axis measurements on TTE and MRI.

Methods: We performed a retrospective analysis of 50 consecutive patients (29 males and 21 females; age 58 ± 14) referred for CMR at Northwestern Memorial Hospital with asymmetric septal HCM. The 3-chamber (3Ch) balanced steady state free precession (bSSFP) images were cross-referenced with the short axis (SA) bSSFP cine stack to ensure correlation between measured myocardial regions. The basal anteroseptum was measured on the 3-chamber images in diastole using a line parallel with the mitral valve and on the short axis view, a line orthogonal to the myocardium at the region corresponding to that measured in the 3 chamber view. The angulation in degrees between the 3-chamber bSSFP slice position and the orthogonal measurement on short-axis images was recorded. In cases with significant discrepancy between 3Ch and SA, measurements of the basal anteroseptum were performed on parasternal long axis (PSL) images at TTE. Measurements were compared using the student’s t-test, with a p-value of 0.05 considered significant.

Results: On aggregate, there was a difference between CMR derived 3Ch and SA myocardial thickness (p<.0005) with an average difference of 0.99 ± 1.4 mm. Angulation between 3Ch and SA images averaged 18 ± 15°. There was a positive linear correlation between angulation and the difference noted between CMR derived 3Ch and SA measurements (R² = .755, p = .012. See Figure 1). 12 subjects (24%) demonstrated at least a 1.5mm difference between CMR derived 3Ch and SA measurements corresponding to an angulation of 24.7°. 4 subject measurement. TTE measurements showed a close agreement with 3Ch measurements (mean TTE-3Ch = .85mm) while tending to overestimate the short axis measurements (mean TTE-SA = 1.69mm).

Conclusions: Angulation of long-axis imaging may explain differences between long-axis and short-axis measurements. Although the absolute difference averaged 0.99 mm in this study, the reliance on maximal myocardial thickness in the diagnosis of HCM is potentially significant, with nearly ¼ of subjects in our study demonstrating differences greater than 1.5 mm. 3Ch images agreed more with TTE measurements suggesting similar challenges with angulation. Our results suggest that operators should minimize 3Ch angulation; keeping the angulation to < 20 as this corresponds to a difference of 1mm and is within the expected error of repeat measurement.

*Abstracts longer than one page will not be accepted.
Risk Factors for Infective Endocarditis in Surgical Patients with Bicuspid Aortic Valve Disease

Background:
Bicuspid aortic valve (BAV) disease is associated with an increased risk of infective endocarditis (IE) compared to the general population. Although prior studies have estimated a 10-30% risk of IE in BAV disease, antibiotic prophylaxis for IE is no longer recommended in these patients. Few studies have addressed risk factors for IE in BAV disease. We seek to determine risk factors for IE in BAV patients undergoing cardiac surgery.

Methods:
We analyzed clinical, demographic, and imaging variables from a surgical cohort of BAV patients who received care at our institution from April 2004 to June 2014. Among the 762 BAV patients, 41 were diagnosed with native valve endocarditis based on review of patient records. An internally-validated multivariable logistic regression model was created to identify risk factors for IE.

Results:
As shown in Figure 1, moderate to severe aortic insufficiency (AI) was associated with increased odds of IE (odds ratio (OR) 3.25, 95% CI 1.38-7.62, P=0.007), while hypertension (OR 0.37 (0.18, 0.78), P=0.008), aortic stenosis 2+ or higher (0.38 (0.18, 0.79), P=0.009), and female sex (0.21 (0.05-0.91), P=0.038) were associated with lower odds of IE.

Conclusion:
In our cohort of BAV patients referred for surgery, moderate to severe AI was associated with increased odds of IE. These findings suggest that BAV patients with moderate to severe AI may constitute a high-risk subgroup who could benefit from antibiotic prophylaxis to reduce their risk of IE.
Abstracts longer than one page will not be accepted.

Research Day Abstract

Presenting Author:* Daniel Olson, MD
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Position:* Resident
Abstract Category:* Clinical Research
Principal Investigator:* Aparna Kalyan, MBBS
Department:* Oncology

Does this research involve women’s health?* Yes

Abstract Title: * Genomic Aberrations in advanced solid malignancies using Next Generation Sequencing – A single institution experience

Background: The paradigm in the treatment of cancer is changing such that, treatment based on molecular targets and associated pathways is at the forefront rather than chemotherapy. The identification of different molecular “drivers” utilizing NGS technology has led to better understanding of advanced malignancies. Recently, the prevalence of potentially targetable genomic abnormalities in primary and metastatic breast cancer utilizing NGS method found that 84% of the evaluated cancers harbored at least one genomic alteration linked to potential treatment options. Validation of this NGS testing in 2,221 clinical cases revealed clinically actionable targets in 76% of tumors, corresponding to three times the number of actionable targets detected by other current diagnostic tests. It is for these reasons that the genomic landscape needs to be better characterized

Methods: Medical records of all patients referred to the phase 1 clinic at our institution who had NGS performed were reviewed retrospectively from January 2014 to December 2015.

Results: 159 cases were identified; 65 males and 94 were females. Mean age was 54.51 Years (Range 25-83 years). Gastrointestinal cancers accounted for 47.2% cases while gynecological, lung and breast cancer accounted for 11%, 10% and 9% respectively. There was an average of 15.31 aberrations per cancer (range: 4- 66). An average of 4.73 aberrations per cancers were found to be clinically relevant, while the rest were variance of unknown significance. FGF, CDK, KRAS, PI3K and FGFR were the most common clinically relevant aberrations and they accounted for 6%, 5.2%, 4.9%, 3.9% and 1.5% of the clinically relevant aberrations respectively. Breast cancer and Colon cancer accounted for 31% and 21% of the PIK3 aberrations. Cholangiocarcinoma, breast cancer accounted for 90% (45% each) of FGFR aberrations.

Conclusions: In this single institution study for phase 1 trials, we found a small but significant number of patients amenable to targeted therapy. Multi-gene NGS panel testing can identify targetable aberrations such as PIK3 and FGFR genetic aberrations, justifying their use in clinical care for screening patients for early phase clinical trials.
Venous thromboembolism (VTE) following spinal surgery has been identified as a significant source of morbidity; however, using anti-coagulant therapy is a well-established measure against these serious complications. Surgeons often avoid early use of chemoprophylaxis due to the dreaded risk of spinal epidural hematomas. In this study, we examined the timing and risks of chemoprophylaxis following spinal surgery.

Records from 6870 consecutive spinal surgeries at one institution were respectively reviewed. Data was collected pertaining to patient demographics, surgical and hospital course, timing of chemoprophylaxis, and complications including DVTs, PEs, and spinal epidural hematomas. Patients receiving anti-coagulant therapy from one day before to three days after surgery (prophylactic group; n=1904) were compared to the remaining patients (non-prophylactic group; n=4968).

Patients receiving chemoprophylaxis were older, had multiple comorbidities, underwent longer surgeries, and were more likely to be admitted to the ICU. Chemoprophylaxis was started following 1.46 days on average. The rate of VTEs was 4% (n=69) in the prophylactic group and 2% (n=101) in the non-prophylactic group (p<.001). Of the prophylactic patients, 0.20% (n=4) developed epidural hematomas, while 0.20% (n=9) of the non-prophylactic group developed epidural hematomas (p=0.619). Only one patient in the prophylactic group (25%) suffered from neurological deficit due to epidural hematoma compared to seven in the non-prophylactic patients (78%). The average timing of hematoma was 10.84 days for prophylactic group and 6.2 days for the non-prophylactic group.

The risk of spinal epidural hematomas between patients receiving chemoprophylaxis and those who do not is low and is the same. This highlights that administering anti-coagulant therapy from one day before to three days after surgery is safe for high-risk patients.

Figure 1. The timing of VTEs in the chemoprophylactic group (n=1904; orange) and non-chemoprophylactic group (n=4968; black). Average timing of developing VTEs in the chemoprophylactic group was 8.52 days and 5.83 days in the non-chemoprophylactic group (p>.05).
**Abstract Title:** Use of adjuvant radiotherapy in women with Stage I endometrioid adenocarcinoma of the uterus: a National Cancer Database study

**Background:** Randomized controlled trials have consistently shown that the use of post-operative radiotherapy in stage I endometrial cancer leads to a reduction in the incidence of pelvic recurrences without a corresponding reduction in mortality. We hypothesized that a reduction in mortality associated with the receipt of radiotherapy could be identified in a large dataset with greater statistical power.

**Methods:** The National Cancer Database was queried to identify women with stage I endometrial adenocarcinoma diagnosed between 2003 and 2011 and treated with total hysterectomy. A Cox regression analysis was performed to determine the impact of known prognostic factors and receipt of radiotherapy (pelvic radiotherapy or vaginal brachytherapy) on mortality.

**Results:** A total of 43,188 eligible women were identified (33,081 stage IA and 10,107 stage IB). Of these, 89.2% of women with stage IA and 55.8% of women with stage IB tumors received no radiotherapy. Older age, co-morbid disease, higher histologic grade and larger tumor size were independently associated with an increase in mortality. Receipt of vaginal brachytherapy was independently associated with a reduction in mortality in both stage IA (HR 0.81; 95% CI 0.67-0.97) and stage IB disease (HR 0.62; 95% CI 0.51-0.74).

**Conclusions:** Analyses from this large database support the utility of post-operative radiotherapy for many women with stage I endometrial cancer. Radiotherapy appears to be underused in this population. Greater adherence to consensus guidelines may lead to improved outcomes.
Abstract Title: The Electrophysiologic Manifestations and Outcomes in Patients with Cardiac Sarcoidosis

Introduction:
Symptomatic atrioventricular (AV) block is a commonly reported initial manifestation of cardiac sarcoidosis requiring permanent pacemaker implantation. However, there is little data on the long term arrhythmic outcomes in this specific patient population.

Methods:
We performed a retrospective assessment of consecutive patients diagnosed with cardiac sarcoidosis with an initial manifestation of symptomatic AV block to characterize the incidence of subsequent ventricular arrhythmias or sudden cardiac death.

Results:
Sixty consecutive patients were enrolled with biopsy-proven or clinically diagnosed cardiac sarcoidosis. Twenty-one (35%) patients presented with an initial manifestation of symptomatic AV block. Of patients with AV block, the average age was 58 years with 15 (71%) males and 5 (24%) African-American patients. Sixty-four percent (n=9) of patients undergoing PET imaging had evidence of metabolically active disease and 91% (n=10) of patients undergoing cardiac MRI had evidence of late-gadolinium enhancement. The average LVEF by transthoracic echocardiogram on presentation was 47.5%. Over a mean follow up of 49 months, 10 patients (47.6%) developed subsequent VT or VF. Among these patients, the average baseline LVEF was 37.1%, and ultimately, >50% in 5 of the 10 patients at follow up. There were 8 (38%) patients in the overall cohort who underwent initial implantation of a permanent pacemaker for AV block that subsequently required upgrade to an implantable cardioverter-defibrillator. One patient underwent cardiac transplantation for advanced heart failure and one patient died of a non-cardiac cause.

Conclusions:
In a cohort of patients with newly diagnosed cardiac sarcoidosis, 35% presented with an initial manifestation of AV block. The long-term outcomes for these patients are poor with a large percentage developing subsequent VT or VF despite a LVEF >35%. Although the clinical impetus in patients with symptomatic AV block is to implant a permanent pacemaker, these findings suggest the need to consider proactive ICD therapy in patients with cardiac sarcoidosis due to the risk of subsequent ventricular arrhythmias.
**Background:** Persons with human immunodeficiency virus (HIV) have twice the risk for myocardial infarction and four-to-fivefold greater risk for sudden cardiac death compared with the general population. Associations between coronary artery disease (CAD) and myocardial fibrosis – a mediator of sudden cardiac death – in the setting of HIV are unknown. We hypothesized that CAD-associated myocardial fibrosis is more extensive for HIV-infected persons than matched uninfected controls.

**Methods:** HIV-infected persons with at least moderate CAD (50% or greater stenosis of at least one coronary artery segment >2mm in diameter) on angiography who also underwent cardiac magnetic resonance imaging (cMR) were frequency matched by demographics with uninfected controls. Extent of fibrosis in each myocardial segment was assessed by cMR with late gadolinium enhancement. Patients with known or suspected non-ischemic cardiomyopathies were excluded.

**Results:** HIV-infected patients (N=12) and uninfected controls (N=22) with at least moderate CAD on angiography who underwent cMR with contrast had similar indications for angiography and cMR as well as similar distributions of CAD. HIV-infected persons had a significantly greater burden of myocardial fibrosis than controls; the mean overall percent of fibrotic myocardium (± SE) and percent per number of coronary arteries with at least moderate CAD were 22.8% ± 3.9% and 11.3% ± 1.1%, respectively, for HIV-infected persons, compared with 11.3% ± 2.4% and 5.0% ± 0.9% for uninfected controls (P value 0.01 and <0.001, respectively). Fibrosis burden in the left anterior descending territory was particularly greater for HIV-infected persons (30.6% ± 6.6%) compared with uninfected controls (9.3% ± 2.9%; p=0.002). Findings were similar in sensitivity analyses including only persons with adjudicated MI.

**Conclusions:** HIV-infected persons have more myocardial fibrosis associated with CAD than uninfected matched controls, which may explain some of the increased risk for sudden cardiac death in these patients. Understanding the mechanisms underlying greater myocardial fibrosis in HIV requires further investigation.

Figure 1. Segmental Myocardial Fibrosis: HIV-Infected vs. Uninfected Patients with similar Coronary Artery Disease Burdens

*Abstracts longer than one page will not be accepted.*
Neural network underlying abnormal syntax processing in primary progressive aphasia: physiologic evidence from resting state functional MRI

**Abstract**

We investigated brain neural network breakdown underlying impaired processing of sentence grammar (syntax) in a group of 48 individuals with primary progressive aphasia (PPA). Using resting state functional magnetic resonance imaging (fMRI), we identified a correlation between decline in connectivity of a left hemisphere parieto-frontal network and impairment in syntax processing. This correlation was not found between control networks and syntax processing measures, proving specificity of our finding.

**Objective:** To determine the neural network underlying abnormal syntax processing in individuals with primary progressive aphasia.

**Background:** PPA is a syndrome of progressive decline of language function due to neurodegenerative disease. Individuals with PPA may make grammatical errors when producing sentences (agrammatism). Once attributed to Broca’s area, evidence has been growing that processing of grammar relies on a network of regions located at the dorsal aspect of left sylvian fissure (dorsal language stream). Brain volume loss (atrophy) within these regions has been found to correlate with the degree of agrammatism. This however, has not been well investigated at physiologic large-scale network level. In this study, we investigated the relationship between functional connectivity of dorsal language stream nodes and processing of syntax in a group of individuals with PPA using task-free fMRI. We hypothesized that decline in syntax processing in PPA would correlate with decreased resting state functional connectivity (RSFC) within the dorsal language network but not in the control non-language-related networks.

**Methods:** A diagnosis of PPA was reached only if the primary clinical feature was language impairment that could not be accounted for by nondegenerative etiologies. Forty-eight individuals with PPA (Age= 64.92± 6.54; 23 women, and 25 men) were recruited and underwent task-free fMRI scanning (i.e. resting state fMRI). Average Western Aphasia Battery Aphasia Quotient (WAB-AQ) in this group was 77.51 ± 17.20 (/100), and they scored 14.65 ± 6.64 (/30) on a composite score of grammatical processing (based on the Northwestern Assessment of Verbs and Sentences [NAVS], and the Northwestern Anagram Test [NAT]). Nodes from the dorsal perisylvian language stream were chosen based on previous fMRI studies of syntax processing and atrophy maps related to agrammatism in PPA. Using Pearson test, we investigated correlation between NAT-NAVS score and strength of RSFC between two 10 mm spherical nodes: the supramarginal gyrus (SM) of the parietal lobe, and pars opercularis portion of the inferior frontal gyrus (PO), both thought to be involved in syntax processing. Additionally, we investigated correlation between NAT-NAVS score and strength of RSFC in two non-language networks: (1) Network connecting right hemisphere counterparts of the PO and SM (contralateral) nodes; and (2) network connecting left PO/SM nodes and a ventral sensorimotor node.

**Results:** The RSFC between the left hemisphere IFG-PO and SM was found to correlate significantly with NAT-NAVS scores (r= 0.409, p=0.0088). This was in contrast to the contralateral RSFC between right PO and SM, which did not correlate with NAT-NAVS scores (r= -0.127, p=0.433). Similarly none of the sensorimotor connections (r= -0.09, p=0.580 for OP, and r=0.027, p=0.868 for SM) correlated with NAT-NAVS results.

**Conclusions:** In individuals with PPA, scores of syntax processing correlated with a left lateralized parieto-frontal network but not with its contralateral right hemisphere counterpart or with sensorimotor connections, confirming specificity of our finding. Historically processing of grammar was attributed to Broca’s area (mostly PO). However, by providing physiologic evidence, our finding adds to a growing literature that supports involvement of a network (containing both PO and SM) in syntax processing. By providing targets for intervention, this study may be useful for guiding therapeutic neuromodulation of the language network (e.g. repetitive transcranial magnetic stimulation).
Abstract Title: Outcomes Associated With Electrical Cardioversion for Atrial Fibrillation When Performed Autonomously by an Advanced Practice Provider

Background: Advanced Practice Providers (APPs) have emerged as an integral part of cardiovascular Team-Based Care. The purpose of this study was to determine the feasibility, safety, and efficacy of elective direct current cardioversion (DCCV) for atrial fibrillation (AF) when performed autonomously by a trained APP using a guideline directed protocol. Methods: A licensed Advanced Practice Nurse-Clinical Nurse Specialist with Advanced Cardiac Life Support certification was trained by an attending electrophysiologist utilizing core competencies based on the 2014 Clinical Practice Guidelines for Management of Patients with AF. A guideline directed protocol that included a pre/post procedural check list was developed. Prior to being credentialed by the hospital to independently perform DCCV, the APP performed 227 DCCVs with direct physician supervision over a ten-month period. After credentialing and privileges were granted, the APP performed all electively scheduled DCCVs in a noninvasive procedure room with the attending electrophysiologist immediately available in an adjacent Electrophysiology Lab. Deep sedation was administered by an anesthesiologist. When a pre-procedural transesophageal echocardiogram (TEE) was required prior to DCCV, the TEE was performed in a separate venue and the patient transferred to the DCCV room. The APP was accountable for the pre-procedural evaluation of the patient and reviewed each patient with the supervising electrophysiologist prior to DCCV. The APP autonomously performed a history and physical, explained risks and benefits of DCCV and obtained informed consent. The APP coordinated the discharge process and follow-up care with the patient and family. A major complication was defined as a complication that required intervention, prolonged hospital stay or resulted in permanent impairment or death. Results: 317 DCCVs were performed by the APP autonomously. There were no major complications or adverse events. One patient suffered a minor stroke 2 days after DCCV, but fully recovered. 2013, 2014, and 2015 average Press Ganey scores were 4.833, 4.840 and 4.875 out of 5.00 respectively. Conclusions: With appropriate clinical training, a protocol that includes a guideline directed pre/post procedural check list and physician supervision, an APP can safely perform DCCV autonomously with excellent patient outcomes.

*Abstracts longer than one page will not be accepted.*
Abstract Title: **Focal characteristics in Childhood Absence Epilepsy Patients**

**Introduction:**
The 3Hz spike and wave pattern seen on EEG was described as early as 1935 by Gibbs, Davis and Lennox and has become diagnostic in Childhood Absence Epilepsy (CAE). However, there are other electrographic features that have been described, including focal or multifocal abnormalities and fragments of discharges. Sadleir, et al found almost 50% of discharges were focal at their onset, despite CAE being characterized as a “generalized” genetic epilepsy. We sought to determine the frequency of focal patterns and describe them in a consecutive series of children with CAE evaluated at our institution.

**Methods:**
Patient’s were identified by a keyword search (“CAE”, “absence”) in the central EEG database of EEG recordings performed at our center from 2007-2011. The diagnosis of CAE was confirmed by review of clinical information. Data on age at seizure onset, sex, medications and sleep deprivation was collected for each patient. Each eligible EEG was reviewed for number of discharges, discharge duration, focal lead presence and duration and fragment presence and location.

**Results:**
98 patient EEGs from 2007-2011 were selected, with a total of 1615 bursts and fragments recorded. 96 patients had bursts and of those, 69/96 (71.8%) had a focal lead in. 58/96 (60.4%) of focal leads were frontal. 57/98 (58.2%) of patients had fragments noted in their record. Of the patients with fragments, a higher percentage were on medications than those who were untreated (62% vs 37%, p=0.04). Presence of fragments did not differ by age or type of medication. Records without fragments tended to have discharges with longer duration (mean of 8.66 seconds vs 5.01 seconds , p=0.001). Duration of discharges did not vary in those who were treated verse who were not (6.8 vs 5.1 sec, p=0.25). 86/98 (87%) of patients in the cohort were sleep deprived and all completed hyperventilation. There was no difference in the number of bursts or length of bursts in sleep deprived verse non-sleep deprived patients (p=0.62, p=0.13). 80/98 (84%) had discharges during hyperventilation. Of the 18 patients who did not have discharges during hyperventilation, 2 had no discharges and 16 had discharges occurring outside of hyperventilation.

**Conclusion:**
CAE, while considered a “generalized” epilepsy, is typically characterized by minor focal features. These findings should be understood by those diagnosing children as they are still consistent with the diagnosis of a generalized genetic epilepsy and should not weigh against the diagnosis and treatment.
Abstracts longer than one page will not be accepted.

**Research Day Abstract**

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**Position:** Research Assistant Professor

**Abstract Category:** Clinical Research

**Principal Investigator:** Abel N. Kho, MD

**Department:** Medicine – General Internal Medicine and Geriatrics

**Does this research involve women’s health?** No

**Abstract Title:** Methods and Initial Practice Characteristics in a Comparative Effectiveness Trial of Strategies to Improve Cardiovascular Care

**BACKGROUND:** Heart disease and stroke are the first and fifth leading causes of death in the United States. The Millions Hearts initiative aims to prevent heart attacks and strokes by improving the ABCS of heart health: Aspirin when appropriate, Blood pressure control, Cholesterol management, and Smoking cessation. The Healthy Hearts in the Heartland (H3) study is being conducted to provide quality improvement services that can improve ABCS performance at small- and medium-size primary care practices in Illinois, Indiana and Wisconsin.

**OBJECTIVES:** The first objective of this study is to evaluate the ability of practices in our region to implement quality improvement strategies to improve ABCS performance and to implement software that evaluates ABCS performance and conducts regional benchmarking. The second objective of this study is to conduct a practice-randomized trial to evaluate the comparative effectiveness of:

A) Point of care (POC) strategies to improve ABCS performance, versus;

B) Point of care plus population management (POC+PM) strategies.

**METHODS:** The H3 study will use an evidence-based, comprehensive approach to quality improvement support to accelerate improvement in the ABCS measures in 250 Midwestern primary care practices. Each participating practice will be paired with a practice facilitator, who will work with the practice to implement quality improvement strategies and to install popHealth, a population management software providing each site with a clinical performance measurement dashboard including national and best practice benchmarks. Practice recruitment and randomization will proceed in three waves over 2015-16. In each wave, practices will be equally allotted to the POC only and POC+PM trial arms. All practices will receive 12 months of active facilitation, followed by a 6-month sustainability period in which study outcome data are collected but the facilitator does not actively support practice quality improvement efforts.

**INTERVENTIONS:** Practices randomized to the POC arm will work with the facilitator to implement strategies such as notifying individual providers of their performance on ABCS measures, implementing clinical decision support alerts in the electronic health record and revising practice workflows to intervene in patients who have uncontrolled hypertension or use tobacco. Practices randomized to the POC+PM study arm will work with the facilitator to implement both POC strategies and population management strategies such as proactive outreach to patients who are not meeting individual ABCS measures and referrals to community-based resources. Facilitators will conduct a combination of onsite visits and remote practice coaching.

**RESULTS:** Thus far, one wave of 42 practices has been enrolled and randomized (21 randomized to POC only and 21 to POC+PM), all of which have an electronic health record. Among POC only practices, 13 (62%) are in Illinois, while 14 (67%) of POC+PM practices are in Illinois. A majority of practices in both study arms are solo practices (i.e. have 1 provider). Among POC only practices, the median proportion of the practice population that is uninsured or has Medicaid insurance is 15% (interquartile range [IQR], 7-40%); among POC+PM practices, the median is 30% (IQR, 10-42%). In both study arms, the median proportion of the practice population that is African American race is 10% (POC only IQR, 2-15%; POC+PM IQR, 1-30%).

**DISCUSSION:** Practice recruitment is ongoing for the second and third waves of H3 study randomization. We will randomize the second wave of participating practices in Spring 2016 and the final wave of participating practices in Summer 2016. Forthcoming quantitative analyses will examine results of practice surveys, staff surveys, implementation tracking data and practice-level ABCS performance. In our forthcoming qualitative evaluation, we will conduct interviews with physician leaders at participating practices to investigate practices’ ability to initiate and manage change, as well as barriers and facilitators to implementing the POC and POC+PM interventions. Over the next 24 months, this study is positioned to provide important new evidence on primary care practices’ ability to implement evidence-based quality improvement strategies and to improve performance on common measures of cardiovascular risk.

**Acknowledgment:** Funding support for this study is provided by the Agency for Healthcare Research and Quality (AHRQ #R18 HS023921)
There is growing interest in religious/spiritual (R/S) matters as they relate to CBT (Rosmarin, Green, Pirutinsky, & McKay, 2013). Whereas diversity issues related to gender and race/ethnicity are often incorporated into clinical training (Bergin, 1991), issues of religion have lagged, perhaps because of their transcendent nature. And yet, religion and spirituality are valued by a large portion of the U.S. population; research indicates that clients would often like to discuss R/S matters in therapy (Rose, Westefeld, & Ansley, 2001). Shafranske (1996) reports that while most psychologists believe such matters could be clinically relevant, only 30% report competence in working with these topics. Rosemarin et al. (2013) surveyed 262 members of ABCT regarding R/S matters: 36% of respondents reported some discomfort in addressing R/S topics in treatment; 71% reported little or no training as to how to do so; and yet 47% indicated a high level of interest in further training in this area. Thus, analysis of the benefits and consequences of R/S integration with empirically supported treatments such as CBT is warranted.

Methods
A literature review was performed in the PsycINFO, PubMed, and Google Scholar databases. Articles addressing the following questions were included for review: 1) What is meant by terms such as “spiritually integrated CBT” and “CBT with religious components?” 2) What do these practices or frameworks entail in terms of interventions and techniques? 3) What is the given rationale for adaptation? 4) How do issues of evidence-based practice, ethics, efficacy/effectiveness, and values in psychotherapy relate to such adaptation? After abstract review, twenty-five publications met the above criteria.

Results
Authors report a) using sacred writings and concepts to support techniques used in CBT, including cognitive restructuring, coping self-statements, and challenging maladaptive thoughts; b) using religious imagery in relaxation training; c) using religious activities in behavioral activation; d) assessing for religious and spiritual concerns early in treatment; and e) incorporating religious or spiritual values into treatment (e.g., forgiveness of self and others, hope). With some notable exceptions, the majority of R/S CBT integrative practices occur outside a conceptual framework. Rationales for integration differ, though many authors cite empirical evidence for efficacy/effectiveness, along with client preference.

Discussion
There are benefits and consequences of integrating empirically supported approaches such as CBT with R/S material; implications are in the realms of efficacy, ethics, values, and evidence-based practice. Some authors argue that R/S adaptations represent a "superficial re-packaging" of CBT which unwittingly transforms it into an altogether novel approach (Beshai et al., 2013). Conversely, this may in fact represent an adaptation of an empirically supported treatment for use in culturally sensitive evidence-based practice. Kazantzis et al. (2013) reframed the process of tailoring therapeutic techniques based on client characteristics, culture, and preferences as a responsive “level of empiricism” within CBT. Hodge’s (2011) theory of collaborative translation is discussed as a practical
Abstract Title: Association between neuraxial analgesia and perineal trauma after vaginal delivery of patients with intra-uterine fetal demise (IUFD)

Introduction: Neuraxial analgesia has been cited as a risk factor for perineal trauma during vaginal delivery, although studies have shown conflicting results. Furthermore, the association between neuraxial analgesia and perineal trauma in patients with intrauterine fetal demise (IUFD) has not been carefully studied. The purpose of this study was to evaluate the incidence of perineal trauma with and without neuraxial analgesia and to model the relative risk of perineal laceration among risk factors in this patient population.

Methods: Patients with a diagnosis of IUFD from 2007 through 2016 were included in this retrospective study. The primary outcome was the incidence of perineal trauma in patients with IUFD in relation to the analgesic modality during labor and delivery. Secondary outcomes included the degree of laceration and the association of bupivacaine concentration with the incidence of laceration.

Results: A total of 442 patients met the definition of IUFD. There were 329 patients (78%) that received neuraxial analgesia. The incidence of perineal laceration was 20.2% (n=79); of those, 71 parturients received neuraxial analgesia compared to 8 patients in non-neuraxial group (23.1% vs. 9.5%, P<0.001). Among patients with perineal trauma in the neuraxial group, 38 patients (53.5%) received an infusion of bupivacaine 0.11% compared to 32 patients (45.1%) with bupivacaine 0.0625% (P=0.36). Multivariate logistic regression identified increased birth weight (OR=3.6, 95% CI [2.0, 6.6], P<0.001), lower BMI (OR=0.93, 95% CI [0.87, 0.99], P=0.014) and lower parity (OR=0.44, 95% CI [0.28, 0.69], P<0.001) as independent predictors of perineal laceration. The predictive accuracy (c-statistic) of the model was 0.91 (95% CI [0.87, 0.95]).

Conclusion: Neuraxial analgesia had a strong association with perineal injury. However, its causality is unclear due to selection bias from our clinical practice. Increased instrumental vaginal delivery related to neuraxial analgesia could play a role even though this technique is infrequently used in IUFD delivery at our institution. High birth weight was found to increase the incidence of perineal trauma significantly, while high BMI and increased parity appear to be protective.

Table 1. Incidence of perineal trauma and the degree of laceration in patients with and without neuraxial analgesia

<table>
<thead>
<tr>
<th>Laceration Degree</th>
<th>Incidence of Perineal Trauma</th>
<th>Difference (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neuraxial Group</td>
<td>Non-Neuraxial Group</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>27 (9.1%)</td>
<td>4 (4.9%)</td>
<td>4.2 (1.9 to 10.3)</td>
</tr>
<tr>
<td>2</td>
<td>28 (9.5%)</td>
<td>2 (2.4%)</td>
<td>7.1 (1.9 to 12.2)</td>
</tr>
<tr>
<td>3</td>
<td>5 (1.7%)</td>
<td>0</td>
<td>1.7 (-0.4 to 3.8)</td>
</tr>
<tr>
<td>Missing Data</td>
<td>14 (4.3%)</td>
<td>2 (2.4%)</td>
<td>1.8 (-2.6 to 6.4)</td>
</tr>
</tbody>
</table>

Table 2. Association of bupivacaine concentration in patients with perineal trauma in neuraxial group

<table>
<thead>
<tr>
<th>Bupivacaine Concentration in Epidural Infusion Bag</th>
<th>Patients with Perineal Trauma in Neuraxial Group (71)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No Infusion Bag</td>
<td>1 (1.4%)</td>
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Reference:
Research Day Abstract

Presenting Author:* Brian Trinh, BA
E-mail:* brian.trinh@northwestern.edu
Position:* Medical Student
Abstract Category:* Clinical Research
Principal Investigator:* Jeremy Collins
Department:* Radiology
Does this research involve women’s health?* No

Abstract Title: * Early Experience with a Third Generation Dual Source CT for TAVI treatment planning

Background: 3rd generation dual-source (3GDS) CT scanners have technical advances compared to 1st generation dual source (1GDS) CT scanners that allow potential increases in temporal and spatial resolution.

Objective: To compare radiation dosage and image quality between a 3GDS system and a 1st generation dual-source (1GDS) system in patients undergoing CT evaluation for transcatheter aortic valve implantation (TAVI).

Methods: Retrospective analysis of 60 patients undergoing pre-TAVI CT evaluation: 20 consecutive patients imaged on a 3GDS system and 40 BMI-matched patients imaged on a 1GDS system. CT dose metrics including kVp, mAs, CT dose index volume, and dose length product were recorded. Contrast volume and BMI were noted. CNR and SNR were calculated.

Results: Age (78±9 vs 79±11, p=0.79), BMI (33±7 vs 31±6, p=0.47), and GFR (45±10 vs 39±14, p=0.16) were similar between patients scanned on 3GDS and those on 1GDS. 3GDS annulus scans utilized 120 kVp more frequently (45% vs 40%), and had greater CTDIvol (65±32 vs 50±26, p=0.048) with similar DLP (1188±860 vs 1024±566, p=0.38). Less contrast was given to 3GDS-scanned patients (81±27 vs 97±31, p=0.05). CNR and SNR on the 3GDS were significantly greater than 1GDS at the aortic root, common iliac, and common femoral arteries.

Conclusions: Despite lower volumes of contrast used, greater z-axis coverage, and conservative kVp settings, scans on a 3GDS system demonstrate superior image quality with comparable radiation doses to scans on a 1GDS system. Patient specific scan optimization is warranted to realize the full potential utility of lower kVp settings, and alternative contrast administration strategies in the pre-TAVI evaluation.
Research Day Abstract

Presenting Author:* Eileen Hu-Wang  
E-mail:* Eileen.hu-wang@northwestern.edu  
Position:* Student  
Abstract Category:* Clinical Research  
Principal Investigator:* Dr. Kai Lin MD and Dr. Michael Markl PhD  
Department:* Radiology  
Does this research involve women’s health?* No

Abstract Title: * The Reproducibility of Heart Deformation Analysis for the Evaluation of Global Cardiac Function

Background:
Analysis of global cardiac function is important for cardiovascular risk estimation but can be time-consuming. Using deformable image registration (DIR) algorithms, Heart Deformation Analysis (HDA) is a recently developed method for measuring cardiac function and motion on existing cardiac cine MR images. With a totally automatic workflow, HDA has the potential to be useful in clinical practice. In this study, the inter-study reproducibility of Heart Deformation Analysis will be analyzed.

Methods:
With IRB approval, 17 healthy volunteers were recruited to participate in the study. Each subject underwent two cardiac MR scans, the second scan taking place 14 days after the first scan. All participants underwent MRI examinations using the same cardiac cine protocol on a 1.5 T scanner (Avanto, Siemens AG, Germany). At four-chamber, two-chamber, and short-axis views, Segmented bSSFP cine sequences were acquired in the cardiac imaging planes with breath-holding. Imaging parameters were as follows: TR/TE = 2.8/1.1 ms; flip angle = 65°, voxel size = 2.1 x 2.1 x 8.0 mm³, bandwidth = 930 Hz/pixel. Eight to ten short-axis myocardial slices were set to cover the entire LV from base to apex. Each cine acquisition was acquired with retrospective ECG-gating and reconstructed into 25 phases. Left ventricular ejection fraction (LVEF) and left ventricular mass (LV mass) were automatically calculated by using the HDA tool. LVEF and LV mass were correlated between the two scans using SPSS software. SPSS intraclass correlation coefficient (ICC) was used to assess variations in LVEF and LV mass values between scans, with an alpha of 0.05 chosen to demarcate statistical significance.

Results:
A moderate to high correlation was found between LVEF and LV mass between the first and second scans. The LVEF ICC was found to be 0.636, p=0.03. The LV mass ICC was found to be 0.527, p=0.08.

Conclusions:
Good inter-study reproducibility was found for evaluating global cardiac function. A moderate to high correlation was found between LVEF (ICC=0.636) and LV mass (ICC=0.527) between the first and second scans. There was statistical significance for correlation of LVEF between scans (p=0.03) but no statistical significance was found for correlation of LV mass between the two scans (p=0.08). The LV mass correlation was probably not found to be significant in this study because of the small sample size of 17 subjects; it is possible that a larger sample size could increase statistical power of the study.

In conclusion, the inter-study reproducibility and totally automatic workflow of HDA give this analysis method the potential to be useful in clinical practice, where a more time-efficient analysis method can be more easily incorporated into patient care.

*Abstracts longer than one page will not be accepted.
OBJECTIVE: The objective of this study is to characterize pregnancy outcomes following hysteroscopic resection of retained products of conception (RPOC), especially as it relates to abnormal placentation and preterm delivery.

SAMPLE: All women who underwent hysteroscopic resection of retained products of conception at Northwestern Prentice Women’s Hospital between January 2004 and December 2014.

METHODS: This is a retrospective study. The medical records of all cases of hysteroscopic resection of RPOCs between January 2004 and December 2014 were reviewed. Demographic characteristics, operative findings, surgical procedure, surgical pathology and pregnancy outcomes for preceding and subsequent pregnancies were obtained. Our primary outcomes were abnormal placentation and preterm delivery in the pregnancy following the procedure.

RESULTS: There were a total of 55 subsequent pregnancies. Among these pregnancies, 54.5% (n=30) were vaginal deliveries, 34.5% (n=19) were cesarean delivery and 7.3% (n=4) were early pregnancy loss. Twenty percent (11/55) of subsequent pregnancies were complicated by preterm delivery. Abnormal placentation was present in 18.1% (10/55) of subsequent pregnancies. This consisted of 3 patients with placenta previa, 2 with placenta accreta and 5 with retained placenta. History of a D and C and a history of abnormal placentation in a prior pregnancy were associated with higher odds of abnormal placentation OR 15.72 (95%CI 0.84-295.3, p=0.066) and OR 6.26, (95%CI 0.89-43.63, p=0.064) respectively, although this finding was not statistically significant.

CONCLUSIONS: Women who undergo hysteroscopic resection of RPOC have a higher rate of preterm delivery and abnormal placentation when compared to the general population. Although the etiology is likely multifactorial, the underlying pathology leading to the initial diagnosis of RPOC is believed to play a major role.

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MRI Gadobutrol Contrast Dose and Intracranial Metastases Detection Prior to Stereotactic Radiosurgery

Shamit Desai, MD

Background
Gadolinium-based contrast agent enhanced T1 3D MRI is the standard protocol for detection of intracranial metastases in planning for stereotactic radiosurgery (SRS).

Three research centers in the United States have shown that gadolinium-enhanced MRI is useful in detecting more lesions at increased lesion size.

Gadobutrol, a macrocyclic gadolinium-based contrast agent, was approved for use by the FDA in 2007.

Objective
To determine the incidence of increased metastases detected on double dose gadobutrol-enhanced pre-SRS MRI using the contrast agent gadobutrol.

Methods
A prospective, retrospective cohort of patients treated with stereotactic radiosurgery for intracranial metastases between 1/1/2012-12/31/2013 with 182 patients (median 58, 28-85) were included. Additional inclusion requirements include a biopsy-proven primary cancer, six cases of SRS in 57 patients (median 61, 26-85) (males 32, females 24) included in the analysis. The most common primary neoplasm included: lung (23), melanoma (19), breast (9), renal cell (8), colon (8), ovarian (4), sarcoma (2), liver (2), thyroid (1), and esophageal (1).

Results
Median contrast dose of pre-SRS MRI to initial MRI was 2 (range 1.6-2.6) (Fig 1).

In 66 cases, 28 showed no new lesions, 28 did show an increase in lesion number (42% of cases).

Mean increase in detected lesion number in 28 positive cases = 3.1 (range 1-9).

Conclusions
Double-dose gadobutrol contrast on pre-SRS MRI for brain metastases resulted in an increased number of metastases. This has significant implications for an institutional pre-SRS brain metastases protocol. Additionally, gadobutrol is a macrocyclic contrast agent, a consideration warranting further study.

References
Abstract Title: Preliminary Data on the Rate of Spontaneous Resolution of Idiopathic Ileocolic Intussusception

Background:
Idiopathic ileocolic intussusception is a common cause of abdominal pain in young children. The gold standard for making this diagnosis is ultrasound of the abdomen. If ileocolic intussusception is identified on ultrasound, the most common next step is barium or hydrostatic enema performed by interventional radiology; subsequent surgical intervention is performed in cases where enema fails to reduce the intussusception. There is a small and underreported percentage of patients who are found to have intussusception on abdominal ultrasound but have no evidence of intussusception when they undergo contrast enema, or when they proceed to the operating room for manual reduction. These situations are sometimes referred to as “spontaneous resolution” of intussusception, and are not adequately described in the existing literature on ileocolic intussusception. This study aims to identify the rate of spontaneous resolution of idiopathic ileocolic intussusception and identify features consistent among patients whose intussusception spontaneously resolved, such as age, duration of symptoms, or other features. Our hypothesis is that the rate of spontaneous resolution of idiopathic ileocolic intussusception in children is not insignificant and should be taken into consideration when managing patients with this diagnosis.

Methods:
This study is a retrospective chart review of all patients ages 3 months to 36 months evaluated for intussusception at Children’s Memorial Hospital/Lurie Children’s Hospital Emergency Department during the time period of January 2007 through July 2015. Patients were identified using diagnosis codes for “intussusception” and “rule out intussusception,” and were also identified by order codes for contrast enema. A total of 632 charts were identified. Details about outcome, time intervals between symptom onset, imaging diagnosis, and outcome, as well as physical exam and demographic factors are collected using a REDCap data collection instrument.

Results:
Data collection is ongoing. Preliminary results of the first 11% (80 of 632) of charts reveal that the rate of spontaneous resolution of idiopathic ileocolic intussusception is 21%. Fifty-five percent of patients had reduction of their intussusception with air or contrast enema, and 24% required intervention in the OR. When comparing the patients with spontaneous resolution to those who require enema or surgical reduction, there is still insufficient data to determine whether age, duration of symptoms, presence of fever, presence of abdominal mass, history of blood stools, or use of narcotic medication differ between the two groups. We hypothesize that one or more of these factors will emerge as statistically significantly different between the spontaneous resolution group and the group that required enema or OR intervention.

Conclusions:
Spontaneous resolution occurs in approximately 21% of cases of idiopathic ileocolic intussusception. This data is preliminary and does not reflect the full set of data to be included in the final version of this study. However, this preliminary data suggests that spontaneous resolution is more common than previously recognized. This information may help inform guidelines or ED practices when approaching the management of a patient with suspected or image-proven ileocolic intussusception.
Abstract Title: Frequency of non-melanoma skin cancer recurrence in cancer patients receiving Niacinamide or Niacin: a retrospective case-control study

Summary: Niacinamide (NCM) has been shown to enhance repair of UV-radiation induced DNA damage in human keratinocytes and has reportedly decreased non-melanoma skin cancer (NMSC) incidence in high-risk patients by 23%. Niacin (NC) has been used to decrease cholesterol in high risk cancer patients.

Objective: The aim of this study was to retrospectively assess NMSC recurrence in cancer patients exposed to NCM or NC.

Methods: We searched a large (3 million patients), urban, academic electronic medical record (EMR) repository (01/2010-12/2014) to select all individuals (age 18-89) with cancer (who have a known high risk for development of NMSC) identified by ICD9 code (excluding melanoma and NMSC). Exposed population consisted of patients receiving NCM or NC. Patients who were exposed to both NCM or NC were excluded. We then determined which patients were documented with at least 2 recurrences of NMSC (NMSC removal procedure on 2 separate dates) after first exposure to NCM or NC. A control population consisted of age and gender matched patients from the same cancer cohort (ratio 1:5), with no documented NCM or NC exposure in the EMR. Association was assessed by Fisher’s exact test while mean number of NMSC removal procedures were assessed by the independent sample test.

Results: While a total of 106,950 patients with a cancer diagnosis were detected, of these, 39 were documented exposed to NCM, with 2 of these patients reported to have multiple recurrences of NMSC post-NCM exposure (5.1% vs 2.1% in control group). 903 patients were exposed to NC, of which 38 had multiple NMSC recurrences (4.2% on NC vs 3.8% in control group). No significant effect on frequency of NMSC recurrence was found in those exposed to NCM or NC (Fisher’s exact test p=0.26 and p=0.57, respectively). The mean number of NMSC removal procedures post-NC exposure was 1.76 + 1.42 compared to 1.90 + 1.93 in the control (p=0.59).

Conclusions: No correlation between the use of Niacinamide or Niacin and a protective effect against NMSC recurrence was detectable in this large population of cancer patients. However, the retrospective nature of this study, and the inability to establish or rule out exposure to multivitamins containing NCM or NC, are study limitations. Regardless of the study limitations, these findings point to the need for further exploration with even larger prospective studies to more clearly establish the role of NCM or NC and NMSC recurrence in high risk cancer patients.
Melanoma and non-melanoma skin cancer association with Alzheimer’s disease: a large single center retrospective cross sectional study

Summary and Objectives:
Although prior literature has demonstrated a decreased risk of cancer, specifically non-melanoma skin cancer (NMSC), in individuals with Alzheimer’s disease (AD), characterization of the relationship between malignant melanoma (MM) and AD is unknown. The aim of this study is to explore the relationship between melanoma and non-melanoma skin cancer and Alzheimer’s disease, and discuss the mechanistic aspects related to association between Alzheimer’s disease and melanoma and/or-melanoma skin cancer.

Methods:
We searched a large urban academic center Electronic Medical Record repository (4.4 million patients), the Northwestern Medicine Enterprise Data Warehouse (NMEDW), to explore the relationship between NMSC and MM with AD. All individuals, ages 60+ with known race, gender, and at least one year of documented follow-up, who had an in person encounter between Jan 2001 and Dec 2015, disease-free at the time of the first encounter, were included.

Results:
A total of 91,738 individuals, ages 60+ with known race, gender, and at least one year of documented follow-up, between Jan 2001 and Dec 2015 were detected for analysis. 1,257 were MM, of whom 7 were also AD. 2,458 were basal cell carcinoma (BCC), of whom 23 had AD, and 1,027 were squamous cell carcinoma (SCC), of whom 8 had AD. After adjusting for confounding factors (race, sex, age, cardiac disease, peripheral vascular disease, and diabetes), there was a significant inverse relationship between MM and AD (OR: 0.43; 95%CI: 0.20-0.90; p=0.02). No association was detectable for BCC or SCC and AD (p=0.17 and p=0.18 respectively).

Conclusion:
These findings of a specific inverse relationship between MM and AD support historical findings of the association of AD with cancer in general. The mechanistic relationship between melanoma and Alzheimer’s disease warrants further exploration.
Background: Ustekinumab is an interleukin (IL)-12 and IL-23 inhibitor, approved for the treatment of moderate to severe psoriasis and for active psoriatic arthritis. Randomized controlled trials (RCT) long-term studies, with up to 5 years of follow-up, concluded that ustekinumab did not increase the rate of malignancy in patients with psoriasis.\textsuperscript{1-3} According to the Full Prescribing Information (FPI), occurrence of malignancies other than non-melanoma skin cancer in ustekinumab-treated patients was similar for that would occur in the general U.S. population (breast cancer, prostate cancer, colon cancer, rectal cancer, and melanoma). The aim of this study was to determine what associations were detectable for ustekinumab and malignancy in the Food and Drug Administration Adverse Event Reporting System (FAERS) database.

Methods: We retrieved adverse drug events reports that were voluntarily submitted to FAERS between January 2004 and June 2014 for terms related to ustekinumab combined with cancer or malignancy. Medical Dictionary for Regulatory Activities Preferred Terms (MedDRA) was used to define the terms related to malignancy or cancer. We calculated the proportional reporting ratio (PRR) for detection of a safety signal, defined as the number of events (>3), chi-square results (>4) and the PRR (>2). Using this threshold minimized the likelihood of detecting false-positive signals, especially for rare events.

Results: A total of 4,970 adverse event reports were submitted for ustekinumab between January 2004 and June 2014. Safety signals were detected for B-cell lymphoma (N=14), epithelioid sarcoma (N=5), lung cancer (N=21), esophageal cancer (N=5), ovarian cancer (N=10), renal cancer (N=6), testicular cancer (N=6) and thyroid cancer (N=20). But no association was detectable for myeloid leukemia (N=10), bladder cancer (N=9), cervix carcinoma (N=2) and gastric cancer (N=5).

Conclusions: Safety signals from the FAERS database exist for ustekinumab association with several malignancies not recognized in the FPI. Limitations to the interpretation of FAERS data include the voluntarily-reported aspect of data collection and redundant reporting. The debate whether ustekinumab increases risk of malignancy remains largely unresolved and is further confounded by the theory that a chronic inflammatory disease such as psoriasis or psoriatic arthritis may inherently increase one’s risk for developing cancer.\textsuperscript{4} Further long-term prospective clinical trials and large pharmacoepidemiologic studies, are necessary to more precisely quantify cancer risk associated with ustekinumab.

References:
The Effect of Needle Size on Pain Perception in Patients Treated with Botulinum Toxin A Injections: A Split-Face, Patient- and Injector-Blinded Randomized Controlled Trial

Background: Transcutaneous injection through smaller hollow bore needles may decrease patient discomfort, but current evidence is equivocal.

Objective: This study compares injection discomfort with the use of 30- versus 32-gauge needles.

Method: In this double-blinded, split-face, randomized controlled trial, one side of the subject’s forehead received botulinum toxin in saline injected with a 32-gauge needle; other side with a 30-gauge needle. In addition, each subject received randomized injections of saline to their upper inner arms. Subjects were between the ages of 25 to 70, in good health, female, and with moderate dynamic forehead/glabellar wrinkles.

Results: Twenty subjects completed the study. Primary outcomes measured patient-reported pain on a visual analog scale (VAS) on either side of the face and arms, and the proportion of patients with clinically significant pain. Secondary outcomes included patient-reported characterization of the pain at both sites. Overall, facial and arm injections were nominally but not significantly more painful with 30-gauge needles (face: 4.16 vs. 3.41, p=0.33; arm: 1.66 vs 1.21, p=0.45). For facial injections, 40% of subjects reported clinically significant pain (VAS>=5.4) with the use of 30-gauge needles versus 15% of subjects with the use of 32-gauge needles (OR:3.80, CI:1.05-13.78, p=0.0424). Arm injections did not exhibit a difference in pain associated with needle type. There was no difference in character of pain associated with needle bore.

Conclusion: For facial injections of neurotoxin in saline, 30-gauge needles were associated with a greater incidence of clinically significant pain than 32-gauge needles. For patients prone to experience clinically significant pain upon facial injections, use of 32-gauge needles may minimize this discomfort.
Abstract Title: Evaluation of the Influence of Pregnancy on Vitiligo Vulgaris Disease Activity

**Background:** Vitiligo vulgaris (VV), an acquired disease resulting from an autoimmune process against melanocytes, is a common disorder of pigmentation affecting approximately 0.5-1% of the world population. Autoimmune diseases often improve during pregnancy—a state of relative immunosuppression. Our objective was to assess vitiligo disease activity during pregnancy—an association not fully characterized.

**Methods:** Eligible subjects were identified using the Northwestern Medicine Enterprise Data Warehouse (NMEDW) repository for electronic medical records. Subjects included in the study were women > 18 years and < 55 years old with a diagnosis of VV who either became pregnant or delivered a child during the period September 1, 2011 to September 1, 2013. A telephone survey of 24 vitiligo subjects was conducted with questions that pertained to vitiligo history, pregnancy history, and vitiligo disease activity prior to, during, and after pregnancy. Additional questions pertained to demographics, history of autoimmune disease and family history of vitiligo.

**Results:** Seventeen subjects were self-reported as Caucasian/White (70.8%), three were Asian/Pacific Islander, two were Hispanic/Latino, one was African American/Black, and one was of mixed ethnicity. Three subjects (12.5%) reported improving vitiligo during pregnancy. These three all described one or more lesions decreasing in size with the remaining lesions neither improving nor worsening. Fifteen subjects (62.5%) reported that their disease was stable with no new lesions or changes to preexisting lesions over the course of their pregnancies.

**Conclusions:** The majority of subjects surveyed reported either stable or improved vitiligo activity during pregnancy. A minority (21%) reported worsening disease, and one subject reported disease onset during pregnancy.

Figure 1. A majority of subjects (75%) reported their VV activity to be stable or improved during pregnancy. A minority (21%) reported worsening disease, and one subject reported disease onset during pregnancy.
Research Day Abstract

Presenting Author:* Ryan Buck, MD
E-mail:* ryan.buck@nm.org
Position:* Assistant Professor
Abstract Category:* Clinical Research
Principal Investigator:* Ryan Buck, MD
Department:* Hospital Medicine
Does this research involve women’s health?* No

Abstract Title: * Impact of a Best Practice Alert on Transfusion Practices for Solid Tumor Oncology Patients

Background: Recent evidence supports a restrictive transfusion strategy in the majority of hospitalized patients, though transfusion practices for oncology patients remain highly variable. We evaluated whether use of a best practice alert for solid tumor oncology inpatients would result in more restrictive transfusion practices and impact patient outcomes.

Methods: We conducted a retrospective, historical control analysis at a large academic hospital in Chicago, IL, where both oncology hospitalist and oncologist-staffed teaching services provide care for oncology patients. We compared transfusion utilization among solid tumor oncology patients before and after implementation of a transfusion alert. Patients with active bleeding, hematologic malignancies and those undergoing surgical procedures were excluded. A best practice alert with clinical decision support encouraging use of a restrictive transfusion strategy (Hgb <7 g/dL) was implemented 6/1/14 with phase-in completed by 9/1/14. We obtained data from the Electronic Data Warehouse for PRE intervention medical records of patients hospitalized from 5/1/13 to 4/30/14 and POST intervention records from 9/1/14 to 8/31/15. Number of units of packed red blood cells (pRBCs) transfused per 100 patient days, readmission rates, incidence of ICU transfer, and inpatient mortality were compared using multiple linear regression. Outcomes were adjusted for age, gender, race, BMI, smoking status and Charlson comorbidity index.

Results: 1296 total patients were included in the analysis (PRE, n=685; POST, n=611). There were no differences in age, gender, BMI, or Charlson comorbidity index among cohorts, although the PRE cohort included more Caucasians (60.2% vs. 46.8%, p <0.0001) and smokers (6.0% vs. 2.5%, p=0.002). PRBCs transfused per 100 patient days were significantly lower in the POST-intervention cohort (6.4 vs. 3.8, p=0.01). The POST-intervention cohort also had fewer 30-day emergency department visits (5.1% vs. 3.3%, p=0.03). Between the PRE vs. POST groups respectively, there were no significant differences in rates of 30-day readmission (37.3 % vs. 34.6 %, p=0.19), ICU transfer (1.1% vs. 0.5%, p=0.08) or inpatient mortality (1.8% vs. 1.7%, p=0.96).

Conclusions: Implementation of a best practice alert among solid tumor oncology patients effectively reduced utilization of packed red blood cells without affecting patient outcomes.

*Abstracts longer than one page will not be accepted.
Abstract Title: Impact of Lichen Sclerosus, Lichen Planus, and Vulvodynia on Quality of Life for Patients Using the Vulvar-Specific Skindex-29 Patient Reported Outcome Measure

Introduction:
Vulvar disease impact on quality of life (QoL) is not well studied. Although vulvar-specific Skindex-29 (vsSK-29), a patient self-administered instrument, has been validated in vulvodynia, its utility has not been reported in other vulvar diseases.

Methods:
Patients seen in a vulvar mucosal specialty dermatology clinic at a tertiary referral center completed the vsSK-29 questionnaire per standard of care. This instrument has 29 items divided into functioning, symptoms and emotions domains. vsSK-29 data for patients diagnosed with vulvodynia (V, ICD9 625.7), lichen sclerosus (LS, ICD9 701.0) or lichen planus (LP, ICD9 697.0) between 2010 and 2014 were analyzed. Patients diagnosed with two or more of these conditions or those with squamous cell carcinoma were excluded. vsSK-29 mean total score and mean score for each domain were calculated for each disease.

Results:
238 subjects were evaluable. Analyzed subjects included 179 (75.2%) LS, 49 (20.6%) LP and 10 (4.2%) V. Mean age was 53 years for LS, 66 years for LP and 50 years for V. Mean total vsSK-29 score for LS was 46.39, with domain scores of 50.53, 49.66 and 38.98 for emotions, symptoms and functioning, respectively. Mean total score for LP was 43.49, with domain scores of 46.24, 47.58 and 36.63 for emotions, symptoms and functioning, respectively. Mean total score for V was 53.62 with domain scores of 49.20, 60.00 and 51.67 for emotions, symptoms and functioning, respectively.

Limitations:
Limitations include a single academic center, varying sample size per subgroup, comorbid conditions, and concomitant treatment.

Conclusion:
Women with vulvodynia, lichen sclerosus and lichen planus have poor quality of life in all domains measured. Mean total QoL score was highest for vulvodynia indicating poorest QoL when compared to lichen sclerosus or lichen planus. These data support prior vsSK-29 validation reporting and indicate that the impact of vulvodyina on QoL may differ from that of lichen sclerosus or lichen sclerosus. Within vulvodynia, the symptoms domain exhibited the highest mean domain score indicating greatest effect on QoL, similar to lichen planus but in contrast with lichen sclerosus. While all women with vulvar diseases may experience severe impact on quality of life, the specific nature of this impact may vary with disease process.
Melanoma in men treated with PDE5A inhibitors: A Report from the RADAR (Research on Adverse Drug Events And Reports) Project.

Introduction:
The phosphodiesterase 5 (PDE5A) inhibitors such as sildenafil (S), vardenadil (V), avanafil (A), and tadalafi (T) are all FDA-approved for the treatment of erectile dysfunction without caveats for melanoma risk in the Full Prescribing Information (FPI). However, an increased risk of melanoma related to S, V, and T has been reported in literature. The objective of this study is to explore whether melanoma occurs subsequently after exposure to PDE5A inhibitor in a large patient population.

Methods:
We searched a large, academic-based electronic medical record (EMR) repository, the Northwestern Medicine Enterprise Data Warehouse (NMEDW) containing >4 million individuals from January 2010 to December 2014 for male patients exposed to one of the PDE5A inhibitor drugs and were subsequently diagnosed with melanoma (ICD9 codes 172.0-172.0) for at least 3 months after exposure to PDE5A inhibitor.

Results:
Of 525,523 individual males, we found that 8 of 1,117 men exposed to V developed melanoma; 30 of 5,933 men exposed to T developed melanoma; 36 of 5,307 men exposed to S developed melanoma; and 0 of 21 men exposed to A developed melanoma. After adjusting for race and age, a significant association with melanoma was detected for T (OR: 1.6; 1.11-2.31, p=0.01) and S (OR: 2.07; 1.48-2.89, p<0.001). Moreover, a trend towards significance (p=0.058) was detected for V.

Conclusion:
While not currently recognized as a warning, precaution, or possible adverse event on FPI for any of the PDE5A inhibitors, these data indicate significant association with the development of melanoma in patients taking S or T. The findings do warrant exploration to further address safety signals in larger population studies. This study underscores how ongoing, proactive, post-marketing pharmacovigilance plays an important role in the detection of adverse outcomes not previously detected as safety signals in already marketed drugs. Moreover, investigation into causality for possible relationship between PDE5A inhibition and the development of malignant melanoma is warranted.
Abstract Title: A Genome- and Phenome-Wide Study of Diverticulosis

Summary
The exploding growth of available genetic data coupled with longitudinal electronic health records (EHRs) enables the phenome-wide association studies (PheWAS) to discover new phenotype associations for genetic variants. By performing PheWASs on the diverticulosis patients of the eMERGE cohort, we demonstrate its feasibility as a novel tool for not only exploring novel genotype-phenotype associations but also providing a comprehensive catalog of human diseases associated with published variants.

Introduction
Genome-wide Association Studies (GWAS) provide hypothesis-free investigation of the whole genome. However, GWAS have limited ability to identify clinically significant variants, and account only for a portion of the predicted phenotypic heritability. In addition, most GWAS-significant single nucleotide polymorphisms (SNPs) are located in intergenic regions, which make the interpretation of biological mechanisms more challenging. As a complement to GWAS, Phenome-wide association studies (PheWAS) can offer insights into the biological mechanisms that predict one’s susceptibility to disease, and help to determine promising polymorphisms or variants for further study.

Methods
As part of the eMERGE network, we developed and validated an algorithm to find cases and controls for diverticulosis and diverticulitis. At all but two sites, we selected subjects from patients having colonoscopies or abdominal imaging: Natural Language Processing (NLP) was performed on the reports from those procedures, and any subject that had any asserted mention of “diverticul*” in those reports was recorded as cases, plus any with an asserted mention of diverticulitis were noted. Conversely, controls had at least one colonoscopy and no asserted mentions of “diverticul*” in those reports. For two sites where NLP of all reports was not possible, cases were selected as above, plus only those diagnosed (using ICD-9 codes) with diverticulosis or diverticulitis within 7 days after the procedures were selected as cases. Conversely, controls were also the same, but in addition had to have no diagnosis ever for diverticulosis or diverticulitis. Three sites validated algorithm performance by chart review of a combined total of 300 randomly selected charts of cases and controls to ensure a high positive predictive value (PPV). We performed a GWAS of diverticulosis cases, the subset of those with diverticulitis, and controls, selected using electronic health record (EHR) data from all adult eMERGE subjects. We selected the top SNPs associated with diverticulosis, and diverticulitis for the PheWAS. We used logistic regression adjusted for age and sex assuming an additive genetic model, on the eMERGE adult cohort of ~38,000 individuals, and also on various subsets, including just those with diverticulosis, and diverticulitis, using the R PheWAS package.

Results
The GWAS found 39 SNPs to be highly correlated (p<10-8) with either diverticulosis and/or diverticulitis. Our phenotype algorithm identified 6297 diverticulosis cases, of which 734 had diverticulitis, and 5090 controls. Subsequent PheWAS identified several significant associations with skin disorders, including skin cancer. We also identified vitamin deficiency, specifically vitamin D, to be significantly correlated with both diverticulosis subjects at p<10-9 for 2 SNPs, and diverticulitis subjects at 10-4, on one of the two SNPs for diverticulosis.

Conclusions
Our findings reinforce the utility of PheWAS as a tool for not only replicating genotype-phenotype associations but also providing insight into potential promising pathways for further investigation. Recent epidemiologic studies suggest have identified a strong association between vitamin D deficiency and diverticulitis. As a disease of epithelial cells, the correlation of the SNPs associated with diverticulosis and skin disorders is biologically plausible and may suggest a possible disease pathway. Ongoing work is underway to validate the GWAS results for all adult eMERGE diverticulosis case and control subjects with additional PheWAS analyses.
Abstract Title: Development of Automated Methods to Achieve Compliance with IRB, Institutional and Federal Requirements in the De-Identification of Medical Record Narratives Used for Detection of Safety Signals for Drugs and Medical Devices

Introduction: Institutional, legal and regulatory requirements that govern data-mining of electronic medical records (EMRs) include provisions for maintaining data security, preserving patient confidentiality and respecting institutional prerogatives. De-identification algorithms must be expressed in a manner that is clear, validatable and revisable. In the context of proactive pharmacovigilance, much adverse drug or device event (ADE) information requires manual EMR review and data extraction and is therefore often unobtainable.

Automated natural language processing (NLP) provides a means for extraction of data and detection of safety signals. Since the cost of manual EMR review is prohibitive, and important ADE evidence is mostly undetectable from structured data alone, we sought to develop an effective NLP method to help annotate narratives for the purpose of synthesizing with structured data.

Methods: We developed a corpus of automatically de-identified data from EMRs, including both narratives (e.g., clinical notes, pathology reports, imaging reports) and structured data (e.g., demographics, ICD codes, lab values). Our primary endpoints were to effectively demonstrate NLP reliability in the detection and extraction of secure, de-identified and IRB-compliant key ADE data using prediction and monitoring tools in order to advance pharmacovigilance capability with big data. To assess NLP capabilities, we used information about known ADEs to evaluate accuracy, robustness, and completeness of extracted EMR information and then applied this methodology to test the ability to automatically extract ADE-related data for a drug recently FDA-approved, romidepsin.

Results: From a single institution data repository of 3 million individual EMRs, we automatically detected and extracted de-identified data from 52 EMRs (1,581 documents) for exposed patients. We used these data to evaluate effectiveness of two independent automated software processes, a de-identification process and a previously-trained machine-learning NLP tagger to identify relevant terms such as medication name, dosage, method of administration, and ADEs.

Conclusions: The NLP tagger provides a basis for using EMR narrative text to augment structured data fields already present in the EMR and the automated de-identification program shows advanced pharmacovigilance capability with well-supported sensitivity and specificity.

Limitations: While this automated process effectively removes PHI, the methodology continues to undergo further development and sophistication. In doing so, we have devised a workflow that combines manual expert annotation of EMR text with a final relatively short manual de-identification step following time-saving automated de-identification of big data.

Directions for Future Study: Next steps are to develop fully automated detection, extraction and de-identification of ADE-related narrative and structured EMR data for research purposes.
Research Day Abstract

Abstract Title: Smoking Cessation Treatment in Adults with Cancer: Do Disease Factors Matter?

Background: Adherence to smoking cessation treatment predicts successful abstinence. However, adherence may be especially challenging for smokers with chronic diseases. We hypothesized that disease factors would predict adherence to and success with smoking cessation treatment among individuals diagnosed with cancer.

Methods: Participants were smokers (≥5 cigarettes/week) diagnosed with cancer within the past 5 years who were recruited for an ongoing clinical trial of extended treatment with varenicline and behavior therapy. Data from 117 participants who completed the 12-week open-label phase were included in this study. Disease variables measured at baseline included tumor site (smoking-related vs. not), cancer stage (0-4, remission, not specified), past month treatment (surgery, chemotherapy, radiation, hormone therapy), and perceived health status (Short Form Health Survey [SF-12]). Abstinence was bioverified (carbon monoxide exhalation <8 parts per million) at Week 12. 12-week adherence was determined by 80% compliance (medication: 132 of 165 pills; behavior counseling: 4 of 5 sessions). Logistic regression was used to assess the relationship between disease variables with adherence and abstinence outcomes.

Results: Overall, 47.0% of participants were medication adherent, 74.2% were counseling adherent, and 41.6% were abstinent. Adherence to medication was positively associated with adherence to counseling, and both indices were positively associated with bioverified abstinence at Week 12, ps<.001. SF-12 scores were associated with medication adherence (OR: 1.12, 95% CI: 1.03-1.22) and counseling adherence (OR: 1.12, 95% CI: 1.03-1.22), ps<.05, but not with abstinence ps>.05. Other disease variables were not associated with medication adherence, counseling adherence, or abstinence (ps>.05).

Conclusion: In this sample, adherence to and success with smoking cessation treatment among adults with cancer was similar to healthy populations. Of the disease factors, only perceived health status predicted medication and counseling adherence. Perceived health status may be related to self-efficacy, which is an important factor for successful smoking cessation. Findings indicate that disease factors should not be barriers to patients with cancer being referred to, enrolled in, and ultimately successful in smoking cessation treatment.

FUNDING: This research was supported by the National Cancer Institute (R01CA165001, Robert A. Schnoll).
Research Day Abstract

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Does this research involve women’s health?* No

Abstract Title: * Right Ventricular Strain in Intermediate to High-Risk Pulmonary Embolism

Background:
Echocardiographic assessment of right ventricular (RV) function is frequently used in the assessment of patients with acute pulmonary embolism (PE). RV dysfunction associated with PE is independently associated with increased risk of adverse events including death. 2-dimensional right ventricular strain (RVS) may add prognostic information to traditional echocardiographic parameters of RV size and function. We sought to describe RVS pattern in individuals presenting with intermediate to high-risk PE, compare to those who received catheter directed thrombolysis (CDT), and analyze the post-treatment RVS pattern.

Methods:
We reviewed 98 consecutive cases of intermediate to high-risk PE for whom a TTE was completed within 72 hours of diagnosis at a single tertiary care academic institution. Intermediate and high risk PE were defined by European Society of Cardiology 2014 guidelines on PE. Analysis of RVS was performed on all patients at frame rates of at least 40 fps on the Epsilon ™ processing system. Global longitudinal (GLS) and free wall strain values were reported for the RV. Analysis of RVS of post-CDT was also performed with median time to follow up TTE of 2.5 days. A total of 67 participants were included in the final analysis.

Results:
A total of 17 (25%) underwent CDT for treatment of PE. By TTE, 17 patients (25%) had severe RV systolic dysfunction and 20 (30%) had severe RV dilation. McConnell’s sign was present in 43% of subjects. Mean pulmonary artery systolic pressure (PASP) was 43.1. Mean RV basal dilation was 3.9. Mean fractional area of change (FAC) was 25.5. For strain analysis, average GLS was -10.46. Regional strain values were similar.

In the CDT subgroup (n =17) compared to the overall population, mean BNP (745 vs 449, p = 0.07) and PASP (55.67 vs 39.6, p = 0.001) were significantly higher in the pre-treatment thrombolytic group. TAPSE, S’ and fractional area of change were not significantly different. GLS and free wall strain trended worse in the CDT group but also were not statistically different.

In the subgroup that received CDT, median time to follow-up TTE was 2.5 days. Following CDT, severe RV systolic dysfunction decreased from 41% to 12%, McConnell’s reporting decreased from 65% to 18% and PASP decreased from 56.4 mmHg to 49 mmHg (p = 0.17). There was no change in GLS (-11.2 vs -11.1) or RV free wall strain (-12.99 vs -13).

Conclusion
In intermediate to high-risk pulmonary embolism, RVS abnormalities appear to correlate with other markers of RV impairment on initial presentation, but in the short-term may persist despite improvements in other measurements of RV function.

*Abstracts longer than one page will not be accepted.
Research Day Abstract

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Department: * Transplant Surgery
Does this research involve women’s health? * No
Abstract Title: * Observation for assessment of clinician performance: a review

Background: Video-recorded and in-person observations are methods of quality assessment and monitoring that have been employed in high risk industries. In the medical field, observations have been used to evaluate the quality and safety of various clinical processes. This review summarizes studies utilizing video-recorded or in-person observations for assessing clinician performance in medicine and surgery.

Methods: A search of MEDLINE (PubMed) was conducted using a combination of medical subject headings (MeSH) terms. Articles were included if they described the use of in-person or video-recorded observations to assess clinician practices in three categories: (1) teamwork and communication between clinicians; (2) errors and weaknesses in practice; and (3) compliance and adherence to interventions or guidelines.

Results: The initial search criteria returned 3,215 studies, 223 of which were identified for full text review. A total of 69 studies were included in the final set of literature. Observations were most commonly used in data dense and high risk environments, such as the emergency department or operating room. The most common use was for assessing teamwork and communication factors.

Conclusions: Observations are useful for the improvement of healthcare delivery through the identification of clinician lapses and weaknesses that affect quality and safety. Limitations of observations include the Hawthorne effect and the necessity of trained observers to capture and analyze the notes or videos. The comprehensive, subtle, and sensitive information observations provide can supplement traditional quality assessment methods and inform targeted interventions to improve patient safety and the quality of care.

*Abstracts longer than one page will not be accepted.
Major Depressive Disorder is one of the most common complications of pregnancy, with 7.5% of women having an incident episode during the 9 months of pregnancy and 6.5% with an episode in the first 3 months postpartum. The overarching goal in this newly-funded Obstetric-Fetal Pharmacology Research Center is to develop guidelines to optimize the safety and efficacy of SSRI antidepressant treatment in pregnant women. This application addresses priorities for research during pregnancy: Establish interdisciplinary approaches to understand the pharmacokinetics and/or pharmacodynamics of medications. There are 3 main OPTI-MOM projects identified below, which are complementary:

1. Clinical Research Project—Assess the safety and toxicity of drugs during pregnancy and postpartum. The progressive changes in plasma SSRI and metabolite concentrations across pregnancy and after birth will be determined in an observational study. Serial evaluations of depressive and anxiety symptoms and side effects will be obtained to evaluate their association with plasma concentrations at monthly intervals in pregnancy and twice post-birth. To assess the subjects’ metabolic phenotypes, a probe drug cocktail will be given to determine activities of CYP2D6, 2C19, 2C9 and 3A4 during the third trimester (when activity change is maximal) compared to the non-pregnant state after birth.

2. The Basic/Translational Research Project—Perform clinical research to understand mechanisms of pregnancy related changes in drug response and disposition and --Identify biomarkers for safe and effective treatment of pregnancy-related conditions. We will investigate the impact of genomic variability on inter-individual differences in SSRI dosing, plasma concentrations and pharmacodynamics during pregnancy, with a focus on genes involved in the metabolism of SSRIs, drug transporters responsible for SSRI access to the CNS, and genes encoding SSRI targets involved in therapeutic efficacy.

3. The Pilot Project—Assess the safety and toxicity of the drugs during pregnancy, postpartum, and in postnatal periods of development. This project will determine the maternal-fetal plasma concentrations and pharmacogenetic characteristics associated with neonatal SSRI abstinence syndrome. Maternal and fetal CYP and P-glycoprotein genotypes will be assessed for their relationship to SSRI drug concentrations and neonatal abstinence syndrome.
**Research Day Abstract**

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**Abstract Category:** Clinical Research  
**Principal Investigator:** Sanjiv Shah, MD  
**Department:** Cardiology  
**Does this research involve women’s health?** No

**Abstract Title:** Identification of Candidates for Novel Interatrial Shunt Device Through Non-Invasive Testing in Patients with Heart Failure with Preserved Ejection Fraction

**Intro:** Interatrial shunt devices (IASD) are a novel therapeutic option for heart failure and preserved ejection fraction (HFpEF). IASDs work by decompressing the overloaded left atrium (LA) via shunting of blood to the right atrium (RA). Thus, optimal candidates for the IASD intervention will have an elevated pressure gradient between the LA and RA. We hypothesized that increased LA-RA gradient could be diagnosed noninvasively by echo.

**Methods:** A total of 293 consecutive patients with HFpEF who also underwent invasive hemodynamic testing were identified. All patients underwent comprehensive echo, including tissue Doppler. Patients were categorized into 2 groups based on the LA-RA pressure gradient (PCWP-RA pressure) at time of invasive hemodynamic testing (PCWP-RAP > 10 mmHg [large pressure gradient] vs. PCWP 0-5 mmHg [low pressure gradient]), and clinical, laboratory, and echocardiography parameters were compared between groups.

**Results:** Mean age was 64±12 years, 59% were female, 36% were African American, and comorbidities were common. Of the 293 patients, n=58 had PCWP-RAP gradient of 0-5 mmHg and n=114 had PCWP-RAP > 10 mmHg, with the rest of the patients (n=56) in the PCWP-RAP 5-10 mmHg range. Patients with an elevated PCWP-RAP gradient were more often female and obese and less likely to have a history of atrial fibrillation. On echocardiography, the 2 parameters that were most different between groups were TAPSE and lateral e’ velocity such that an elevated ratio of TAPSE to lateral e’ velocity identified patients with HFpEF who were most likely to have an elevated PCWP-RAP gradient > 10 mmHg (area under the ROC curve = 0.69 [95% CI 0.600.78]; P=0.001).

**Conclusions:** An elevated TAPSE/lateral e’ velocity ratio on echo in HFpEF is associated with invasive PCWP-RAP gradient > 10 mmHg at rest and may aid in the identifying suitable HFpEF candidates who would benefit from an IASD.
**Abstract Title:** Changes in psoriasis level of activity for both pre- and post-menopausal state in women: a single-center retrospective study

**Summary:**
Sex hormones are known to modulate immunity and influence the pathophysiology of numerous disorders. Yet the effect of fluctuating estrogen levels throughout a woman’s life on the level of psoriasis activity (LoPA) remains poorly elucidated. This study assessed whether the LoPA varied in pre-menopausal compared to post-menopausal women. Our results suggest that estrogen depletion associated with menopause does not confer a protective benefit for women who had psoriasis prior to the onset of menopause.

**Objective:**
The aim of this study was to determine if the LoPA varied in pre-menopause females compared to post-menopause females.

**Sample:**
Women diagnosed with psoriasis (ICD-9 code: 696.1) at least 3 years prior to diagnosis of menopause (ICD-9 base code: 627) with at least a 3-year follow-up post-menopause.

**Methods:**
We searched a large urban academic center electronic medical record (EMR) repository (> 3 million individuals), the Northwestern Medicine Enterprise Data Warehouse (NMEDW), for existing data (January 2001 to December 2014). Inclusion criteria included diagnosis of psoriasis (ICD-9 code: 696.1) at least 3 years prior to diagnosis of menopause (ICD-9 base code: 627) with at least a 3-year follow-up post-menopause. Systemic therapy for psoriasis was utilized to assess LoPA. Women who were exposed to systemic (oral or injectable) therapy were compared to women who had no exposure to systemic therapy.

**Results:**
51 adult women were included in the analyses. Post-menopause, 5.9% (N=3) of women improved their LoPA (changed from systemic therapy to no systemic therapy), 15.7% (N=8) showed worsening of LoPA (changed from no systemic therapy to systemic therapy), and 78.4% (N=40) showed no difference for LoPA.

**Conclusion:**
These findings suggest that post-menopausal estrogen depletion does not appear to be associated with a protective effect for women with pre-menopausal psoriasis. Given the long-standing history for gender bias in biomedical studies, further exploration of issues related to sex hormone activity and LoPA (including pregnancy state and hormone replacement therapy exposure) seems warranted. Assessing how various estrogen-based treatments and physiological reproductive changes (such as menopause and pregnancy) affect LoPA will enable physicians to optimize treatment options for women throughout their lives.
Abstract Title: A quantitative metric of magnetization transfer homogeneity as a marker of spinal cord changes in chronic whiplash

Summary
Whiplash Associated Disorders (WADs) have been commonly treated as homogenous injuries; no structural mechanism of WADs has been found. However, recent evidence has identified degenerative changes in neck muscles specific to 50% of persons with WAD, suggesting a core biological contribution. Precise mechanisms, however, remain elusive. Magnetization Transfer (MT) imaging is a method of investigating white matter integrity in multiple pathologies, including demyelination in the spinal cord. MT ratio (MTR) analysis in the spinal cord could refine diagnosis in WAD.

Objective
The goal of this work is threefold: 1 introduce quantitative MTR methods by which patients with WAD can be characterized; 2 promote quantitative metrics in the study of WAD; 3 present degeneration in regional spinal cord pathways which may be present in a subpopulation of persons with chronic WAD.

Methods
15 subjects, 5 chronic WAD, 5 recovered and 5 controls were recruited into this study. Images were gathered perpendicular to the cervical spinal cord at the superior aspect of the fifth vertebra using MEDIC MRI. The MT pulse was 1.5kHz off-resonance with Flip angle/duration of 5400/10ms. Scan time was 8 minutes for MT and non-MT imaging. Ventral, dorsal, and lateral (left & right) aspects of the cord were segmented, and MTRs were calculated. The range in MTR values (dMTR) was then recorded.

Results
dMTR differences were significant between WAD versus control and recovered groups (P < 0.01). Average dMTR values were dMTR: 18.87, recovered: 7.45 and control: 6.59. Control and recovered were not distinguishable (P = 0.37).

Conclusions
A quantitative imaging technique was introduced and preliminary findings suggest that the group of concern demonstrates reductions of magnetization transfer ratios in white matter of the spinal cord. Recovered and healthy controls do not have such findings.
Neonatal Cord Blood Methylation: Maternal Pre-Pregnancy BMI Downregulates LEP Gene Transcription Start Site Methylation

**Background:** Epigenetic changes are one mechanism by which the maternal metabolic environment can contribute to fetal genetic programming. Maternal pre-pregnancy BMI has been associated with alterations of metabolic genes within cord blood DNA. *LEP* is one gene of interest whose function may be affected by epigenetic modifications induced by maternal factors.

**Objective:** Identify *LEP* gene methylation patterns in neonatal cord blood that are associated with maternal metabolic factors.

**Hypothesis:** The maternal metabolic environment can impact the methylation of metabolic-related genes in neonatal DNA.

**Design/Methods:** 114 healthy mothers with normal glucose tolerance and their full term neonates were studied. Neonatal cord blood was collected after birth and later assayed for leptin. Methylation levels of the candidate gene *LEP* were measured using the Infinium HumanMethylation 450K Beadchip array. Maternal and gestational characteristics were collected and neonatal body composition by air displacement plethysmography was obtained between 24-72 hours of life. Multiple linear regression models were used to identify associations between maternal exposures and neonatal characteristics and differentially methylated CpG sites accounting for blood cell subtype proportions and batch effect.

**Results:** Maternal pre-pregnancy BMI was negatively associated with methylation at 5 CpG sites within the transcription start site of the *LEP* gene (FDR<0.05 for all sites). Cord blood leptin was positively associated with birth weight (r=0.45, p<0.001), fat mass (r=0.47, p<0.001), and neonatal percent body fat (r=0.44, p<0.001) when adjusted for neonatal sex, gestational age, race, and maternal age at delivery. A positive relationship between cord blood leptin and maternal pre-pregnancy BMI approached significance (p=0.054).

**Conclusions:** Increased maternal pre-pregnancy BMI is associated with decreased methylation within the neonatal *LEP* gene transcription start site. This suggests that maternal metabolic factors may impact neonatal *LEP* gene expression.
Research Day Abstract

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Principal Investigator:* Luis Z. Blanco Jr., M.D.
Department:* Pathology
Does this research involve women’s health?* Yes

Abstract Title: * Androgen Receptor, Survivin, and Mesothelin are Targetable Markers Expressed in Pregnancy Associated Breast Cancer

Summary: Pregnancy associated breast cancer (PABC), diagnosed during gestation to 5 years postpartum, is aggressive, often triple negative (TN), and has a poor prognosis, which is worst when diagnosed within the first 2 years postpartum. Androgen receptor (AR), survivin, and mesothelin are currently being investigated as appealing targetable therapeutic and prognostic markers in breast cancer that have minimal expression in normal cells. AR and mesothelin expression have been reported in a subset of breast cancers, particularly those with a TN phenotype, in which hormonal therapy, and occasionally, chemotherapy regimens, are ineffective. Likewise, survivin has been described to be over-expressed in some breast cancers, correlates with HER2 and EGFR expression, and predicts resistance to chemotherapy and radiation. These three are especially desirable markers since their expression in a tumor can be determined with immunohistochemical (IHC) stains. IHC stains are ideal since they are regularly performed in histology laboratories, have short turnaround times, and can be easily evaluated by pathologists at their microscopes.

Objective: To identify the expression of novel markers AR, survivin, and mesothelin in PABC using IHC stains in order to evaluate their potential as therapeutic targets.

Methods: 23 patients with PABC diagnosed within 2 years of pregnancy (mean age=35.8 years, range=26-48 years) and control age-/grade-/stage-matched nulliparous women (mean age=37.5 years, range=29-51 years) were evaluated. Slides were reviewed and pathologic tumor characteristics including tumor histology, grade, size, lymph-vascular space invasion, lymph node involvement, and hormone receptor status were assessed. IHC stains for AR, survivin, and mesothelin were evaluated for extent (percentage of tumor cells positive) and intensity (1=weak, 2=moderate, or 3=strong), and an H-score (product of extent and intensity) was calculated for each marker.

Results: AR was expressed in the majority of PABC cases (15/23, 65%) and controls (11/14, 79%). Survivin was expressed in almost one-third of PABC cases (7/23, 30%) and in only one control (1/14, 7%). Mesothelin was expressed in two PABC patients (2/23, 9%) and in one control (1/14, 7%). The mean H-scores for all markers were similar for both groups. Expression of all three markers did not correlate with the TN status (0% of TN PABC cases expressed all three markers).

Conclusions: 1. AR is expressed in a majority of PABC. 2. Survivin is expressed in almost one-third of patients with PABC. 3. Mesothelin is expressed in a small subset of PABC patients. 4. The expression of all markers was similar in both PABC and controls, likely attributable to the closely matched tumor characteristics. 5. All three markers are rarely expressed in the same tumor, so a panel involving the three markers would be useful not only in PABC, but in all breast cancers with similar high-grade characteristics. This expression of novel markers AR, survivin, and mesothelin by IHC in a subset of PABC and matched control cases provides potential additional unique targets for directed therapy and prognostication in these aggressive tumors that pathologists can easily and efficiently evaluate.
Research Day Abstract

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Abstract Category:* Clinical Research
Principal Investigator:* David C. Mohr, Ph.D.
Department:* Department of Preventive Medicine
Does this research involve women's health?* No

Abstract Title: * MoveMe: Results of User Feedback on a Fitness-Promoting App Supporting Mood Management

Background: Research suggests that physical exercise may reduce symptoms of depression. While it remains unclear which particular types of movement procure the greatest benefits for those with depression, and which physiological mechanisms underlie mood management, there may be a more pressing question to consider: what are the psychobehavioral barriers impeding motivation to engage in such physical activity in the first place and how can we help overcome them? In light of this, we designed an app called MoveMe to encourage daily bouts of planned physical activity. The app assists users by identifying a variety of personal and group activities to perform, along with providing a queue of dynamic exercise routine videos linked to YouTube. This app also syncs with the user’s personal calendar, allowing him or her to schedule and then mentally prepare for upcoming activity, whereby increasing the likelihood of subsequent behavioral activation.

Methods: MoveMe was made publicly available on the Google Play store and included as part of a field trial evaluating a suite of mobile apps teaching skills and offering tools to treat depression and anxiety, with minimal support from a human coach. Individuals who consented to be contacted for future research purposes and used the app on multiple occasions were invited to provide user feedback. The questionnaires and qualitative interviews included Likert-scale ratings of the app’s likability, ease of use, learnability, and perceived helpfulness, in concert with open-ended questions surrounding benefits and barriers to MoveMe app use.

Results: 17 adult MoveMe users (M age=37.58 years, SD=12.64 years, 82.35% female) provided feedback on the app. At the end of an 8 week program, on a 1 to 7 Likert-type scale, users rated the app as moderately likeable (M = 3.41, SD = 1.54) and helpful (M = 3.59, SD = 1.87). The app’s ease of use (M = 5.41, SD = 1.46) and learnability (M = 5.24, SD = 1.56) were both rated highly too. On the other hand, qualitative feedback revealed several shortcomings of the app features. These included desires for more flexibility and customization of offered exercises, such that less active or physically restricted users would feel more empowered and could see and feel benefit from whichever type and however much activity they were capable of. Also, users wished to be able to log unplanned episodes of activity throughout the day, as well as log successful completion of planned activity with the opportunity to describe thoughts and feelings related to the behavior.

Conclusions: Results demonstrate the positively perceived usability of a generalized fitness-promoting app, yet highlight limitations related to customization and the capacity to capture behavioral activation outcome and associated mood states. Future research may benefit from collecting outcome measures centered on completion of pre-planned activities, and daily self-report of post-exercise affect.

*Abstracts longer than one page will not be accepted.
**Research Day Abstract**

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**Does this research involve women’s health?** No

**Abstract Title:** Hypertension, obesity, diabetes, and heart failure-free survival: The Cardiovascular Disease Lifetime Risk Pooling Project

**Background:** Quantification of years lived free from heart failure in the context of risk factor burden in mid-life may improve risk communication and prevention efforts.

**Objectives:** To quantify the relationship between the absence of HF risk factors in middle age and incident heart failure, heart failure-free survival, and overall survival.

**Methods:** We conducted a pooled, individual-level analysis sampling from communities across the US as part of four cohort studies: the Framingham Heart, Framingham Offspring, Chicago Heart Association Detection Project in Industry, and Atherosclerosis Risk in Communities studies. Participants with and without hypertension (blood pressure ≥140/90 mmHg or treatment), obesity (body mass index ≥30 kg/m²), or diabetes (fasting glucose ≥126 mg/dL or treatment), and combinations of these factors, at index ages of 45 and 55 through 95 years. Competing risk-adjusted Cox models, a modified Kaplan-Meier estimator, and Irwin’s Restricted Mean were used to estimate the association between the absence of risk factors at mid-life and incident heart failure, heart failure-free survival, and overall survival.

**Results:** For participants at age 45 years, over 516,537 person-years of follow-up, 1,677 incident heart failure events occurred. Men and women with no risk factors, compared to those with all three, had 73% to 86% lower risks of incident heart failure. Men and women without hypertension, obesity, or diabetes at age 45 years lived on average 34.7 and 38.0 years without incident heart failure, and they lived on average 3 to 15 years longer free of heart failure than those with one, two, or three risk factors. Similar trends were seen when stratified by race and at index age 55 years.

**Conclusions:** Prevention of hypertension, obesity, and diabetes by age 45 and 55 years may substantially prolong heart failure-free survival, decrease heart failure-related morbidity, and reduce the public health impact of heart failure.
Abstract Title: * Disease Characteristics and Prognosis of Myelodysplastic Syndrome Presenting with Isolated Thrombocytopenia

Patients with myelodysplastic syndrome (MDS) who present with isolated thrombocytopenia (TCP) are a poorly described patient subgroup. The aim of this study was to retrospectively evaluate the disease characteristics and prognosis of patients with MDS and isolated TCP. In this tertiary care center, there were 50 patients (12%) with MDS that presented with isolated TCP. Patients had varying MDS sub-classifications and cytogenetic profiles. The most common IPSS-R risk score was low (n=24), though half of the patients had either IPSS-R intermediate (n=18), high or very high-risk disease (n=7). Leukemic transformation occurred in 10 patients and there were 14 deaths (28%) amongst all IPSS-R risk scores. Therapeutic agents used in this patient subgroup included hypomethylating agents and thrombopoietin receptor agonists. Overall, MDS with isolated TCP did not appear to have an inherently indolent course as previously suggested. Future studies are needed to improve risk stratification, identify relevant contributors to disease pathogenesis, and better define treatment modalities.
Abstract Title: Association between small particle air pollution, climate and childhood eczema prevalence and severity: a US population-based study

BACKGROUND:
We sought to determine the relationship between childhood eczema, climate and environmental pollutants.

METHODS:
We analyzed data from the 2007-2008 National Survey of Children’s Health including a representative sample of 91,642 children age 0-17 years and the 2006-2007 Environmental Protection Agency measurements of carbon monoxide (CO), nitrate (NO3 ), nitrogen dioxide (NO2 ), organic carbon (OC), sulfate (SO3 ), sulfur dioxide (SO2 ), particulate matter ≤2.5 micrometer (PM-2.5) and <10 micrometer (PM-10) and tropospheric ozone levels, and the National Climate Data Center measurements of relative humidity (%), issued UV index, outdoor air temperature and precipitation levels.

RESULTS:
In multivariate survey logistic regression models controlling for age, sex, race/ethnicity, household income, US birthplace and history of moving to a new location, eczema was associated with higher mean annual NO2 (P=0.008), SO2 (P=0.006), SO3 (P=0.0002), arsenic (P=0.0007), nickel (P=0.0002), lead (P=0.03), vanadium (P<0.0001) and zinc (P=0.003), but lower NO3 (P=0.002), OC (P=0.03), PM-2.5 (P=0.006), cadmium (P<0.0001), copper (P=0.004) and potassium (P<0.0001). In contrast, moderate-severe eczema was associated with higher NO3 (P=0.03), OC (P=0.008) and PM-2.5 (P=0.01), copper (P=0.04), lead (P=0.008) and zinc (P=0.01), but lower CO (P=0.03). Principal component analysis was used and identified 4 combinations of pollutants and climate factors occurring in the US, of which 1 was associated higher prevalence and 2 were associated with lower prevalences of eczema (P<0.05).

CONCLUSIONS:
Pollutants in conjunction with climate factors may differentially impact eczema prevalence and severity, some with apparent harmful effects.
Abstract Title: Long-term effects on the basal ganglia in youth with perinatally-acquired HIV infection

Background: HIV affects multiple brain regions. Pathological studies have demonstrated prominent and differential distribution patterns of HIV in the basal ganglia. Neuroimaging studies in adults have also demonstrated a correlation between atrophy of these subcortical structures and clinical measures of systemic disease severity. Whether these effects are observed in adolescents with perinatally-acquired HIV (PHIV) has not been well-studied.

Methods: We conducted structural magnetic resonance imaging (MRI) in 40 youth with PHIV (median age=17.1 years, 48% male) at one PHACS Adolescent Master Protocol study site. Current and past HIV severity measures were obtained from medical charts. Median peak HIV-1 viral load was 522,000 copies/ml. Median nadir CD4+ T-lymphocyte percentage was 17%. Subcortical surfaces and vertex deformation referenced to a population mean for each region of the basal ganglia (nucleus accumbens, caudate, putamen and globus pallidus) as well as the hippocampus, amygdala and thalamus were obtained via automated FreeSurfer-initiated Large-Deformation Diffeomorphic Metric Mapping (FSLDDMM) pipeline. Univariate regression was performed for each vertex on each subcortical surface with deformation as the dependent variable and peak plasma HIV RNA load as the independent predictor, adjusting for sex, age, and substance use. Significant clusters, after family-wise error correction, were identified and visualized on the specific surfaces. Mean deformation within significant structures was correlated with cognitive performance.

Results: Peak viral load showed significant correlations with the shape of the putamen, globus pallidus, caudate, and thalamus (all p<0.001, corrected). Visualization revealed that in youth with PHIV, higher peak viral load was associated with increased inward deformity (i.e., localized volume loss) in contiguous patterns, primarily in anterior and posterior aspects of these structures (Figure 1). Cognitive performance correlated with mean deformation in the caudate (p = 0.04) and thalamus (p = 0.03).

Conclusions: Among PHIV youth with a history of higher peak viral loads were associated with greater localized volume loss in multiple regions of the basal ganglia. These neuroimaging findings are consistent with histopathologic and clinical studies in adults, and suggest similar patterns of brain dysmorphology in adolescents with life-long HIV given antiretroviral therapy during brain development.

Figure 1. Higher peak HIV viral load is correlated with inward deformation in subcortical structures
Here, inward deformation (localized volume loss) is in the bluer colors, and outward deformation is in the redder colors. In our vertex-wise analysis, we found that there was significant inward deformation in the anterior and medial thalamus, the tail of the caudate, and lateral putamen.
**Purpose:**

The evaluation, management and follow-up of adolescent idiopathic scoliosis (AIS) occur frequently within clinical practice. Curve status can be assessed non-radiographically with Scoliometer measurements of angle trunk rotation (ATR), which are reliable and reproducible to within 3 degrees and correlate generally with radiographic Cobb angles. This study assessed the longitudinal efficacy, safety and cost savings of integrating ATR measurements to monitor curve status and progression in AIS, and suggests a quality-based management strategy.

**Methods:**

A retrospective review of medical records between 2004 and 2014 included patients with AIS between 10-17 years and excluded those with Cobb angle > 52 degrees at presentation. Data included sex, menarchal status, ATR measurements, radiographic Cobb angle and Risser stage. Two cohorts were analyzed: Group PRE (pre-menarchal females and males with Risser <5) and POST (post-menarchal females and males with Risser ≥5). “Unstable” was defined as patients with ≥4 degrees of change from initial to final ATR measurement. The cost of a single PA thoracolumbar radiograph ($36.27) was defined by the 2015 CMS fee schedule. Safety was defined based on the effective radiation dose avoided (0.14 millisieverts/radiograph).

**Results:**

A total of 60 children were included with 46 (76.7%) presenting pre-menarchal (n=42) or males with Risser <5 (n=4) and 14 presenting post-menarchal. There were no unstable curve patterns in the POST group. See Figure 1 for averages of the cohorts. The use of ATR measurements provided a cost benefit in both the PRE Stable and Unstable cohorts, by avoiding radiographs with an average savings of $161.76 and $137.83 respectively. Similarly within POST, there was an average cost savings of $105.18 per patient. The safety benefit of using ATR measurements included avoiding an average of 0.62, 0.53 and 0.4 millisievert of radiation in the PRE Stable, PRE Unstable and POST groups respectively.

**Conclusion:**

An evaluation strategy that includes (non-radiographic) ATR measurements provides a reliable, cost-effective and safety advantage in the monitoring of curve progression in both skeletally mature and immature patients with AIS. The findings suggest that stable ATR measurements (without radiographs) are a safe and cost effective alternative to serial radiographs in the clinical monitoring of AIS.

**Significance:**

Recent evidence from 25 years of scoliosis treatment in Denmark noted a cancer rate 17 times that of an age-matched population. Thus, reducing radiation exposure during scoliosis monitoring by using ATR measurements has important clinical significance for cancer risk reduction.

**Abstract:**

Angle of Trunk Rotation (ATR) Measurements Improve Quality and Safety in the Clinical Management of Adolescent Idiopathic Scoliosis (AIS)

<table>
<thead>
<tr>
<th>AVERAGES</th>
<th>n</th>
<th>Age at presentation (years)</th>
<th>Cobb Angle at presentation (degrees)</th>
<th>Duration of Observation (years)</th>
<th># of Encounters</th>
<th>Time between encounters (months)</th>
<th># of XR Encounters</th>
<th># of Non-XR Encounters</th>
<th>Change in Cobb Angle (degrees)</th>
<th>Change in ATR (degrees)</th>
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</thead>
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<tr>
<td>PRE Stable</td>
<td>30</td>
<td>12.2</td>
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<td>1.4</td>
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<tr>
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<td>16</td>
<td>11.0</td>
<td>22.6</td>
<td>3.96</td>
<td>8.6</td>
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</tr>
<tr>
<td>POST Stable</td>
<td>14</td>
<td>13.7</td>
<td>22.6</td>
<td>2.54</td>
<td>5.7</td>
<td>5.3</td>
<td>2.8</td>
<td>2.9</td>
<td>4.4</td>
<td>0.7</td>
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<tr>
<td>Unstable</td>
<td>0</td>
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</tbody>
</table>
Mitochondrial DNA and Cancer in the Normative Aging Study

Background: Mitochondrial DNA (mtDNA) is a potentially sensitive marker of damage by reactive oxygen species (ROS). Two biomarkers in mtDNA, copy number (mtDNAcn) and 8-OHdG, have therefore been proposed as potential markers of oxidative stress and therefore carcinogenesis. Prospective human studies subjects of mtDNAcn have found inconsistent results, but many suggest that the interval between mtDNAcn measurement and cancer diagnosis affects the association. Moreover, prior studies suggest that the interplay of mtDNAcn and 8-OHdG reflect ongoing oxidative stress related to carcinogenesis, suggesting their potential use in tandem as an early detection biomarker of cancer. Our objective was to examine longitudinal associations between mtDNAcn and 8-OHdG measured in whole blood in relation to both cancer incidence and mortality.

Methods: We studied 526 Normative Aging Study participants who had blood drawn 1–4 times from 1999 through 2012 and who were cancer free at first blood draw (median 9.7 years between blood draw and cancer diagnosis/censoring). mtDNAcn and 8-OHdG were measured using quantitative real-time PCR. We used Cox proportional hazards regression models to examine associations between mtDNAcn and mitochondrial 8-OHdG measured at the first blood draw only as well as time-dependent associations across a total of 1043 blood draws and time to all-cancer diagnosis. We ran a second set of models stratified by time between blood draw and diagnosis/censoring, and a third set that explored possible interaction between mtDNAcn and 8-OHdG via inclusion of a product term. All models adjusted for age, BMI, white blood cell count, proportion neutrophils, race, education, smoking status, pack-years of smoking, and alcohol consumption.

Results: We found no significant associations between pre-diagnostic mtDNAcn and time to cancer diagnosis or death. When measured at the first blood draw only, 8-OHdG was inversely associated with all-cancer (HR: 0.17; 95% CI: 0.03-0.87) and prostate cancer incidence (HR: 0.05; 95% CI: 0.00-0.97). In the time-dependent models, mitochondrial 8-OHdG was inversely associated with time to all-cancer diagnosis (HR: 0.31; 95% CI: 0.10-1.01) and positively associated with time to all-cancer death (HR: 1.83; 95% CI: 1.13-2.98), while mtDNAcn was positively and independently associated with time to all-cancer death (HR: 1.59; 95% CI: 1.17-2.15; pinteraction=0.96). In the stratum of 4-6 years between blood draw and diagnosis, 8-OHdG was associated with cancer incidence (HR: 0.01; 95% CI: 0-1.00). Modeling 8-OHdG and mtDNAcn together produced no noteworthy changes in results. Similarly, the test for interaction was non-significant across all models.

Conclusion: Pre-diagnostic mtDNAcn does not appear to be significantly associated with cancer, however mitochondrial 8-OHdG may be a significant predictor of cancer several years prior to diagnosis. Mitochondrial markers of oxidative stress may also be significant predictors of cancer mortality, possibly related to metastasis and/or treatment. Additional prospective studies in larger cohorts with greater racial/ethnic, gender, and socioeconomic diversity are needed to validate the utility of 8-OHdG as an early detection biomarker of cancer. Future studies of mitochondrial oxidative stress markers measurable in blood and cancer mortality are warranted.
Introduction
Psoriasis is a chronic inflammatory condition with several possible co-morbidities including multiple sclerosis (MS), a chronic demyelinating disease of the central nervous system (CNS). TNF-α is a pro-inflammatory cytokine intimately involved in the pathogenesis of psoriasis and reported to be elevated in the CSF of patients with MS. Increased MS disease activity and demyelinating disease of the CNS has been reported to occur in patients using TNF-α blocking drugs.

Aim
We sought to determine if an association exists between psoriasis and MS in a large, urban, single center, electronic medical record (EMR) repository: the Northwestern Medicine Enterprise Data Warehouse (NMEDW).

Methods
We searched the NMEDW (> 4 million patients) to detect all patients who had an in-person clinic or hospital encounter (index date) between January 2001 and December 2014, with at least one follow-up encounter > 30 days after the index date, and were diagnosed with both psoriasis and MS (using ICD-9 codes 696.1 and 340, respectively). Individuals with a diagnosis of psoriasis or MS before the index date were excluded. Age, gender, race, concomitant psoriatic arthropathy (ICD-9 code 696.0) and at least one prescription TNF-α agent FDA-indicated for both psoriasis and psoriasis arthritis (etanercept, infliximab, adalimumab) or psoriatic arthritis alone (certolizumab pegol, golimumab) were also collected. Adjusted odds ratio (OR) was calculated to assess the association between psoriasis and MS by using logistic regression analysis.

Results
A total of 667,480 individuals were detected that met inclusion criteria. 5,988 were coded as psoriasis, of which 2 persons were also coded as psoriatic arthropathy, while 2,331 patients were coded as MS. Of these, 31 patients were diagnosed with both psoriasis and MS. A significant association between psoriasis and MS was detected in this population after adjusting for confounding variables including sex, age, psoriatic and TNF-α agent exposure (OR=1.51; 95%CI 1.04 -2.19; p =0.02).

Conclusions
These findings are supportive of the prior reported association for MS and psoriasis. TNF-α blocking agents are commonly used for moderate to severe psoriasis with or without concomitant psoriatic arthropathy. Despite the reported cases of demyelinating diseases during TNF-α blocking agents therapy, and the precautions in the Full Prescribing Information for etanercept, infliximab, adalimumab, certolizumab pegol and golimumab stating that “demyelinating disease, exacerbation or new onset, may occur”, in our study population, exposure to TNF-α agents did not affect the statistical association between MS and psoriasis. A limitation to this study includes absence of data on exposure to biologic agents used for psoriasis that are not TNF-α agents and other biologic agents not used for psoriasis, including those that are used for cancer and for MS, thus their role in the statistical association between psoriasis and MS cannot be excluded. Based on these findings, further exploration of the association between psoriasis and multiple sclerosis is warranted to ensure optimal therapeutic management, especially with biologic agents, for such patients.
Abstracts longer than one page will not be accepted.

Research Day Abstract

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Abstract Category: Clinical Research
Principal Investigator: Stefania Fatone, PhD, BPO(Hons)
Department: Physical Medicine & Rehabilitation, Feinberg School of Medicine
Does this research involve women’s health? No

Abstract Title: Stakeholder Input on Development of a Residual Limb Monitoring System

Summary: The interface between a prosthetic socket and residual limb is often problematic with socket fit and suspension issues leading to skin problems, reduced daily prosthesis use, mobility and quality of life (Meulenbelt et al. 2006). Sensing inside the socket is proposed as a way for prosthetists to both monitor and troubleshoot these socket fit and suspension problems (Hafner & Sanders 2014). Recent development of thin, flexible, ‘skin-like’ sensors (Kim et al. 2011) may address these problems by leading to the development of a residual limb monitoring system. However, to ensure clinical utility of any such system, input from stakeholders is necessary.

Objective: To gather information from prosthetists and prosthesis users about the residual limb problems they encounter, how a residual limb monitoring system might be used in clinical practice, and how it might best be configured.

Methods: Two focus groups were held, one with certified prosthetists (CP) and one with lower-limb prosthesis users (Px Users). An experienced moderator guided focus group discussions using scripts comprising of 8-9 open-ended questions. The questions solicited information about residual limb problems and management; how users and clinicians might want to measure conditions within the sockets; and how a sensor/monitoring system might look to end users. Discussions were audio recorded and transcribed. A team of four investigators participated in thematic data analysis (Guest et al. 2012) to assess prosthetists’ and prosthesis users’ perceptions, feelings, knowledge, and behavior of residual limb problems and potential methods for monitoring socket issues and residual limb health.

Results: Participants in the CP group (n=7) came from a mix of practice settings and had 4 to 33 years of clinical experience. Participants in the Px Users group (n=7) were diverse in their level of amputation (transtibial and transfemoral amputation) and etiology (trauma, vascular, infection, congenital), and had <1 to 40 years of experience using lower-limb prostheses.

The residual limb problems reported by focus group participants, including skin breakdown, pain, and volume fluctuation, were similar to findings from the literature regarding problems reported by users that interfere with prosthesis use (Meulenbelt et al. 2006; Klute et al. 2009). Both prosthetists and prosthesis users indicated that in-socket temperature and pressure were priorities for measurement and that the most immediate benefit was in troubleshooting socket fit issues. They were generally in favor of a wireless sensor system to monitor residual limb health in the clinic and perhaps short term at home so long as the system was easy to use and inexpensive.

Conclusion: In order to develop a user-friendly residual limb monitoring system for widespread clinical use, system benefits would need to strongly outweigh any inconveniences with use for both the prosthetist and prosthesis user. Focus group input is being used in the development of a residual limb monitoring system using wireless, ‘skin-like’ sensors (Kim et al. 2011) that can measure temperature and pressure inside a prosthetic socket, helping to detect issues before they become problematic.
Research Day Abstract

Abstract Title: Adipokines as serum markers of fatigue in systemic lupus erythematosus: A pilot study

Background: Fatigue, a common symptom in systemic lupus erythematosus (SLE) patients, is ameliorated by physical activity, but the mechanism by which this occurs is unknown. Adipokines, cytokines produced by adipose tissue, have established pro- and anti-inflammatory roles. Adiposity and adipokines are also associated with patient-reported fatigue in other chronic diseases. We describe associations between adipokines (leptin, adiponectin, and resistin), fatigue, and physical activity in SLE patients.

Methods: We examined adipokines, self-reported fatigue, and objectively-measured physical activity in 129 patients meeting American College of Rheumatology revised criteria for definite SLE from the cross-sectional Activity in Lupus to Energize and Renew (ALTER) study. Body mass index (BMI), disease activity (Safety of Estrogens in Systemic Lupus Erythematosus National Assessment—Systemic Lupus Erythematosus Disease Activity Index [SELENA-SLEDAI]), and disease damage (Systemic Lupus International Collaborating Clinics Damage Index [SDI]) were measured. Fatigue was assessed by the Fatigue Severity Scale (FSS). Patient-reported sleep disturbance was determined with the Patient Reported Outcomes Measurement Information System (PROMIS) 8a short form. A triaxial accelerometer was worn for 7 days, and physical activity was estimated by total accelerometer vector magnitude (VM) counts. Six patients with <4 valid days of accelerometer wear were excluded from physical activity analyses. Leptin, adiponectin, and resistin were measured in stored serum with a Luminex bead-based assay. Leptin/adiponectin (L/A) ratio was calculated. Adipokine data were logarithmically transformed for inclusion in linear regression models describing relationships between FSS and adipokines. Spearman correlation coefficients estimated associations between adipokines, physical activity, and SELENA-SLEDAI.

Results: Participants were predominantly female (94%), Caucasian (53%), and mean age 45.5 years (SD 10.9). Mean BMI was 28.1 kg/m² (8.2). SELENA-SLEDAI was 2.4 (2.8) and SDI was 1.7 (2.2) consistent with low disease activity and damage, respectively. FSS score of 4.4 (1.6) was consistent with clinically relevant fatigue. PROMIS-sleep disturbance T-score of 56.1 (10.3) indicated higher levels of sleep disturbance in our SLE sample compared to the general U.S. population. Mean adipokine levels were: leptin 44.2 ng/ml (47.6), adiponectin 13.5 microg/ml (10.8), and resistin 1.9 ng/ml (1.5). L/A ratio was 5.9 (10.3). No significant associations were found between leptin, adiponectin, L/A ratio, or resistin and FSS in regression models adjusting for BMI, age, sex, race/ethnicity, SELENA-SLEDAI score, physical activity, or PROMIS-sleep disturbance score. BMI >30 kg/m² (obesity) was associated with FSS in adjusted models (p<0.05, data not shown). Weak correlations between physical activity and a) leptin, b) adiponectin, and c) L/A ratio were not significant after adjusting for BMI (Table).

Conclusion: No significant associations were found between adipokines and fatigue in SLE patients. This study demonstrates that adipokines are correlated with physical activity (leptin, adiponectin, and L/A ratio), but most of these associations can be explained by BMI.

<table>
<thead>
<tr>
<th>Spearman correlation coefficients for adipokines and physical activity</th>
<th>Adjustment Variables</th>
<th>Correlation coefficient</th>
<th>Leptin</th>
<th>Adiponectin</th>
<th>L/A Ratio</th>
<th>Resistin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total accelerometer wear time</td>
<td>95% CI</td>
<td>-0.25</td>
<td>0.20</td>
<td>-0.27</td>
<td>-0.07</td>
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</tr>
<tr>
<td>VM counts (n=123)</td>
<td>Accelerometer wear time, BMI</td>
<td>95% CI</td>
<td>-0.24, 0.12</td>
<td>-0.08, 0.28</td>
<td>(-0.27, 0.09)</td>
<td>-0.22, 0.14</td>
</tr>
</tbody>
</table>

L/A ratio = leptin/adiponectin ratio; VM = vector magnitude; r = Spearman correlation coefficient; CI = confidence interval. Bolded r-values (95% CI) indicate statistical significance.
Abstracts longer than one page will not be accepted.

Research Day Abstract

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Position:* Medical Student, Class of 2018
Abstract Category:* Clinical Research
Principal Investigator:* Lubna Choudhury, MD
Department:* Bluhm Cardiovascular Institute
Does this research involve women’s health?* No

Abstract Title: * Late Gadolinium Enhancement and Extracellular Volume as Markers of Arrhythmia Risk in Hypertrophic Cardiomyopathy

Background:
Late gadolinium enhancement (LGE) and extracellular volume (ECV) by T1 mapping are cardiac magnetic resonance (CMR) techniques to quantify fibrosis in hypertrophic cardiomyopathy (HCM). While LGE reflects focal fibrosis, ECV represents a diffuse pattern of interstitial fibrosis. We studied the relationships of LGE and ECV with ventricular arrhythmia and risk factors for sudden cardiac death (SCD) in HCM.

Methods:
Retrospective analysis identified patients with a diagnosis of HCM referred for CMR at Northwestern Memorial Hospital from 1/1/2012 to 12/31/2014. Conventional segmented, inversion-recovery gradient recalled echo imaging was used to generate a stack of short axis images for LGE quantification using automated software (Medis) with a threshold of 6 SD. T1 mapping used pre and post contrast balanced steady state free precession (bSSFP) single shot Modified Look-Locker inversion recovery with data acquisition over 11 heartbeats. Patients received 0.2 or 0.1 mmol/kg gadopentetate dimeglumine contrast. A composite arrhythmia endpoint (non-sustained ventricular tachycardia, SCD, or appropriate ICD shock) and composite SCD risk factor endpoint (syncope, maximal wall thickness > 30mm, or family history of SCD) were assessed through retrospective review and compared to LGE and ECV values. Segmental LGE and ECV values were calculated according to the AHA 16 segment model. To characterize ECV in segments without LGE, ECV was averaged over segments with <3% LGE, a cutoff determined by averaging signal noise in segments without visually identifiable scar.

Results:
In 66 patients meeting criteria (37 men, mean age 52.0), average global LGE was 15.6% (0.92-72.2%) of LV mass and ECV was 26.3% (16.4-45.3%). Of 31 patients with LGE < 15%, 5 had ECV > 30%. Global LGE > 15% correlated with increased arrhythmia vs LGE < 5% (p<.05) (1A). We saw a trend towards increased arrhythmia in patients with ECV > 30% in segments with no LGE (1B). Elevated LGE and ECV were associated with an increasing trend in SCD risk factors (1C, 1D).

Conclusions:
LGE and ECV are highly variable in HCM. LGE > 15% correlates with increased arrhythmia. Elevated ECV in the absence of LGE trended toward increased arrhythmia, although small sample size limited evaluation. Larger studies are warranted to investigate ECV and arrhythmia risk in HCM.

Figure 1. A composite arrhythmia endpoint stratified by global %LGE (1A) and %ECV in myocardial segments without LGE (1B). A composite SCD risk factor endpoint stratified by global LGE (1C) and global ECV (1D).

*Abstracts longer than one page will not be accepted.
**Abstract Title:** Establishing survivorship care planning in a comprehensive cancer center to meet clinic needs and accreditation standards.

**Background:**
Standard 3.3 of the American College of Surgeons Commission on Cancer (CoC) patient-centered care guidelines requires that accredited institutions deliver SCPs to all patients completing cancer treatment with curative intent (10% of eligible patients in 2015 and increasing incrementally to 100% in 2019). Implementation of SCP delivery has been challenging and limited to date. We describe our implementation process at the Robert H. Lurie Comprehensive Cancer Center.

**Methods:** We established a multidisciplinary working group which included physicians, nurses, navigators, researchers, administrators, and advanced practice nurses. This group developed and administered a survey of providers’ attitudes towards SCPs and preferences for delivery, assessed clinical workflows, then developed and vetted customized SCP templates within the electronic health record (EHR) and two complimentary SCP delivery models.

**Results:** Twelve providers completed the survey (6 physicians, 5 advanced practice providers [APPs], 1 nurse). 67% viewed SCPs as feasible within workflows, 75% felt designated survivorship clinicians were best equipped to deliver SCPs; All reported SCPs were beneficial to patients; and 92% felt SCPs were beneficial to inter-provider communication. Cited barriers were: time and staff required and non-optimal billing. To harmonize with existing workflows, we established two delivery models: (1) clinical groups with a low volume of survivors relative to available nursing staff complete and deliver SCPs themselves; (2) clinical groups with high volumes of survivors relative to available nursing staff refer patients to a centralized survivorship clinic where SCPs are delivered by designated survivorship APPs. All elements of the American Society of Clinical Oncology (ASCO) templates were incorporated into our EHR templates. We reduced free-text data entry by designing templates where 20% of the fields are auto-populated from existing EHR data and another 65% use drop-down menus. Mean completion time is 12 minutes (range 10-30 minutes; n=30). Routine metrics including total number of referrals, SCPs completed, and downstream referrals (i.e. labs, imaging, supportive oncology, specialty care) are tracked via the Enterprise Data Warehouse of Northwestern to monitor compliance and productivity.

**Conclusions:** CoC-accredited institutions across the nation are working to meet Standard 3.3. We present our experiences developing and implementing SCP delivery models, including lessons learned to inform models of survivorship care under development at other institutions.
**Research Day Abstract**

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**Abstract Category:** Clinical Research  
**Principal Investigator:** Jonathan I. Silverberg, MD, PhD, MPH  
**Department:** Dermatology

Does this research involve women's health? No

**Abstract Title:** Assessing quality of life disturbance from contact dermatitis in a patch testing clinic

**METHODS:** This prospective study was approved by the Institutional Review Board at Northwestern University. Subjects were adult patients referred to the patch testing clinic at Northwestern Medicine. Responses from initiation of the study in January 2014–December 2015 were included. The participation rate for the survey was 96.4%; partial responses were excluded. Data were de-identified, confidential and posed minimal risk to participants. Requirement for informed consent was waived by the institutional review board.

Patients were administered a survey in the waiting area prior to clinical evaluation. The questionnaire included questions about socio-demographics, health behaviors, history of atopic dermatitis, the distribution of their dermatitis, Visual Analog Scale (VAS) for itch, and the 10-question Dermatology Life Quality (DLQI) survey as a measure of quality of life impairment. Feasibility was assessed in 27 patients, including time to completion, comprehension and representativeness of questions to the patients.

The DLQI was analyzed as both interval and ordinal variables (no/small: 0-5; moderate: 6-10; very or extremely large: >10). To determine the relationship between the extent of the dermatitis and QOL impairment, ordinal logistic regression models were constructed with the total DLQI score as the dependent variable and number of body parts affected by dermatitis as the independent variable. The proportional odds assumption was met (Score test, P>0.05). Multivariate models included the patient’s age, race/ethnicity, gender, birthplace, insurance status and history of atopic dermatitis. Adjusted OR and 95% CI were estimated.

To determine the relationship of the distribution of dermatitis on QOL, ordinal logistic regression models were constructed with DLQI as the dependent variable and binary logistic regression models with self-consciousness and sexual dysfunction. The independent variables were site affected with dermatitis. Multivariate models included the abovementioned variables as well as the number of body parts affected with dermatitis as covariates. Adjusted OR and 95% CI were estimated.

All data analyses and statistical processes were performed using SAS version 9.4 (SAS Institute, Cary, NC). A two-sided value of p < 0.05 was used to indicate significance for all estimates.

**RESULTS:** The questionnaire was completed by all patients in < 3 minutes, and did not interrupt the clinical workflow with good patient and provider satisfaction. Of 553 subjects, age distribution was 36.0% (18-39 years), 40.7% (40-59 years), and 23.3% (> 60 years). Females represented 79.8% of subjects. History of atopic dermatitis was found in 36.2%.

The mean (SD) DLQI score was 5.9 (5.2), with 45.2% reporting moderate to extreme effects on QOL (DLQI score > 5). In ordinal logistic regression models controlling for age, gender, race/ethnicity, country of birth, insurance and history of atopic dermatitis, QOL impairment was significantly higher in patients with ≥10 body parts (adjusted odds ratio [95% confidence interval]: 2.13 [1.27-3.58]) affected by dermatitis compared with only a single body part, but not 2-9 body parts affected (1.02 [0.69-1.49]).

In models that controlled for the abovementioned covariates and number of body parts affected, total DLQI scores were not worse in patients with a specific body part affected (P ≥ 0.09 for all) or higher intensity of itch (P = 0.65). The distribution of dermatitis lesions was associated with different patterns of QOL disturbance. For example, genital lesions were associated with significantly higher odds of sexual dysfunction (4.59 [1.93-9.86]), and lip lesions were associated with significantly higher odds of self-consciousness (2.12 [1.13-4.00]).

**CONCLUSIONS:** Assessing QOL impairment in contact dermatitis using DLQI is feasible and can be used to guide therapeutic management. Among patients with contact dermatitis, the strongest predictor of poor QOL was increased lesion extent. There were site-specific associations with specific aspects of QOL impairment. Sexual dysfunction was particularly associated with dermatitis affecting the genitalia, while cheilitis was associated with self-consciousness.

Background: Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are life-threatening blistering disorders associated with significant morbidity and mortality. Most epidemiological studies of these disorders have been limited to case series. We sought to determine risk factors, comorbidities, inpatient burden and mortality in US children with SJS, SJS/TEN and TEN.

Methods: We analyzed data from the 2009-2012 Nationwide Inpatient Sample (NIS), containing a representative 20% sample of all hospitalizations in the US. SJS, SJS/TEN and TEN were identified by a validated algorithm using ICD-9-CM codes. Patients with a LOS <3 days or a concomitant diagnosis of any bullous dermatosis or erythema multiforme major were excluded. Sample weights that were created by the NIS to provide representative estimates of hospital discharges across the US were used. Socio-demographics, inflation-adjusted cost, length of stay, comorbidities and mortality were analyzed using descriptive statistics and multivariate regression analysis. Calculation of incidence and mortality excluded patients who had been transferred to another hospital (3.2% of overall cohort).

Results: The incidences of SJS, SJS/TEN and TEN ranged from 4.4-6.0 (mean 5.5), 0.6-1.4 (0.8), and 0-0.7 (0.4) per million children per year, respectively. The strongest shared predictors for increased rates of hospitalization – when analyzing SJS, SJS/TEN, and TEN individually – were increasing age and increasing number of chronic conditions (linear regression; P<0.05 for all), although TEN was not associated with increasing number of chronic conditions. Significantly prolonged length of stay and higher costs of care (SJS: 9.2±0.6 days, $24,589±3113; SJS/TEN: 15.7±1.5 days, $63,787±8014; TEN: 20.4±6.3 days, $102,243±37,588) were observed in comparison with all other admissions (4.6±0.1 days, $10,496±424). Mean sex and age-adjusted mortality was 0% for SJS, 3.7% [1.4-6.1] for SJS/TEN and 24.8% [11.8-37.8] for TEN. In multivariate regression models, SJS was associated with Herpes Simplex Virus (OR [95% Confidence Interval] 18.46 [7.54-45.19]) and Mycoplasma infection (9.70 [4.46-21.12]). All cases of HSV and Mycoplasma occurred in SJS patients. SJS was not associated with renal failure or septicemia, but SJS/TEN & TEN were significantly associated with septicemia (11.69 [6.34-21.54]), renal failure (7.63 [2.71-21.54]), and liver damage (3.47 [1.26-9.58]). In logistic regression models with stepwise selection controlling for comorbidities, predictors of mortality included renal failure (>999.99 [57.01->999.99]), malignancy (13.63 [2.98-62.30]), septicemia (57.29 [14.25-230.27]), any bacterial infection (27.88 [6.77-114.85]), and epilepsy (34.66 [8.38-143.39]).

Discussion: Pediatric SJS/TEN are a substantial health burden in the United States in terms of costs, length of stay and mortality. Incidences of SJS, SJS/TEN, and TEN were lower in children than previously observed in adults. Renal failure, septicemia, and bacterial infections were the strongest predictors of mortality. Mortality in TEN was substantially higher than in SJS/TEN or SJS patients, suggesting that BSA over 30% -- not just 10% -- is an additional mortality risk factor. Future studies are needed to improve prognostication and reduce the incidence and mortality of SJS/TEN.
Introduction: A meta-analysis of perioperative outcomes following ambulatory surgery in obese subjects concluded a lack of evidence regarding the effect of obesity on outcomes following ambulatory surgical procedures. The purpose of this study was to evaluate the independent association of body mass index (BMI) with pulmonary complications following ambulatory surgery.

Methods: The National Surgical Quality Improvement Project (NSQIP) database is a prospectively maintained surgical outcomes data that includes more than 400 participating community and academic hospitals. A review of the 2012 NSQIP dataset was performed for all patients with “ambulatory” recorded as their surgical setting and home as their discharge destination. We removed cases that were coded such as ventilator dependent, emergency surgeries and current pneumonia. The primary outcome of interest was aggregate pulmonary complications (PC) (pneumonia, unplanned intubation, ventilation > 48 hours, pulmonary embolism) for 30 days following surgery. Variables selected for the analysis had demonstrated a significant association with major complications following ambulatory surgery. The association between BMI and PC was assessed using binary logistic regression, and the WMW odds and confidence intervals for a random pair of BMI values from a PDPH subject compared with a non-PDPH subject were calculated from the area under the receiver operator characteristics curve. A parsimonious logistic regression model was constructed to identify independent variables associated with PC (c-statistic 0.68, 95% CI 0.66 to 0.71). A conditional tree analysis was constructed using variables identified by logistic regression.

Results: 316,690 cases were included in the analysis. PCs were identified in 498 (0.2%) of patients (pneumonia 243 (0.1%), unplanned intubation 103 (0.03%), pulmonary embolus 186 (0.1%), ventilation > 48 hours 38 (0.01%). The WMW odds of the ratio of a BMI from a subject with a PC compared to one without a PC was 1.15 (95% CI 1.04 to 1.28, P=0.005). The optimal cut-off value of BMI for PC was 28.25 (P=0.04). The logistic regression mode identified age, bleeding disorder, BMI, disseminated cancer, dyspnea, female gender, functional status prior to surgery, COPD, CHF, HTN requiring treatment, renal failure, current steroid use and weight loss >10% of body weight in the prior 6 months independent predictors of a PC.

Conclusion: Increased BMI was associated with an increase in PC following ambulatory surgery by univariate but conditional tree analysis demonstrated the effect of obesity is less important than other co-morbidities for risk stratification following ambulatory surgery.

Abstract Title: Brain Activation During Facial Affect Perception Differentiates High vs. Low Functioning Individuals with Schizophrenia

A recent study suggests that individuals with 'high functioning' schizophrenia (HF-SCZ) may have preserved facial affect perception (FAP) compared to individuals with 'low functioning' schizophrenia (LF-SCZ). However, it is unclear whether the neural mechanisms supporting FAP for HF-SCZ remain preserved or if HF-SCZ recruit additional neural resources to preserve behavior. This study evaluated if brain activation during FAP task performance differed in HF-SCZ when compared to controls and LF-SCZ, and whether FAP-related brain activation was related to FAP task performance. Seventeen HF-SCZ, thirteen LF-SCZ, and 24 controls completed a FAP task during functional magnetic resonance imaging. Group-level analyses compared the neural activity corresponding to accurate FAP trials between HF-SCZ and LF-SCZ. Post-hoc analyses evaluated the neural activity of controls in the regions showing differential activation between HF-SCZ and LF-SCZ. We evaluated the associations between brain activation and FAP accuracy using Spearman correlations. HF-SCZ demonstrated preserved FAP task performance and were characterized by similar activation in the left insula and right superior frontal gyrus compared to controls, which was significantly greater than LF-SCZ. Both SCZ groups demonstrated similar patterns of activation in the precuneus, which differed from controls. Lastly, FAP task accuracy was correlated with fusiform gyrus activation among HF-SCZ (ρ =.48, p<.05), but negatively correlated among LF-SCZ (ρ =-.58, p<.04). These results suggest that individuals with 'high functioning' schizophrenia demonstrate similar patterns of brain activation during accurate FAP task performance compared to controls. Our findings suggest that these brain regions may be possible neuroimaging markers for monitoring interventions aimed at improving community functioning in schizophrenia.
Background: Sudden infant death syndrome (SIDS) is the third leading cause of death among children 0-12 months and the leading cause of death from 28 days to 1 year of age. While the etiology of SIDS is unclear, risk factors have been identified that are associated with increased risk of infant death. The American Academy of Pediatrics (AAP) recommends sleeping prone, using a firm sleep surface, breastfeeding, offering a pacifier, avoidance of bed-sharing, eliminating soft objects from the bed or under the infant, prevention of overheating, and avoidance of tobacco, alcohol and illicit drugs to decrease the risk of SIDS. Infant sleep environments should prioritize the ABCs: Alone, on the Back, and in an empty Crib. The Ann & Robert H. Lurie Children’s Hospital of Chicago (LCH) has an infant sleep policy that states that all children under 24 months should be placed in a crib. However, it does not address the position of the child, nor does it describe or recommend other factors and behaviors associated with safe sleep. Parents are allowed to co-sleep with their child if they sign a release. It is not known how often co-sleeping occurs, how often the release is signed, or if hospitalized infants are put to sleep in a safe sleep environment according to AAP guidelines.

Objectives: To analyze the sleep practices of infants admitted to Lurie Children’s Hospital and to examine the prevalence and characteristics of safe sleep policies across children’s hospitals in the United States.

Methods: The primary investigator observed infants 0-12 months who were general medical or surgical patients on 2 floors of the hospital. Variables assessed included age, sex, gestational age, diet, date of admission, primary diagnosis, and problem list. Infants were observed surreptitiously while in their sleeping environment, documenting location and position of the sleeping child, the presence of co-sleeping, home and medical supplies present in the crib, and the room temperature. Infants were excluded from study participation if they had medical or surgical conditions that necessitated a specific sleeping position, or if they were awake or not in their room at the time of observation. In addition, a survey was sent to pediatric hospital administrators and pediatric chief residents at other hospitals asking about their hospital policies on infant sleep safety. Policy details were requested, as well as demographic information about the hospital (e.g., size of pediatric training program, presence of NICU or newborn nursery). The LCH IRB approved this study.

Results: One hundred and sixty seven infants were observed in their sleeping environment between July and October 2015. The median time between admission and observation was 2 days (range 0-176 days). 50% were between 0-2 months, and 57% were male. 34% were Hispanic/Latino. 47% were partially or fully breast-feeding while inpatient. 80% were on a medical, rather than surgical service. Unsafe sleep was common at the time of observation: 20% were co-sleeping at the time of observation (only 6% had a hospital-required signed waiver on file); 56% had medical supplies in their cribs; 93% had home supplies (e.g., diapers, wipes, extra blankets, or clothes) in their cribs; 40% were sleeping with the crib head-of-bed elevated. Of the 167 infants observed during their hospitalization, only 2 (1.1%) met all ABC’s of safe sleep described by the AAP. There was a significant difference between hospital units in crib head-of-bed elevation; 56% of infants on Floor 20 had an elevated head-of-bed (vs. 31% on Floor 21, p=0.0055). Preterm babies were also more likely to have the crib head-of-bed elevated (57% vs. 36%, p=0.0498). Term babies were more likely to be observed co-sleeping than preterm babies (23.4% vs. 33%, p=0.0105). The survey sent to hospital administrators and chief residents received 18 responses. 78% of respondents were from free-standing children’s hospitals, and all hospitals had a NICU. 83% of these hospitals had a policy on infant sleep, and 87% of those policies prohibited medical supplies or items from home being present in the crib. 73% of the policies prohibit co-sleeping.

Conclusions: Despite the presence of a policy on infant sleep environments, 99% of infants at LCH do not sleep in a safe environment when admitted to the general inpatient floors. In addition, unlike many peer institutions, the LCH policy does not address the sleep environment of the infant. A stronger policy with education of physicians, nurses, and other medical caregivers is needed and may help emphasize the importance of safe sleep to parents. Enforcing this policy may lead to safer sleep environments in the hospital and at home.
Abstract Title: Association of Inflammatory Bowel Disease and Hidradenitis Suppurativa: a large single center retrospective study

Summary: Hidradenitis suppurativa (HS) is a progressive, inflammatory skin disease characterized by nodules, abscesses, sinus tracts, and scarring. Reported comorbid disease associations with HS include metabolic syndrome, autoimmune disease, and depression. The association of inflammatory bowel disease (IBD) and HS is known, yet characterization of the relationship between IBD and HS is not well reported. While findings support increased likelihood of HS in patients with IBD, the occurrence of IBD in patients with HS has not been described. The role of anti-TNF-alpha therapy in the management of HS is an area of active investigation and adalimumab has been approved for the treatment of moderate to severe HS, and multiple anti-TNF-alpha therapeutic agents are FDA-approved for IBD.

Objective: The primary aim of this study within a large single center population, is to determine if an association exists between HS and IBD, and the secondary aim is to determine to what extent anti-TNF-alpha exposure influences this association.

Methods: We searched a large urban academic center electronic medical record repository (4.4 million patients), the Northwestern Medicine Enterprise Data Warehouse (NMEDW), to select all individuals who were diagnosed with HS (ICD-9 code 705.83) between January 2005 and December 2015. Only individuals with documented age, race and gender were included in the analysis. Among HS population all individuals that also have a diagnosis of IBD (ICD-9 code 555 – 556.9) were selected. A control population consisted of age-matched controls (ratio 2:1). Fisher’s exact test was used to determine the significance of the association between HS and IBD.

Sample: 1,332 individuals with a diagnosis of HS.

Results: Of 1,332 individuals with HS, 20 were diagnosed with IBD at the time of, or subsequent to diagnosis of HS (mean age 39.8, range 21-65; 75% females, 40% African-American vs 42% females, 10% African-American in the control group). The mean time to IBD diagnosis in those with HS was 9.4 months (range 0 - 72 months). A significant association (Fisher’s exact test) between HS and IBD was determined (OR: 2.11; 95% CI:1.12- 3.95; p=0.02). Of 1,332 individuals with HS, 40 were diagnosed with HS >1 month after IBD diagnosis. Of these, 12 (30%) were treated with an anti-TNF-alpha agent (N=7 adalimumab; N=5 infliximab) prior to diagnosis of HS (mean age 38.9 years, range 21-61; 75% females, 58.3% Caucasian, 41.7% African-American) and 28 (70%) were not treated with anti-TNF-alpha therapy prior to diagnosis of HS (mean age 46.2 years, range 27-70; 78.6% females, 57.1% Caucasian, 39.3% African-American, 3.6% Asian). The mean time to HS diagnosis in those with IBD on anti-TNF-alpha therapy was 43.3 months (range 18 -103) vs 27.6 months (range 1-108) in those not treated with anti-TNF-alpha therapy prior to diagnosis of HS.

Conclusions: The determination of an association for IBD in patients with prior HS diagnosis, as well as findings that suggest IBD patients undergoing treatment with anti-TNF-alpha therapy have less likelihood to subsequently develop HS and/or have a delayed onset of HS, serve to further delineate our understanding of HS comorbidity. Further exploration of the association of HS and IBD, particularly of the possible mechanistic aspects of this clinically important association, and the role of anti-TNF-alpha therapy in delaying and/or preventing development of HS, are warranted.
Abstract Title: Constructing a Robust Index of Walking Ability for Exoskeletons

**Background.** Clinical scores for evaluating walking skills with lower limb exoskeletons are often based on a single variable, such as distance walked or speed, even in cases where a host of features are measured. We investigated how to combine multiple features such that the resulting score has high discriminatory power, in particular with few patients. A new score is introduced that allows quantifying the walking ability of patients with spinal cord injury when using a powered exoskeleton.

**Methods.** Four spinal cord injury patients were trained to walk over ground with the ReWalk™ exoskeleton. Body accelerations during use of the device were recorded by a wearable accelerometer and 4 features to evaluate walking skills were computed. The new score is the Gaussian naïve Bayes surprise, which evaluates patients relative to the features’ distribution measured in 7 expert users of the ReWalk™. We compared our score based on all the features with a standard outcome measure, which is based on number of steps only.

**Results.** All 4 patients improved over the course of training, as their scores trended towards the expert users’ scores. The combined score (Gaussian naïve surprise) was considerably more discriminative than the one using only walked distance (steps). At the end of training, 3 out of 4 patients were significantly different from the experts, according to the combined score (p < .001, Wilcoxon Signed-Rank Test). In contrast, all but one patient were scored as experts when number of steps was the only feature.

**Conclusion.** Integrating multiple features could provide a more robust metric to measure patients’ skills while they learn to walk with a robotic exoskeleton. Testing this approach with other features and more subjects remains as future work.
Research Day Abstract

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Department:* Preventive Medicine
Does this research involve women's health?* Yes

Abstract Title:* Metabolic networks and metabolites underlie associations between maternal glucose during pregnancy and newborn size at birth

Offspring of mothers with pre-existing or gestational diabetes mellitus (GDM) are at risk for higher birth weight (BW) and adiposity as well as childhood metabolic disorders including obesity, impaired glucose tolerance, and dyslipidemia. Mechanisms and mediators underlying these risks are not well defined but likely relate to fetal overnutrition in the setting of available maternal fuels.

One fuel present in increased supply in GDM is glucose. The Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, a population-based study of >23,000 women, and others, demonstrated a linear relationship between maternal glucose and offspring BW and fatness. This is likely mediated through glucose-stimulated insulin secretion in the fetus. Additional fuels also likely contribute. For example, women with GDM have increased circulating triglycerides in the third trimester of pregnancy. Maternal free fatty acids, which are derived from triglycerides, cross the placenta, serve as substrates for triglyceride synthesis, and contribute to fetal growth. Amino acids in maternal fasting plasma have been correlated with BW among women with diet-controlled GDM. The role of these and other fuels in risks associated with maternal hyperglycemia is unknown. To address possible metabolic linkages between maternal hyperglycemia and offspring phenotypes, we performed targeted and non-targeted metabolomics together with pathway, network, and random forest analyses on 400 HAPO mothers of European ancestry.

Amino acids, fatty acids, acylcarnitines and products of lipid metabolism decreased and triglycerides increased following glucose ingestion during the OGTT. Analyses of individual metabolites indicated limited maternal glucose associations at fasting, but broader associations including amino acids, fatty acids, carbohydrates and lipids at 1-hour. Network analyses modeling metabolite correlations (see fig. 5D) provided context for individual metabolite associations and elucidated collective associations of multiple classes of metabolic fuels with newborn size and adiposity, including acylcarnitines, fatty acids, carbohydrates and organic acids. Random forest analyses indicated improved ability to predict newborn size outcomes using maternal metabolomics data beyond traditional risk factors including maternal glucose. Broad scale association of fuel metabolites with maternal glucose is evident during pregnancy, with unique maternal metabolites potentially contributing specifically to newborn birth weight and adiposity.

Fig. 5D. Subnetwork of maternal 1-hour metabolites associated with maternal 1-hour plasma glucose and newborn birth weight. Nodes represent metabolites and edges represent partial correlation >0.25 for metabolite pairs. Nodes are sized according to p-value based node score, with larger nodes corresponding to higher scores. Nodes are colored according to metabolite class, and grouped according to spinglass community within the subnetwork. Direction of association for maternal 1-hour plasma glucose and newborn birth weight is noted by color shading in the left and right sides of the nodes, respectively. Positive associations are darker and negative associations are lighter.
Background: Aggression following penetrating TBI (pTBI) occurs in up to one third of pTBI patients. The link between frontal lobe lesions and aggression has been demonstrated, however oftentimes people with lesions in parts of the brain not generally associated with disinhibition, violence or fear will also show behavioral changes. It has also been noted that some forms of post-TBI aggression and post-traumatic epilepsy may be related to overlapping network connectivity leading some to theorize that the brain areas involved in seizures themselves may also play a role in aggression.

Objective: Compare patients who developed seizures following pTBI to those who did not develop seizures following pTBI on the Neuropsychiatric Inventory (NPI) aggression subscale to determine if presence of seizures predicts aggressive behavior. Determine if location of penetrative lesion has an effect on this correlation.

Methods: 159 patients with pTBI were drawn from the Vietnam Head Injury Study registry. Patients with pTBI were divided according to presence (N=69) or absence (N= 90) of seizures following injury. Aggression was assessed using the aggression subscale of the NPI. Lesion location was determined using voxel-by-voxel assessment of CT scans.

Results: A chi-square analysis indicated that patients who developed seizures following TBI were more likely to have elevated NPI aggression scores than patients without seizures ($\chi^2 = 9.563$, p-value = .003). There was no statistically significant correlation between NPI score and location of initial lesion.

Conclusion: Patients who developed seizures following pTBI were more likely to engage in aggressive behavior post-injury, regardless of lesion location.
Abstracts longer than one page will not be accepted.

Research Day Abstract

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Position:* research staff

Abstract Category:* clinical research

Principal Investigator:* Michael Markl

Department:* Radiology

Does this research involve women's health?* No

Abstract Title:* Aortic hemodynamics in dilated ascending aorta with and without aortic valve stenosis

**Introduction** - Aortic valve stenosis (AS) is a major risk factor for ascending aortic (AAo) dilation. However, even patients without AS can develop AAo dilation.

**Purpose** - To characterize differences in aortic flow velocity, blood flow patterns, and flow eccentricity between patients with and without AS and healthy controls using 4D flow MRI.

**Methods** - 11 patients with dilated AAo with moderate to severe AS (64.8±14.9 years, 10 men, sinus of valsalva [SOV]: 37.6±5.2mm, mid ascending aorta [MAA]: 40.9±3.2mm), 11 patients with dilated AAo without AS (64.5±15.0 years, 10 men, SOV: 42.7±5.1mm, MAA: 42.5±4.9mm), 11 healthy control subjects (60.5±12.7 years, 8 men, SOV: 33.0±3.1mm, MAA: 32.4±3.0mm) were identified via IRB-approved retrospective chart review. All patients underwent in-vivo 4D flow MRI for the measurement of 3D blood flow velocities. Data analysis included the quantification of systolic peak velocities in analysis planes at the aortic root, proximal-, mid-, distal-AAo, proximal-, distal-arch, proximal-, mid-, distal-descending aorta. Aortic flow patterns were visualized using time resolved pathlines (Fig. 1-A) and semi-quantitatively graded for the presence of vortex and helix flow in AAo by two independent observers using a 3-point scale (1, no vortex/mild helix [flow rotation: less than 180°]; 2, 1-2 large vortex/moderate supra-physiologic helix [flow rotation: 180° to 360°]; 3, more than 2 large vortex/prominent supra-physiologic helix [flow rotation: more than360°]). Aortic flow eccentricity was evaluated by identifying regions with systolic peak velocities >1 m/s in four quadrants of analysis planes placed at the proximal, mid, and distal AAo.

**Results** - Peak velocity was significantly greater in the patients with AS in root, proximal AAo, mid AAo, distal AAo, proximal arch, and distal arch compared to those without AS and control subjects (Fig. 1-B). Patients without AS showed significantly elevated vortex flow compared to control subjects (2.18±0.40 vs. 1.45±0.52, p<0.05). Helix flow was significantly elevated for both patients with and without AS compared to control subjects (2.82±0.40 vs. 1.45±0.52 and 3.00±0.00 vs. 1.45±0.52, p<0.05) (Fig. 1-C). Increased flow eccentricity was observed in the patients with AS in mid and distal AAo and those without AS in proximal AAo. Control subjects demonstrated more uniform flow profiles (Fig. 1-D).

**Conclusions** - Patients with AS demonstrated significantly more eccentric flow in the AAo compared to those without AS with similar alterations in blood flow despite matching subjects by age, gender, and aortic size. As expected patients with dilation of the AAo with and without AS demonstrated alterations in blood flow compared with age- and gender-matched healthy controls. The eccentric flow observed in patients with dilated AAo and AS may lead to accelerated aneurysm progression in this group; outcomes studies are warranted to assess the independent influence of blood flow on progression of AAo dilation.

A. Flow visualization

B. Peak velocities

C. Visual grading AAo Vortex

D. Aortic flow eccentricity

*Abstracts longer than one page will not be accepted.*
Abstract Title: Wernicke's Encephalopathy or Creutzfeldt Jakob Disease? Report of Cases with Non-Classic Presentation of Thiamine Deficiency and Challenging Brain Magnetic Resonance Imaging Findings

Objective: To report two unusual cases of thiamine deficiency presenting as acute on chronic cognitive/psychiatric impairment. In both cases, brain MRI also suggested Creutzfeldt Jakob disease (CJD).

Summary: We present a case series on 2 patients with Wernicke's Encephalopathy (WE) from thiamine deficiency that presented atypically. WE does not consistently present as the classic triad of altered mental status, ataxia, and ocular problems. Our patients had underlying cognitive/psychiatric problems whose clinical and radiographic presentations initially was concerning for Creutzfeldt Jakob Disease, but by keeping a broad differential diagnosis, both patients were ultimately found to have thiamine deficiency.

Background: Thiamine (or Vitamin B1) dependent enzymes are found in most cells of the body. These enzymes are particularly critical in the processes of sustaining an osmotic gradient, glucose metabolism, and neurotransmitter synthesis. Despite the requirement of thiamine throughout the body, the nervous system is most notably sensitive because of its increased reliance on oxidative metabolism. Daily thiamine requirement is about 2 mg. In a typical diet, most thiamine intake is primarily through whole grains, but it is also found in a wide variety of foods including sunflower seeds, asparagus, kale, potatoes, oranges, pork, and eggs. Without thiamine intake, the reserves could be depleted in 4-6 weeks. Thiamine deficiency classically presents acutely as Wernicke's encephalopathy (WE), which is composed of the triad of altered mental status, ataxia, and eye muscle weakness. Classic imaging findings include increased T2/FLAIR (fluid-attenuate inversion recovery) signals surrounding the cerebral aqueduct and third ventricle, and within the medial thalamus, dorsal medulla, tectal plate, and/or mammillary bodies. CJD, on the other hand, is a rapidly progressive dementia that can also present acutely with psychiatric prodrome and altered mental status. The typical radiographic findings here are T2/FLAIR hyperintensity of the putamen, caudate head, thalamus, cerebral cortex, cerebellar cortex, and white matter. We present two WE cases which posed diagnostic challenge due to prior cognitive/psychiatric impairment, non-classic presentation, and challenging Magnetic Resonance Imaging (MRI) findings.

Methods: Case series.

Results: Our cases include two women, ages 58 and 62 years old, with underlying schizophrenia and Alzheimer disease respectively. Both stopped eating due to their underlying conditions and presented with acute changes in mental status. Neither patient had ocular signs or ataxia. In both cases, brain MRIs showed diffusion restriction and T2/FLAIR hyperintensity in bilateral thalami. The clinical and radiographic findings together suggested CJD as the underlying cause. Both patients were later diagnosed with thiamine deficiency, and CJD was ruled out.

Conclusions: Both of our patients presented as worsening of their underlying disease, in the setting of decreased nutritional intake. However, since both presented with only a portion of the typical WE triad, and brain MRI highly suggested CJD, further work up was necessary to rule out the possibility of CJD. WE is likely under-recognized, as the classic triad occurs in only 16-38% of patients. It should be in the differential diagnosis of acute cognitive decline in patients with underlying conditions that can result in decreased nutritional intake. Early recognition is crucial, and if treated in a timely manner, prognosis is usually favorable.
In-depth diagnostic immune-profiling of two X-linked SCID siblings identified through the Illinois newborn SCID screening program

Mandatory statewide newborn screening for T cell-deficient Severe Combined Immunodeficiency (SCID) was implemented in Illinois in January 2014. This entails molecular analysis for T cell Receptor Rearrangement Excision Circles (TREC) from heel-stick derived dried blood spots collected at birth at the state public health laboratory followed by confirmatory flow-cytometry testing at our institution’s CLIA and CAP-certified diagnostic immunology laboratory (and a Jeffrey Modell Foundation designated diagnostic and research laboratory for primary immunodeficiency diseases) for neonates that register < 250 TRECs/microliter of blood.

In July 2014, we analyzed a peripheral blood sample from a male neonate with a TREC count of 0. Flow-cytometry revealed markedly reduced numbers of T cells and Natural Killer cells but normal B cell counts, raising the possibility of T-B-NK SCID, arising due to a mutation in either the gene encoding for the common gamma chain [CD132; signaling sub-unit shared by the receptors for IL-2, IL-4, IL-7, IL-9, IL-15 and IL-21 (X-linked SCID)] or the Janus Kinase 3 gene [JAK3 (Autosomal Recessive SCID)]. Phenotypic analysis of the few T cells available revealed a preponderance of a memory phenotype as well as normal surface expression of CD132 and cytosolic expression of JAK3. However, functional immune profiling demonstrated depressed phytohemagglutinin-induced proliferation of the T cells, as well as marked hypo-phosphorylation of B cell-associated STAT6 following IL-4 treatment, suggestive of a severe attenuation of the signaling potential in the CD132-JAK3 axis. Subsequent sequencing of the patient’s genomic DNA revealed a non-sense mutation in the CD132 gene [(c.375C>A); (p.Y125X)], which would have resulted in the production of a common gamma chain completely lacking the transmembrane and intracellular domains, confirming the prediction based on the immune profiling results.

In September 2015, our index patient’s infant brother was referred to our institution following his abnormal newborn screen, also with a TREC count of 0. Phenotypic and functional assessment of his lymphocyte subsets demonstrated an immune profile that was almost exactly the same as that of his older brother. After the diagnosis of X-linked SCID was made in each case, the siblings underwent unrelated donor stem cell transplant following reduced-intensity conditioning with fludarabine, busulfan and anti-thymocyte globulin. Both siblings attained full donor engraftment and immune reconstitution after the transplant and are now clinically well.

In conclusion, functional immune profiling of patients' lymphocytes, including phosphorylation studies of receptor signaling molecules, is a rapid and effective way to diagnose immunodeficiency and should be considered a routine part of the work-up for newborns with possible SCID.
Introduction: Thanks to modern methods of cancer treatment, women diagnosed with cancer today have a greater chance of long-term survival than in previous years (1, 2). It is important that cancer survivors maintain a high quality of life after diagnosis and completion of treatment. However, lifesaving treatments such as chemotherapy, radiation, and surgery may negatively impact survivors by impairing endocrine and reproductive health, specifically the neuroendocrine axis, immature and growing follicles in the ovaries, and reproductive organs (3-7). For patients with cancer, preserving the ability to start a family at a time of their choosing is especially important and may influence decisions pertaining to cancer treatment (8-11). Controlled ovarian stimulation (COS) followed by oocyte or embryo cryopreservation is a method of fertility preservation (FP) available to women facing a cancer diagnosis that are interested in giving birth in the future. Emerging research in FP is providing clinicians an increasing number of reproductive and hormonal management tools. The type of cancer or the urgency to initiate treatment as soon as possible may ultimately limit or greatly influence FP treatment. Initiating in vitro fertilization (IVF) cycles in FP patients regardless of menstrual cycle phase, a “random-start” (RS) protocol has been proposed to decrease the time to initiate cancer treatment, but has not been thoroughly studied. In this method of treatment, the patient would undergo COS for oocyte or embryo cryopreservation regardless of menstrual cycle phase, minimizing delays and completing FP within 2-3 weeks (12, 13). This is in contrast to the conventional cycle-specific (CS) protocols, which must initiate at the beginning of the follicular phase and may require up to 6 weeks. Even with the use of GnRH antagonists to shorten the time between initial presentation and oocyte or embryo cryopreservation, the patient must still experience a delay in cancer treatment under CS protocols. In this study we sought to compare FP outcomes of RS protocols in comparison to CS protocols and whether RS protocols prevent significant delay in the initiation of cancer treatment. We hypothesized that RS protocols would have the same cycle outcome as conventional, CS protocols, and would decrease the time from fertility preservation referral to initiation of cancer treatment.

Methods: A retrospective chart review was performed on all patients undergoing IVF for FP at Northwestern University from 2006-2013. Chi-squared analysis was used to compare outcomes from RS protocols vs CS protocols: days of stimulation, peak estradiol levels, total oocytes retrieved, mature oocytes retrieved, and days from fertility preservation referral to initiation of cancer treatment (surgery or chemotherapy).

Results: A total of 95 patients were included, 14 in the RS group and 81 in CS group. Mean age was 31 in both groups. RS protocols resulted in significantly higher peak estradiol than in CS protocols (1744 vs 1434, p<0.01), but there was no significant difference in eggs retrieved (13 vs 12), number of mature eggs (11 vs 9), or days of stimulation (11 vs 11). There was also no difference in number of days from patient contact to initiation of cancer treatment (44 vs 45).

Conclusion: Random-start protocols are equivalent to cycle-specific protocols in in vitro fertilization cycle outcome, but may not shorten time to cancer treatment, as previously proposed. Further research is necessary to identify modifiable causes which may delay fertility preservation patients from initiating cancer treatment.
Introduction: Age-related decrease in the amount of slow-wave sleep has been postulated to play a role in impaired cognitive function. Acoustic stimulation during sleep has been shown to increase slow-wave activity (SWA) and improve memory retention in young adults, but has not been examined in older adults. The aim of this study is to examine the ability of acoustic stimulation to increase SWA and improve declarative memory in older adults.

Methods: Thirteen healthy and cognitively intact adults (age 75.2 ± 60-84, 3 men) completed one night of acoustic stimulation and one night of sham stimulation in counterbalanced order. During sleep, an adaptive phase-locked loop (PLL) algorithm was used to lock on to endogenous slow-waves recorded from the midline frontopolar electroencephalogram in real time. Bursts of 1/f noise were delivered when the PLL system predicted the positive upstate of the slow-wave. Tones occurred in blocks of 5 pulses (“ON blocks”) followed by a refractory period of equal length (“OFF blocks”). Participants completed an 88-word pair recall with feedback, before and after sleep, to assess declarative memory. Power spectral analysis was used to identify power in delta frequency band (0.5 Hz-4 Hz). Performance was measured as percent change in word recall from evening to morning. Non-parametric t-tests were used to evaluate differences between stimulation and sham conditions.

Results: There was a significant increase in delta power in the ON blocks relative to OFF blocks during the stimulation night compared to the sham night (16% v. -2.3%, p=0.002). Delta power during ON blocks of the stimulation night was 8% higher compared to ON blocks of the sham night (p=0.002). Overall delta power across the entire night was not significantly different. Participants recalled significantly more words following a night of acoustic stimulation compared to a night of sham stimulation (27.2% v. 4.5%, p=0.008).

Conclusions: Acoustic stimulation delivered during sleep increases SWA and improves declarative memory performance in older adults. These findings may have clinical implications for improving sleep and cognition in populations with cognitive or sleep disorders.

*Abstracts longer than one page will not be accepted.
Abstracts longer than one page will not be accepted.

Research Day Abstract

Presenting Author:* Travis DeSa MS3
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Position:* Medical Student 3
Abstract Category:* Clinical Research
Principal Investigator:* Michael Markl PhD
Department:* Cardiac Imaging

Does this research involve women’s health?* No

Abstract Title:* Comparison of Cardiac Perfusion and Heart Global Functional Parameters between Healthy Volunteers and Cardiac Transplant Patients

Background:
Recently, myocardial perfusion using MRI has become a promising non-invasive method to evaluate myocardial ischemia in cardiovascular diseases (CVDs). However, assessment of CMR’s effectiveness in differentiating quantitative metric of regional myocardial perfusion in patients with CVD and comparison of regional myocardial perfusion indices to cardiac global functional parameters has not been thoroughly studied. To address this unmet clinical need, we evaluated myocardial perfusion and cardiac function in 12 healthy volunteers and 9 cardiac transplant patients.

Methods:
12 healthy volunteers (10 males, mean age 52±17 years old, Body weight: 93±20 Kg ) without documented history of CVDs and 9 cardiac transplant patients were recruited following IRB approval and written informed consent. MRI scans were performed at 1.5 T systems (Magnetom Aera, Siemens Medical Solutions, Erlangen, Germany). Each volunteer and patient underwent a cardiac MRI enclosing first pass perfusion imaging after injection of Gd contrast agent and short axis CINE SSFP imaging for the assessment of global cardiac function.

Perfusion images were acquired in left ventricular (LV) short axis orientation with three slices positioned at basal, mid-chamber, and apical level after the injection of a single dose of gadopentetate dimeglumine (Magnevist, 0.1 ml/kg). Perfusion data reconstruction included inline and fully automated motion correction to compensate for the effects of cardiac and respiratory motion. Perfusion Imaging parameters were as follows: FOV = 360 x 360 mm2, Slice thickness = 8mm, TR/TE/flip angle = 168/1.14ms/12degree. Measurements = 60

All CINE data were transferred to a computer (Siemens Leonardo Syngo) for analysis using ARGUS software. A single reviewer semi-automatically drew the borders (endo and epicardial) of the LV at each slice for each study and global cardiac function parameters were calculated.

Cardiac global functional parameters including absolute EF, absolute and normalized EDV, absolute and normalized ESV, absolute and normalized SV, absolute CO, and normalized CI were measured based on short-axis cine images. Perfusion data analysis include LV contour segmentation, and calculation of peak perfusion signal intensity, peak slope of the signal change, and time to peak perfusion (TTP). Perfusion data were evaluated in myocardial segments based on the AHA 16-segment model.

Differences in perfusion on a segmental and global level were assessed between volunteers and patients using an unpaired two-tailed t-test. In addition, differences in global functional parameters were assessed between volunteers and patients using an unpaired two-tailed t-test. Finally, correlation between perfusion and global functional parameters was assessed by using Pearson correlation coefficient (r) for volunteers and cardiac transplant patients.

Results:
The results for t-tests assessing differences between volunteers and patients for perfusion, slope, and time to peak perfusion are shown in Table 1. The most significant differences were seen in the perfusion parameter, with 7 of the 16 segments showing significant differences between patients and controls. However, few significant differences were seen in slope and time to peak perfusion parameters. The average perfusion (averaged over entire LV) for volunteers and patients is shown in Table 2 and was significantly different between controls and patients (85.27 +/- 19.6, 63.07 +/- 14.07, p = 0.016). The results for differences in cardiac global functional parameters between volunteers and controls as well as the results for correlation between functional parameters and perfusion are shown in Table 3. No significant differences were seen in functional parameters between volunteers and patients. No significant relationships between perfusion and global functional cardiac parameters were found except normalized SV (0.508, p = 0.039).

Conclusion:
Cardiac MR detected significant differences in regional myocardial perfusion indices between healthy volunteers and recipients of cardiac transplantation, as evidenced by the significant differences measured in segmental and average perfusion. The absence of significant correlations of perfusion with cardiac functional parameters indicates that metrics of myocardial perfusion may be more sensitive to detect early changes in LV dysfunction prior to the onset of impairment in global cardiac function. Additional studies in larger cohorts are warranted to further evaluate relationships among various cardiac indices.

*Abstracts longer than one page will not be accepted.
Summary: Maternal adiposity and glycemia during pregnancy influence the developing fetus, impacting birthweight and adiposity, and potentially adversely affect the long term metabolic health of the child. However, the mechanisms underlying these associations are not fully characterized. Using serum collected as part of the Hyperglycemia and Adverse Pregnancy Outcome (HAPO) Study, we sought to identify maternal and newborn metabolites associated with maternal BMI and glucose measured during an oral glucose tolerance test (OGTT) at ~28 weeks’ gestation via targeted metabolomics in women of Afro-Caribbean, Northern European, Mexican-American, and Thai ancestry. Meta-analysis of cohort specific newborn data revealed significant associations of maternal BMI with fetal amino acid metabolism. Meta-analysis of mother metabolites revealed broad perturbations of amino acid, acylcarnitine and conventional metabolite levels associated with maternal glucose, consistent across ancestry groups. Large scale perturbations across metabolite classes associated with BMI were also observed, but with a distinct metabolic signature exhibited by the Thais compared to other ancestry groups.

Objective: To characterize maternal and newborn metabolic profiles associated with maternal BMI and glycemia during pregnancy.

Sample: 1600 HAPO mother/newborn pairs, 400 each of Afro-Caribbean, Northern European, Mexican-American and Thai Ancestry.

Methods: HAPO was an observational study (conducted 1999-2006) of >23,000 pregnant women at 15 international field centers that examined associations of glucose levels during pregnancy with adverse outcomes in mothers and newborns and to derive criteria for gestational diabetes diagnosis. Mothers underwent a 2-hr 75 gm OGTT at ~ 28 weeks gestation, and blood was obtained at fasting and 1-hr after Trutol consumption. Newborn cord blood samples were obtained within 5 mins of delivery and prior to delivery of the placenta. Conventional clinical metabolite assays were performed using a Beckman-Coulter Unicell DxC 600 clinical analyzer. Acylcarnitines and amino acid panels were analyzed by tandem mass spectrometry with addition of known quantities of stable isotope-labeled or non-natural internal standards. Associations of maternal BMI and glucose levels with metabolite levels were assessed using linear regression for each ancestry group, and random-effects meta-analysis was used to combine results across cohorts.

Results: On meta-analysis, maternal BMI demonstrated significant positive associations with newborn branched chain amino acids (leucine/isoleucine, valine), phenylalanine, and three acylcarnitines that arise from amino acid catabolism (FDR adjusted p < 0.05). Maternal fasting glucose was not significantly associated with newborn metabolites. Maternal BMI was positively associated with maternal acylcarnitines (most significantly C16:1 and C4-OH), conventional clinical metabolites (most significantly glycerol and 3-hydroxybutyrate), and amino acids (most significantly glutamine and phenylalanine) (FDR adjusted p < 0.05). Notably, of the 30 significant maternal metabolite – BMI associations identified via meta-analysis, only three were significant in the ancestry specific analyses for the Thai cohort compared to ten or more in the remaining ancestry groups (see Figure to the left). Maternal fasting glucose demonstrated significant positive associations with several amino acids (alanine, proline, glutamine, valine, asparagine) and lactate, and showed significant negative associations with a group of acylcarnitines, most significantly C16:1 and C16 (FDR adjusted p < 0.05).

Conclusion: Across four ancestry cohorts, maternal BMI was associated with significantly altered amino acid metabolism in newborns. Maternal BMI and glucose were also significantly associated with broad-scale perturbations of mother metabolites, with largely overlapping associations across ancestry groups for glucose. Interestingly, the maternal metabolic profile associated with BMI was distinct for the Thai ancestry cohort compared to other ancestries, and is worthy of further investigation.
Research Day Abstract

Abstract Title:  Placental pathologic features in fetomaternal hemorrhage detected by flow cytometry

Background: Fetomaternal hemorrhage (FMH) occurs when fetal blood enters the maternal circulation during pregnancy or delivery. It can have significant effects including maternal sensitization to red blood cell antigens and fetal anemia, which may lead to fetal hydrops, neurologic injury or death. However, the pathophysiology of FMH remains largely unknown. Traditionally the diagnosis was confirmed by Kleihauer-Betke testing; however, flow cytometric analysis has recently emerged as a more sensitive and specific method. The placental pathology associated with FMH detected by flow cytometry has not been investigated. Our aim was to correlate placental pathology with FMH detected by flow cytometry.

Methods: All patients with maternal blood sent for FMH flow cytometric testing with available placentas (H&E slides), from 2009 – 2015, were retrospectively reviewed. Twin placentas were excluded. Cases were defined as ≥0.10% hemoglobin F (HbF) in the maternal circulation while controls contained <0.10% HbF. The placental pathologic findings were coded and the pathologic findings associated with FMH were determined. Statistical analysis used chi-squared and t-tests.

Results: 35 cases and 79 controls were identified. The mean volume of FMH was 109.10 mL ± 117.01 mL, and 17% of the FMH cases experienced intrauterine fetal demise. The mean gestational age and mean placental weight of the cases were greater than those of the controls (37 vs 33 weeks; p=0.001 and 451 vs 318 grams; p<0.001, respectively). When the FMH cases were compared to the controls, the only placental variable associated with FMH was villous dysmaturity/immaturity (present in 14.3% of cases vs 1.3% of controls; p=0.01). The incidence of intervillous thrombi, a finding that has been reported in the literature in association with FMH, was not significantly different between the cases and controls (present in 14% of cases and 13% of controls; p=0.813). Placentas with villous edema and nucleated red blood cells (nRBCs) in the fetal vasculature had significantly higher mean %HbF (1.33% vs 0.32%; p=0.01 and 1.54% vs 0.21%; p=0.01, respectively) and greater volumes of fetal blood in the maternal circulation (69.50 vs 17.26 mL; p=0.012 and 78.25 vs 12.37 mL; p=0.002, respectively). Fetal vascular pathology, maternal vascular pathology and chronic inflammation were significantly more frequent in the controls. Additionally, when the FMH cases were stratified into mild (<30 mL; n=12), moderate (30 – 100 mL; n=10) and severe (>100 mL; n=13) FMH, a significant difference in the presence of nRBCs was seen (0% of mild, 30% of moderate, 92% of severe cases displayed nRBCs; p<0.001). Villous dysmaturity/immaturity and villous edema were associated with severe FMH (4 of 5 cases with villous dysmaturity/immaturity [p<0.001] and 10 of 13 cases with villous edema [p=0.001] were associated with severe FMH).

Conclusions: Villous dysmaturity/immaturity, villous edema and nRBCs in the fetal vasculature, findings compatible with fetal anemia, are the most significant placental findings in FMH detected by flow cytometry. In addition, when the FMH cases were stratified into mild, moderate and severe, all three findings were significantly associated with severe FMH. Interestingly, a background of chronic placental pathology, such as maternal or fetal vascular pathology or chronic inflammation, does not seem to predispose a pregnancy to FMH. In fact, the control population showed significantly more chronic placental derangements than the study group, suggesting that patients who have FMH testing performed often have significant placental disease. The presence of villous dysmaturity/immaturity, villous edema and nRBCs in fetal vessels in addition to a relative lack of other placental pathologic findings should alert the pathologist to the possibility of FMH.

*Abstracts longer than one page will not be accepted.
OBJECTIVE: This retrospective review identifies the clinical presentation and outcomes of transient osteoporosis (TO) in peripartum women to increase awareness of TO of the sacrum (TOS) and sacral insufficiency fractures as a cause for low back pain in peripartum women.

STUDY DESIGN: A retrospective case series of 18 peripartum women presenting to Women’s Health Musculoskeletal (MSK) Physiatrists (2010-2013) who were diagnosed with transient osteoporosis of pregnancy (TOP).

RESULTS: There were 18 cases of women presenting with symptomatic TOP. The most common location was the sacrum (13 cases – 72%) including 10 unilateral sacral insufficiency fractures, 2 bilateral insufficiency sacral fractures, and 1 unilateral sacral stress reaction. Of the remaining 5 cases of TOP, there were 2 involving the hip without fracture (1 unilateral, 1 bilateral), 1 involving the hip and knees without fracture, and 2 unilateral pubic fractures. Average onset of symptoms during pregnancy was 28 weeks gestation. Average onset of symptoms in postpartum was 1 month. Lumbosacral pain was the most common presenting complaint in patients with TOS.

CONCLUSION: Transient osteoporosis of pregnancy has classically been described involving the hip. This retrospective case series identifies that a predominance of presenting cases to a robust Women’s Health MSK clinical practice involved the sacrum. This suggests that transient osteoporosis of the sacrum may be an under-diagnosed and underreported cause of low back pain in peripartum women.
Objective: To study longitudinal impact of changes in childhood adiposity on cardiac geometry and function.

Background: There has been a dramatic increase in childhood and adolescent obesity in the United States since 1980. Recent NHANES data shows that 17% of children and adolescents have a BMI greater than 95th percentile. National Heart Lung and Bone Institute released guidelines in 2011 for cardiovascular health and risk reduction in children and adolescents that included recommendations for obesity screening (including recommendations for lipid, weight, diet, physical activity). Studies have demonstrated that the presence of obesity in childhood and adolescence is associated with increased cardiovascular morbidity and mortality in adulthood with evidence of atherosclerosis at autopsy, elevated blood pressure, dyslipidemia, and insulin resistance. In the adult population, echocardiographic studies have demonstrated that obesity leads to cardiac remodeling and alterations in the myocardial function characterized by eccentric left ventricular hypertrophy, diastolic and systolic dysfunction. The relation between adiposity and cardiac structure and function in children, however, is less well documented.

Hypothesis: There is progressive worsening of left ventricular hypertrophy and myocardial dysfunction with increases in adiposity measure during childhood.

Methods: Project HeartBeat! recruited 678 healthy children grouped into cohorts aged 8, 11, and 14 years at baseline. Anthropometric and transthoracic echocardiographic data was collected at 4-month intervals for up to 4 years (1991–1995). Standardized 2 dimensional (2D), M-mode, and Doppler echocardiography was performed at each visit measuring cardiac geometry and function. Of the 678 children enrolled in Project Heartbeat! at baseline, 28 were excluded for having fewer than two exams and 1 was excluded for missing a baseline BMI value, leaving 649 eligible for analysis. In analyses examining echo parameters at year 2 only the 512 children who attended the 2 year follow-up were included.

The exposures we considered were BMI percentile (calculated using CDC criteria), waist circumference, skinfold thickness, and waist-to-hip ratio. Eight echocardiogram parameters were considered as outcomes. Left ventricular diameter (systolic and diastolic) and left atrial diameter were measured. Wall stress, fractional shortening, EME Myocardial Performance Index, Modified Tei index, and left ventricular mass were derived from existing variables. All eight outcomes were tested for normality. Variables that were both significantly non-normal and had skewness greater than 0.50 were transformed using the natural log. Parameter estimates were then exponentiated for ease of interpretation. Linear regression models were used to examine the cross-sectional association between baseline adiposity and baseline outcomes as well as to examine the association between baseline adiposity and echo parameters at the 2 year follow-up. Models were sequentially adjusted for demographics (gender and ethnicity) and baseline blood pressure. To model the association between baseline exposure and the change in outcome over time, as well as the association between the change in exposure and outcome over time we compared repeated measures to random effects models. Using this approach, we could use every measurement occasion; the 649 children contributed a total of 5779 measurement occasions. Data were assumed to be missing at random. When compared, both the repeated measures and random effects models had identical Akaike information criterion (AIC) using BMI percentile as the exposure.

Results: Analysis in process
INTRODUCTION: Current transfemoral (TF) prosthetic sockets restrict function, lack comfort and cause residual limb problems. Although designed to support the body and enable effective load transfer during walking and other activities, prosthetic sockets interface with soft tissues that are neither accustomed nor well-suited to the high pressure and shear loading that occurs during prosthetic ambulation.2 Despite high daily use, lack of socket comfort is the most common complaint of prosthesis users.3-6 Residual limb skin problems such as cysts, calluses, verrucous hyperplasia, allergic reactions, and bacterial or fungal infections have been reported by 25 to 63% of persons with amputation with a negative influence on ability to perform household tasks, prosthesis use, social functioning, and participation in sports. The development and availability of a more comfortable and possibly functional socket may contribute to improving quality of life of persons with TF amputation.

METHODS: A TF socket technique was developed aimed at improving comfort. The Northwestern University Flexible Sub-Ischial Vacuum (NU-FlexSIV) Socket has lower proximal trim lines that do not impinge on the pelvis; is flexible so muscles can move comfortably within the socket as they contract during activity and improve sitting comfort; and is held securely to the residual limb by vacuum pump suction as well as compression of an undersized liner and socket. The socket includes a highly compressive, cylindrical fabric covered silicone liner, a flexible inner socket, and a shorter rigid outer socket with vacuum applied between liner and inner socket. An algorithm and rectification mapping were developed to facilitate decision making for socket fabrication. Socket comfort score, gait analysis, and clinical outcome measures (Rapid-Sit-To-Stand, Four-Square-Step-Test and T-Test of Agility) were used to assess socket performance. A hands-on workshop to teach this technique was piloted.

RESULTS: The undersized liner and socket are used to compress the residual limb, stiffening the soft tissue and decreasing relative motion of the limb within the socket. The impression is taken over the liner with the patient seated and the limb flexed and slightly abducted, allowing gravity to pre-modify the tissues. Rectifications were quantified using a program that aligned a series of 30 scans of rectified and unrectified negative molds and calculated changes in shape. A color coded scale on the rectification map indicates the depth and contours of the rectifications required for the NU-FlexSIV Socket, showing that plaster is primarily removed from the proximal-lateral and posterior regions, while the medial and anterior regions remain relatively untouched. No plaster is added. For 2 subjects, socket comfort increased in the NU-FlexSIV Socket compared to an ischial containment socket. Walking speed increased for the NU-FlexSIV Socket but other gait variables, including coronal plane trunk flexion and sagittal hip motion, were comparable for level ground walking. Clinical outcome measure performance was comparable in both sockets. Three workshops held in summer 2015 were attended by 31 prosthetists from the US and Canada. Attendees were taught to cast, rectify, fit and align the NU-FlexSIV Socket. Patient models responded positively to the comfort, range of motion and stability of the NU-FlexSIV Socket while prosthetists described the technique as “straight forward, reproducible”.

CONCLUSION: To the best of our knowledge, this is the first attempt to create a teachable subischial socket technique that results in improved comfort and comparable function to ischial containment sockets, confirming previous reports. Color coded rectification maps help communicate an important step in this socket technique, enhancing dissemination. Socket stability during walking was confirmed by lack of lateral trunk flexion and lateral socket gapping at mid stance. Clinical experience fitting this socket to over 100 patients confirms these research findings. Initial evaluation of the NU-FlexSIV Socket with military amputees is promising. Future work includes an assessor-blinded, randomized cross-over trial comparing comfort and functional performance with the NU-FlexSIV Socket to the ischial containment socket in persons with unilateral transfemoral amputation.

This work was funded by the Department of Defense Award #W81XWH-10-1-0744.
**Research Day Abstract**

**Presenting Author:** Laurence Ducharme-Crevier, MD  
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**Position:** Pediatric Neurocritical Care Fellow  
**Abstract Category:** Clinical Research  
**Principal Investigator:** Mark S. Wainwright MD, PhD  
**Department:** Pediatric Neurocritical Care Program  
**Does this research involve women's health?** No

**Abstract Title:** Use of Transcranial Doppler for Management of Central Nervous System Infections in Critically Ill Children

**Purpose:** The primary objective of this study was to characterize changes in cerebral blood flow (CBF) measured using transcranial doppler (TCD) in children with central nervous system (CNS) infections. We hypothesized that children with CNS infections have abnormal CBF, associated with a greater frequency of complications and poor neurologic outcome.

**Methods:** Single center, retrospective study of children admitted to the pediatric intensive care unit with CNS infection and undergoing TCD as part of routine care between March 2011 and July 2015.

**Results:** 21 children with CNS infection underwent 35 TCDs. The mean age was 8.2 ± 6.2 yr, including 12 boys and 9 girls. Most cases were caused by meningitis (n=12, 57%), the remainder comprising encephalitis (14%), meningoencephalitis (19%) and abscess or empyema (10%). Bacterial (n=10, 48%) and viral (n=7) sources were common with only 1 (5%) fungal infection and 3 (14%) unknown but presumed viral etiology. The patients underwent TCD 4 ± 8 days after ICU admission. CBF velocities were overall increased compared to reference values for age (healthy children and critically ill children) mostly due to hyperemia (n=21, 60%) and vasospasm (6%). Hypoperfusion (CBF velocity < 1 SD of normal value) in at least one vessel was associated with morbidity (intubation, vasoactive medications, neurosurgery, cardiac arrest) (p=0.04) and mortality (p=0.03). Two patients had increased intracranial pressure (ICP) and hyperventilation was safely achieved with TCD monitoring to avoid ischemia. Serial TCDs were used to guide blood pressure management.

**Conclusion:** TCD can be used in children with CNS infection as a tool to assess CBF and may help guide medical therapy. Hypoperfusion is associated with increased morbidity and mortality.

*Abstracts longer than one page will not be accepted.*
Abstract Title: Pilot Evaluation: Ultrasound Elastography for Bladder Wall Assessment of the Neurogenic Bladder

Summary
A bladder with sustained elevated intravesical pressure during the storage phase may place the upper urinary tract at increased risk. There is an ongoing need for a non-invasive method without radiation exposure to assess for alterations in the neurogenic bladder wall that may portend development of decreased compliance.

Objective
The objective of this study is to evaluate the feasibility of shear wave ultrasound elastography (SWE) as a novel means to assess bladder wall changes associated with impaired compliance in children undergoing urodynamics. We hypothesized that shear wave velocity measurements (SWV: a proxy measure of tissue stiffness) would increase during the filling phase in a noncompliant neurogenic bladder.

Methods
Following informed consent, eight to 21-year-olds with a history of neurogenic bladder underwent concurrent SWE and routine urodynamics. SWV measurements were taken using a GE LOGIQ E9 with XDclear probe from the anterior (transverse probe, location 1cm superior to the pubic symphysis in midline) and posterior bladder wall (longitudinal probe, trigonal midline location) with the bladder empty, after 25%, 50%, 75% and 100% EBC was infused, at end fill volume and post-emptying. Intravesical and intra-abdominal pressures were monitored throughout filling. Study processing was completed by a radiologist with selection of three ROIs (inner to outer) corresponding to each layer of the bladder wall per measurement obtained.

Results
Six children with neurogenic bladders have been evaluated to date. Mean SWV and SWV of the detrusor layer (graph 1) increased during bladder filling. There was a significant increase in mean anterior SWV from baseline to end fill volume observed in the four bladders with complete data and impaired compliance (mean baseline SWV 1.62±0.19 SEM vs end fill 2.43±0.13m/s, p=0.02) and in SWV of the anterior detrusor layer (1.60±0.27 vs 2.62±0.10, p=0.05) but not of the posterior bladder wall (mean SWV 1.35±0.44 vs 1.66±0.20, p=0.49). Graph 2 illustrates a scatter plot of mean anterior wall SWV versus intravesical pressure (n=6).

Conclusions
A rise in mean SWV and detrusor SWV of the anterior wall is observed with neurogenic bladder filling and may correspond to a rise in intravesical pressure. This study is currently being expanded to include children with compliant bladders that we hypothesize will remain stable with a lower SWV as compared to the noncompliant neurogenic bladder.
Introduction and Objective: Pancreatic resection surgeries remain high-risk procedures, even in well-selected surgical candidates. The importance of risk stratification has been pushed to the forefront given quality-based reimbursement models. In patients undergoing elective pancreatectomy, our aim was to evaluate the effect of gender on intra-operative blood transfusions, estimated blood loss (EBL) as well as post-operative surgical site infections (SSIs). Our hypothesis was that male gender is associated with worse operative and post-operative surgical outcomes in this patient population.

Sample: Twenty nine thousand forty five patients undergoing elective pancreatectomy from 2005 to 2013 were identified in the Participant User File of the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP). In addition, 298 elective pancreatectomy patients were identified from the Northwestern EDW database in order to internally analyze the correlation between transfusions and EBL.

Methods: Univariate and multivariate analyses were conducted to identify the association between gender, operative time, transfusions and SSIs. Demographic and complication profiles were calculated using χ² and standard t-tests for categorical and continuous variables, respectively. Multivariate logistic regression analysis was used to calculate adjusted odds ratios for factors independently associated with SSI and prolonged operative time. Odds ratios were adjusted for gender, age, BMI, operative time, transfusion and histology (when appropriate). Inclusion into the multivariate model was attained if the univariate analysis for a risk factor yielded a p-value < 0.2.

Results: Demographically, of the 29,045 patients, 49.2% were male, 48.4% were 65 years of age or older, 27.7% were obese, 28.4% received blood transfusion during surgery and 58.7% had malignant histology. Male gender (p=0.001), age, type of procedure (whipple, distal, total pancreatectomy), histology (benign or malignant) and operative time (all p<0.001) were all significantly associated with transfusions. Body mass index (BMI) was not associated with transfusions (p=0.201). In addition, male gender, BMI, type of procedure and histology (all p<0.001) were significantly associated with prolonged operative time (over 6 hours). Nearly all of these factors were significantly associated with deep and superficial SSIs (all p<0.05). Notably however, age was not a risk factor for superficial SSIs (p=0.707). Multivariate analyses to control for potentially confounding variables demonstrated that male gender was independently associated with all-type SSIs (OR 1.27, 95% CI 1.19-1.34) and prolonged operative time greater than 6 hours (OR 1.58, 95% CI 1.50-1.66). The internal analysis of transfusions as a proxy variable for EBL showed a moderate correlation (R=0.516), demonstrating its utility in gauging EBL in the ACS-NSQIP pancreatectomy population.

Conclusions: Male gender is a significant predictor of increased operative time, transfusions as well as post-operative surgical site infections in pancreatectomy patients. Surgeons should be aware of the substantial effect of gender on these outcomes when selecting surgical candidates, delivering patient counseling and providing perioperative management and surveillance.
Research Day Abstract

Presenting Author:* Kimberly Showalter, MD
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Abstract Category:* Clinical Research
Principal Investigator:* Monique Hinchcliff, MD MS
Department:* Rheumatology
Does this research involve women’s health?* Yes

Abstract Title:* Identification of an esophageal diameter threshold associated with interstitial lung disease in systemic sclerosis

**Objective.** To determine the esophageal diameter on high-resolution computed tomography (HRCT) of the thorax that is both sensitive and specific for associated radiographic interstitial lung disease (ILD) in systemic sclerosis (SSc).

**Background.**
- ILD is the leading cause of death in SSc. However, lung transplant programs often uniformly exclude SSc patients with esophageal dilatation due to concern for gastroesophageal reflux injury to the transplant [1].
- Analysis of post-transplantation outcomes in SSc patients do not support categorical exclusion [2].
- Prior studies to assess the association between esophageal dilatation and ILD in patients with SSc dichotomized esophageal dilatation as present or absent and extrapolated a 9 or 10mm esophageal diameter threshold from a study that assessed the association between esophageal dilatation and dysmotility [3-6].
- We previously demonstrated an association between esophageal dilatation as a continuous variable and radiographic ILD in patients with SSc [7].
- We hypothesized that a 9 or 10mm esophageal diameter threshold may not be specific for ILD in SSc.

**Methods.** Northwestern Scleroderma Registry subjects who fulfilled American College of Rheumatology 2013 SSc criteria for either diffuse cutaneous or limited cutaneous SSc and had undergone HRCT scans were included (Table 1) [8]. The widest esophageal diameter (WED) was measured on axial HRCT scans (Figure 1) [8]. A published method to quantify ILD was used [9]. ILD was treated as a dichotomous variable. Esophageal diameter was treated as a continuous variable. A receiver operating characteristic (ROC) curve was generated to determine the sensitivity and specificity for ILD at varying esophageal diameters (Figure 2).

**Results.** 270 subjects with SSc fulfilled inclusion and exclusion criteria. The majority (82%) were women. An esophageal diameter ≥19mm had a sensitivity of 68% and specificity of 63% (LR - 0.5098, LR+ 1.8477) for associated ILD. There was no esophageal diameter below which ILD was uniformly absent. A 9 or 10mm esophageal diameter threshold had a sensitivity of 92.47%, and 91.40%, respectively, and specificity of 13.56%, and 17.51%, respectively, for ILD.

**Conclusions.**
- 9 and 10mm esophageal diameter thresholds that have been used in prior studies that assessed the association with esophageal dilatation and ILD in SSc patients are sensitive, but non-specific for ILD.
- Our analysis did not identify an esophageal diameter threshold below which ILD is uniformly absent in SSc.
- A 19mm esophageal diameter threshold has the highest combined sensitivity and specificity for radiologic ILD in SSc.

**Clinical Implications.** Given no threshold exists below which ILD is universally absent, our results support universal aspiration precautions in SSc.

**References.**

*Abstracts longer than one page will not be accepted.
Abstract Title: **Timing of Complications in Patients Undergoing Immediate Postmastectomy Breast Reconstruction and Adjuvant Radiation**

**Purpose/Objective(s):**
Postmastectomy radiation therapy (PMRT) for breast cancer increases survival, decreases local recurrences, and is a pillar of care in locally advanced disease. While immediate postmastectomy breast reconstruction has been shown to significantly improve psychosocial outcomes, it has also been linked to increased complications when followed by PMRT. Though there are multiple studies assessing and comparing the complication rates of immediate tissue expander/implant reconstructions (TE/I) and autologous tissue reconstructions (ATR) when PMRT is utilized, there are few with long term follow up. This study aims to quantify the long term complication rates and timing of complications of PMRT following immediate reconstruction in a large patient population.

**Materials/Methods:**
Between November 1997 and May 2010, we identified 150 consecutive patients with stages I–IIIC breast cancer who underwent mastectomy with immediate reconstruction followed by subsequent radiation therapy. Of these, 139 patients had adequate long term follow up and documentation for inclusion. We aimed to assess rate and timing of major complications defined as events requiring a separate and distinct procedure. Statistical analysis between variables was evaluated using Fisher’s exact test.

**Results:**
The median follow-up for all patients was 76 months. 115 patients underwent TE/I reconstruction, while 24 patients had ATR. Complications included infection, seroma, hematoma, capsular contracture, implant deflation, skin necrosis, implant extrusion, pain, and flap loss. The rate of major complications in this patient population was 46% when followed long term. The overall major complication rate for TE/I vs ATR was not significantly different (48.7% vs 33.3%, P=0.185). Of patients with major complications, the majority (78.1%) were able to undergo a secondary reconstruction and retain a reconstructed breast. In total, 14 patients (10.1%) had a major complication after which a secondary reconstruction was not performed. Of all major complications, 67% occurred within one year of beginning radiation therapy and 84% occurred within two years. The only identified risk factor that was statistically associated with increased complication rates was the use of hormonal therapy (P= 0.017). Other factors including smoking status, axillary radiation, capillary-lymphatic space invasion, the use of bolus, and neoadjuvant chemotherapy were not found to be associated with increased complications.

**Conclusion:**
Our data suggests that there is no statistically significant difference in the long term complication rates of immediate TE/I vs immediate ATR followed by PMRT. The timing of major complications suggests that most of the complication risk is incurred during the immediate post radiation period.
Abstract Title: Whole exome sequencing of benign breast biopsy to identify genomic mutations leading to malignant breast cancer

Summary: Breast cancer prevention is currently a challenge due to the inability to identify high-risk women accurately only based on family history and pathologic evaluation of benign biopsy. Somatic molecular changes in clinically normal breasts have potential value to improve the assessment of truly high-risk women. The identification of risk biomarkers in benign biopsy material will directly benefit the millions of women who undergo benign breast biopsy annually, adding precision to the risk implied by the histologic features of the benign biopsy.

Objective: Our goal is to pursue robust biomarkers for breast cancer risk by whole exome sequencing of pre-cancer benign biopsies, which may lead to discovery of genomic variants responsible for initiation and early progression of breast cancer.

Samples: We assembled 250 case-control set of benign breast biopsy matched by age, race, and duration of follow-up (up to 10 years). The cases were the benign biopsies from women who subsequently developed breast cancer after at least one year, and the controls were the benign biopsy samples obtained from women who remain cancer free. 10-micron sections from formalin-fixed, paraffin-embedded tissue blocks were used for laser capture microdissection (LCM) of epithelial areas and extraction of genomic DNA.

Methods: Genomic library was constructed using Agilent SureSelect V5 kit. Whole exome sequencing with paired-end 100bp was performed using Illumina HiSeq2000 at coverage of 80-100x. FastQC was performed for quality control from the original fastq files. Then high-quality raw reads files were aligned to human reference genome version 19 using Burrows-Wheeler Aligner (BWA) based on GATK best practice for sequence mapping. ANNOVAR was used for gene-based functional annotation of genomic variants. The comparison between benign cases and benign controls, as well as matched malignant cancer was performed.

Results: We have finished sequencing of 24 benign cases, 11 benign controls and 10 matched malignant tumor. In the 45 samples, average 10,313 (range 9,147-14,886) variants per sample were identified. By removing the synonymous SNV, average 9,890 (range 8,762-14,350) mis-functional variants, including non-synonymous SNV, frameshift insertion, frameshift deletion, stopgain and stoploss. The comparison between benign cases and benign controls revealed 120 genes with differential mutation counts, with 111 genes had more mutant variants in benign cases and in matched tumor, and 9 genes with less mutant variants in benign cases and matched tumor. Gene annotation enrichment analysis using DAVID suggested these genes were involed in functions of cell adhesion, phagocytosis, regulation of programmed cell death, and cellular component morphogenesis. Several candidate variants in mutant genes were selected for further validation and functional studies in additional benign biopsy case and control samples.

Conclusion: The whole exome sequencing of benign breast biopsy leads to the discovery of mutations and genomic variants that may be involved in breast cancer initiation and early progression. These mutations can be potential biomarkers and molecular targets for breast cancer prevention.

*Abstracts longer than one page will not be accepted.
Volumetric growth kinetics to estimate the age of colorectal liver metastasis at MDCT

Purpose
To determine the age of colorectal liver metastases from their individual volumetric growth rates determined from serial multidetector computed tomography (MDCT) examinations.

Materials and methods
This Health Insurance Portability and Accountability Act compliant retrospective study was approved by the institutional review board. Twenty-one colorectal cancer liver metastases in eleven patients imaged twice by MDCT before the start of chemotherapy or radiation treatment were evaluated. Liver metastases were analyzed using semiautomated segmentation software and their reciprocal of doubling time (RDT) (growth kinetic parameter) was calculated. RDT was used to determine the time elapsed from the point when the lesion was detectable by CT (5 mm in diameter). Wilcoxon signed-rank test was used for analysis. Significance was set at 0.05.

Results
Mean age for our cohort was 53 ± 13.56 years. Mean interscan interval was 43.5 ± 20.21 days. Mean volume of liver metastases on the second pretreatment scan was significantly greater when compared to the first pretreatment scan (24.72 ± 43.32 mL vs. 13.21 ± 31.46 mL, respectively; P<0.0001). Median time interval (interquartile range [IQR]) from the time point when the lesion was 5 mm in diameter to the initial CT examination was 217.2 days (IQR, 153.1 – 372.2 days).

Conclusion
Growth kinetics may assist in estimating the time that liver metastasis may have become detectable by MDCT.

Keywords:
Colorectal cancer, liver metastasis, growth kinetics, computed tomography
Research Day Abstract

Presenting Author:* Daniel Fort, PhD, MPH
E-mail:* daniel.fort@northwestern.edu
Position:* postdoctoral fellow
Abstract Category:* Clinical Research
Principal Investigator:* Daniel Fort
Department:* Department of Preventive Medicine, Division of Health and Biomedical Informatics
Does this research involve women’s health?* No
Abstract Title: * Using Collaboration Networks to Visualize Patterns in Clinical Trial Recruitment

Background

Feinberg School of Medicine and other research institutions within the Northwestern University Medical Center have been using a common IRB database since 2006. Using this database, collaboration information, such as two researchers being listed as authorized personnel on the same study, can be combined with total patient recruitment on that study. The result can be used to visualize interactions between researchers, departments, and clinical study recruitment. Using available open source software (http://gephi.github.io), this process can be quickly replicated at other institutions.

Methods

For presented visualizations, nodes are defined as any individual listed as authorized personnel on at least two protocols since 2006. Node colors represent the home department of the individual (i.e. if two nodes are the same color then both individuals belong to the same department). An edge is present between two nodes if the two individuals have been listed as authorized personnel on the same protocol, weighted by the number of times this has occurred. Clusters represent patterns of frequent collaboration between the same group of individuals. Edges can also be colored to represent recruitment success or failure (blue for predominantly successful collaborations, red for failed).

Results and Discussion

We will demonstrate a collaboration network of all individuals at the institution with obvious clusters manually labeled by predominant department. We can see, for example, that cancer research represents an area of frequent collaboration between a more exclusive group of individuals while psychology tends not to collaborate with other departments.

We will also provide an example of a single cluster which also encodes study recruitment outcomes. While the cluster represents a group of highly collaborating individuals within Figure 1, within the cluster are patterns of more frequent collaboration which suggest successfully recruiting researchers tend to work with each other.
In August 2015, we launched an iPad App version of the NIH Toolbox for the Assessment of Neurological Behavior and Function (a web-based version is already in use in over 500 research studies and clinics settings). This new technology is available in the iTunes App Store (https://itunes.apple.com/us/app/nih-toolbox/id1002228307?mt=8), and has received glowing feedback thus far. We just passed 300 new subscribers, and are aware of its use in a handful of very large research studies in the US and abroad. We feel that this technology would be useful to many Northwestern researchers and clinicians, and we would love to showcase the software at Research Day. It seems like a demo table/booth would be more appropriate than a poster- is there a space for vendors or technology demos?
Adductor Canal Block for Total Knee Arthroplasty: A Randomized, Double Blind Placebo Controlled Trial

Summary: Total knee arthroplasty is associated with moderate to severe postoperative pain limiting patient activities and delaying discharge. Multimodal analgesia techniques are frequently used in enhanced recovery protocols to improve pain relief and facilitate early discharge. Periarticular infiltration of a mixture of local anesthetics, anti-inflammatory and opioid analgesics have been utilized in multimodal protocols and can improve pain score, reduce total perioperative narcotic consumption, provide early mobilization and increase patient satisfaction. However, periarticular infiltration is often inadequate to provide sufficient analgesia to the anterior and medial aspect of the knee because the operative approach disrupts the medial joint capsule. Femoral nerve blockade has been commonly used for postoperative analgesia after knee surgery but is frequently associated with quadriceps muscle weakness. A single shot adductor canal block can provide postoperative analgesia for patients undergoing total knee arthroplasty (TKA) with reduced incidence of quadriceps muscle weakness.

Objective: The purpose of this study was to assess postoperative outcomes following ultrasound-guided single injection bupivacaine compared to saline adductor canal block for patients undergoing TKA.

Sample: 40 adult patients scheduled to undergo elective Total Knee Arthroplasty

Methods: A randomized double-blind placebo controlled trial. Subjects were randomized into 2 groups: adductor canal blockade with 10 mL of bupivacaine 25mg with epinephrine 33 ug or 10 mL of normal saline. All patients received a local infiltration analgesia mixture intraoperatively and scheduled and prn oral and IV analgesics postoperatively for breakthrough pain. Personnel blinded to group allocation recorded pain scores and opioid consumption every six hours. Pain burden, area under the numeric rating score for pain, was calculated for 36 hours. The primary outcome was postoperative morphine (mg morEq) consumption.

Results: 63 patients were approached to participate in the study and 40 (28 F/12 M) patients were studied. Postoperative opioid consumption was reduced in the bupivacaine 143 (118 to 184) mg morEq compared to saline 180 (148 to 255) mg morEq, difference -38 (-98 to -5) mg morEq (P=.03). Pain burden at rest was decreased in the bupivacaine 71 (37 to 120) score·h compared with saline 131 (92 to 161) score·h, difference -60 (-93 to -14) score·h (P=0.009). Postoperative dizziness was reported in 28.8% of patients who received bupivacaine compared to 55% in the saline (P = 0.02). Median satisfaction scores postoperative day 1 were greater in patients receiving with bupivacaine compared to those who received saline, difference 2 (95% CI 0.5 to 5) P=0.04. There was no difference between groups in physical therapy milestones. Patients that received bupivacaine an adductor canal block were discharge to home earlier than those receiving saline (P=0.04, log rank test). At the three-week follow-up assessment patients who received bupivacaine reported greater patient satisfaction than those that received normal saline P=0.04.

Conclusions: The most important finding of the current study is that when compared to a saline injection, an ultrasound-guided adductor canal block with 10 ml of bupivacaine 25 mg with epinephrine 33 ug can reduce opioid consumption and pain burden during the first 36 hours after surgery without impeding the physical therapy milestones required for hospital discharge. In addition, patients receiving the bupivacaine adductor canal block had less severe opioid related side effects and provided greater patient satisfaction during hospitalization and at three-week follow-up. Our finding suggests that an adductor canal block can be an integral part of an enhanced recovery protocol since it positively impacted pain burden, reduced opioid consumption postoperatively, reduced opioid related side effect severity, facilitated early discharge and improved patient satisfaction.

References
Research Day Abstract

Abstract Title: Dual Window Pattern Recognition Classifier for Improved Partial-Hand Prosthesis Control

Summary: Although partial-hand amputees largely retain the ability to use their wrist, it is difficult to preserve wrist motion while using a myoelectric partial-hand prosthesis without severely impacting control performance. Electromyogram (EMG) pattern recognition is a well-studied control method; however, EMG from wrist motion can obscure myoelectric finger control signals. Thus, to accommodate wrist motion and to provide high classification accuracy and minimize system latency, we developed a training protocol and a classifier that switches between long and short EMG analysis window lengths.

Methods: Seventeen non-amputee and two partial-hand amputee subjects participated in a study to determine the effects of including EMG from different arm and hand locations during static and/or dynamic wrist motion in the classifier training data. We evaluated several real-time classification techniques to determine which control scheme yielded the highest performance in virtual real-time tasks using a 3-way ANOVA.

Results: We found significant interaction between analysis window length and the number of grasps available. Including static and dynamic wrist motion and intrinsic hand muscle EMG with extrinsic muscle EMG significantly reduced pattern recognition classification error by 35%. Classification delay or majority voting techniques significantly improved real-time task completion rates (17%), selection (23%) and completion (11%) times, and selection attempts (15%) for non-amputee subjects, and the dual window classifier significantly reduced the time (8%) and average number of attempts required to complete grasp selections (14%) made in various wrist positions. Amputee subjects demonstrated improved task timeout rates, and made fewer grasp selection attempts, with classification delay or majority voting techniques.

Conclusions: Including wrist motion in a pattern recognition classifier is critical to maximizing performance of partial-hand prostheses while still preserving residual wrist movement. Furthermore, using a dual window classifier maximized classification accuracy when class selection was most important and reduced system delay when additional accuracy was not necessary or fewer grasps were available. Finally, the introduction of classification delays or majority voting techniques also significantly improved real-time prosthesis control and were generally preferred by users. These techniques form the basis for developing a control system for a partial-hand prosthesis that preserves the function of the wrist. The control systems proposed here are simple and can easily be implemented with current devices already available on the market.
Abstract Title: Diurnal Pattern of Nicotinamide Adenine Dinucleotide (NAD+) in Humans

Introduction: Nicotinamide Adenine Dinucleotide (NAD+) is a coenzyme involved in oxidation/reduction reactions in living cells. It is intricately involved in energy metabolism, serving as an electron donor in the generation of ATP and cosubstrate for the Sirtuin class of metabolic regulators. NAD+ synthesis has been shown to have a 24-hour circadian oscillation in mouse tissues. Reduced tissue NAD+ levels are associated with both aging and cardiometabolic disease. Furthermore, studies have shown that the administration of NMN (a NAD+ biosynthetic precursor), can improve metabolic function. Circadian disruption has also been tied to aging and cardiometabolic disease risk, so it is possible that these effects are mediated by disrupted circadian function of NAD+, however, most molecular research in this area has centered on rodent models. The goal of this study is to characterize the 24-hour pattern of NAD+ in humans.

Methods: Two healthy participants, both female, ages 24 and 28 years completed a 29-hour modified constant routine protocol. During wake participants were in dim light (<10 lux), received isocaloric snacks every two hours, and remained in a semi-recumbent position. Participants were allowed to sleep for 8 hours in the dark (<3lux) starting at habitual bedtime. On day 2, starting one hour after wake whole blood was sampled every 4 hours for 29 hours, for a total of 8 samples. The samples were assayed for NAD+ (pmol/mg tissue) using high performance liquid chromatography. NAD+ levels were plotted over the sampling period for both participants, as a function of circadian time (hours after first wake).

Results: NAD+ shows a diurnal pattern in human whole blood (Fig 1). There are two peaks that occur approximately at circadian time (CT) 13 and 25, with a trough in NAD+ levels after sleep onset (CT17).

Discussion: These results demonstrate that there is a diurnal pattern of NAD+ levels in blood in humans. Data in humans is similar to that reported in mice, with two main peaks in the 24-hour period. Further studies with a larger number of both male and female participants, and without sleep, are needed to indicate whether the pattern demonstrated here is stable and circadian-driven. While no significant conclusions can be drawn at this time, these preliminary results provide evidence for the circadian oscillation of NAD+, and warrant further research into whether the disruption of NAD+ rhythms contributes to health outcomes.
**Research Day Abstract**

Presenting Author:* Anna E. Strohl, MD  
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Position:* Fellow  
Abstract Category:* Clinical Research  
Principal Investigator:* Jonathan B. Strauss, MD  
Department:* Obstetrics and Gynecology – Division of Gynecologic Oncology; Radiation Oncology  
Does this research involve women’s health?* Yes  

**Abstract Title:** Adjuvant Chemotherapy and Radiation is Associated with Improved Survival in Women with Node-Positive Endometrial Cancer: A National Cancer Database Study

**Background:** Women with node-positive endometrial cancer have higher rates of disease recurrence and decreased survival compared to those with early stage disease. Adjuvant treatment is considered a mainstay of treatment, yet no standard treatment approach exists. Using a large national cancer database, we aimed to investigate outcomes for women with node-positive endometrial cancer treated with chemotherapy (CT) alone, radiotherapy (RT) alone, or chemoradiotherapy (CRT), compared to patients that received no adjuvant treatment.

**Methods:** The National Cancer Database was queried to identify women with surgically staged IIIC1 or IIIC2 node-positive endometrial cancer diagnosed between 2003 and 2011. Chi-square tests and multivariable logistic regression were performed to analyze factors associated with treatment type. Survival analysis was performed using log-rank test, Cox proportional hazards regression, and Kaplan-Meier estimates.

**Results:** A total of 7,653 patients were identified, among whom 1,502 (19.6%) received no adjuvant treatment, 1,350 (17.6%) received RT, 1,939 (25.3%) received CT, and 2,862 (37.4%) received CRT. Patients were more likely to receive CRT if they were younger, had fewer comorbidities, lived closer to the hospital, had fewer number of positive nodes, had smaller tumor size, and if a single agent chemotherapy regimen was used. Use of CRT was associated with improved survival compared to no adjuvant treatment (HR 2.08, 95% CI 1.73-2.50, p<0.001), RT only (HR 1.28, 95% CI 1.09-1.51, p=0.003), and CT only (HR 1.34, 95% CI 1.15-1.56, p<0.001). Receipt of any treatment was superior to no treatment.

**Conclusions:** In women with node-positive endometrial cancer, modern multimodality CRT appears to confer an additional survival advantage beyond that achieved with CT or RT alone in this large cohort. Our findings suggest that CRT should be the preferred adjuvant treatment strategy in women with node-positive endometrial cancer who are expected to tolerate the toxicities of the combined approach.

*Abstracts longer than one page will not be accepted.*
Abstracts longer than one page will not be accepted.

Research Day Abstract

Presenting Author: Timothy M. Herr, MS
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Position: Graduate Student
Abstract Category: Clinical Research
Principal Investigator: Rex L. Chisholm, PhD
Department: Preventive Medicine
Does this research involve women's health? No

Abstract Title: Translating Omic Data into Patient Care: Implementing Pharmacogenomic Clinical Decision Support

Background: As an element of precision care, genomic medicine has the potential to transform the way healthcare is delivered. However, so-called “omic data” is difficult to work with. Data volume exceeds the cognitive capacity of any individual, and an ever-changing understanding of the human genome makes it difficult to keep up with new, clinically relevant knowledge. This raises the fundamental question, “How can we effectively use genomic data to treat patients?” Our “Omic Funnel” model (Figure 1) provides a theoretical framework for this translation process. Practical implementation of this model includes multiple technical components. These include electronic health records (EHR), omic ancillary systems (OAS) that store and analyze genetic and genomic data and integrate with EHRs, and clinical decision support (CDS) tools that provide relevant genomics-based knowledge to clinicians at the point-of-care.

Objective: Northwestern University (NU), along with other organizations in the Electronic Medical Records and Genomics (eMERGE) Network, sought to demonstrate the feasibility of genomic medicine through the successful implementation and use of pharmacogenomic (PGx) CDS tools.

Methods: NU and other eMERGE sites attempted to implement PGx CDS rules in the clinical setting through a variety of technical approaches. Drug-gene interactions of interest include clopidogrel (CYP2C19), simvastatin (SLCO1B1), warfarin (CYP2C9, VKORC1), and codeine (CYP2D6). After implementation, eMERGE sites participating in the EHR Integration Workgroup completed a formal survey detailing their experiences, which collected information about system characteristics and implementation barriers encountered.

Results: 10 of 11 surveyed sites successfully completed PGx CDS implementations, through a variety of technical approaches. Most sites elected to implement an OAS to manage genomic data, though there was variation in how data was structured when communicating across systems (table to be included on final poster). Implementations completed with minimal unexpected barriers. Most project delays were due to typical IT implementation issues, such as staffing and departmental approval delays (Figure 2).

Conclusions: These results demonstrate that PGx CDS is feasible, but numerous questions remain regarding the technical approach. This includes how to structure omic data when reporting a lab result and/or transferring from an OAS to the EHR, or whether to actively query an OAS for decision support vs. building static CDS rules in the EHR. Despite these questions, NU and other participants in the eMERGE Network have successfully demonstrated first generation PGx CDS. Along with third-party organizations, such as the Clinical Pharmacogenetics Implementation Consortium (CPIC) and ClinGen, a pipeline for genomic decision support is emerging. Future research will move beyond feasibility studies and into effectiveness studies.

Figure 1: The Omic Funnel

Figure 2: Implementation Delays by Impact and Frequency

**Research Day Abstract**

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**Abstract Category:** Clinical Research  
**Principal Investigator:** Robert D. Galiano, MD  
**Department:** Division of Plastic and Reconstructive Surgery  
**Does this research involve women’s health?** No

**Abstract Title:** Satisfaction and Quality of Life in Patients Affected by Skin Scars: A Qualitative Assessment

**Introduction:** Evidence-based clinical recommendations for scar management currently exist, however, the development of these and future guidelines has been limited by a lack of evidence for many interventions. A major reason for the poor quality of evidence is the fact that many aspects of scar outcomes are inherently subjective (e.g. functional deficits such as pain and pruritus as well as psychosocial effects on the patient). Outcomes research in plastic surgery is limited by patient-centered analyses that provide clinicians and researchers an accurate way to measure subjective outcomes. Given the wide variety of scars and the disparate nature of their etiologies as well as differences in patient characteristics, it is not feasible to develop a scar scale that is truly global. However, the purpose of this study is to develop and validate a weighted scar assessment scale that incorporates both the patient’s and the observer’s assessments and is applicable for use on a wide range of scar types in diverse subjects.

**Objective:** This research is part of Stage 1 in a three stage study in which a conceptual framework is being developed to form the basis of the scar assessment instrument. The goal of this initial stage of developing a scar assessment scale is to generate an exhaustive item-pool from semi-structured qualitative interviews with study participants that will serve as a draft questionnaire which will be pretested via cognitive debriefing interviews and focus groups.

**Results:** 29 patients (6 males and 23 females; age range 22-80 years) with skin phototypes II-VI were interviewed between June 2015 and February 2016. The majority of patients had scars resulting from surgery (either elective or medically necessary). Other scar etiologies included acne (n=3) and accidental/traumatic injury (n=3). Linear scars were the most common scar type of interviewed patients (n=19), followed by hypertrophic scars (n=6), keloid scars (n=2) and atrophic acne scars (n=2). Patient self-assessments of their scars ranged from 1-10 (on a 1-10 VAS).

The patient interviews revealed that skin scars impact patients in the following five main areas: satisfaction with success/career; psychological well-being; social well-being; sexual well-being; and physical/functional well-being. These five identified themes will be used to form the basis of a conceptual framework of quality of life in patients with cutaneous scars. 72.4% of the patients interviewed were moderately or severely affected by their scars, with at least two areas of their lives significantly impacted.

**Conclusion:** Our conceptual framework establishes the main areas of life impacted by scarring. This new framework can serve to assess the appropriateness of current scar management strategies will be used to develop evidence-based guidance for the development of a global scar assessment scale. The results of this study highlight the fact that regardless of type or etiology, scars affect patients to an underappreciated degree.
EMG-Based Online Intent Recognition for a Powered Lower Limb Prosthesis

BACKGROUND AND AIM: Pattern recognition has been used to transition powered leg prostheses between locomotion modes seamlessly. Adding EMG signals to mechanical sensor information improves performance, but is not clinically implemented because signal quality degrades over time. We developed a method for detecting detrimental changes in EMG signal quality by comparing new patterns to a model of previous training data. The aim of this study was to evaluate this technique with amputees using an online pattern recognition system to control a powered knee-ankle prosthesis. We investigated whether our method can prevent errors by reverting to using only mechanical sensors to make predictions when EMG changes are detected.

METHODS: Two transfemoral amputees were fitted with a powered knee-ankle prosthesis and completed a protocol that included walking on level ground, ramps, and stairs on two different days. On the first day, an experimenter triggered mode transitions at four gait events (heel contact, mid-stance, toe off, mid-swing). Embedded mechanical sensor and EMG information from four residual leg muscles were recorded during ambulation. Signal features were used to train eight classifiers acting within different modes and at different gait events to predict the transitions between standing, level walking, ramp ascent/descent, stair ascent/descent. Gaussian models of EMG features were developed to inform classifiers when to incorporate EMG into mode predictions. In the second session, an online classifier transitioned the prosthesis between modes. Only mechanical sensors were used if new EMG patterns were significantly different (>3σ) from the model of EMG features. The percentage of steps where EMG was used is reported for each classifier. Steady-state and transitional classification error rates for each classifier were calculated. The average classifier error for heel contact and toe-off is also reported.

RESULTS: EMG signals from the second day were frequently excluded by most classifiers, and none used EMG signals in 100% of its classifications (Table 1). Classifiers operating in standing mode (ST_HC, ST_TO) and the toe-off classifier (TO) incorporated EMG in most classifications. Subjects could successfully transition between modes with low classification error rates (Table 1). The average error rate for all heel contact classifiers was 1.9% [0.9%], (mean [standard deviation]), for steady-state steps and 5.4% [2.1%] for transition steps. The average error rates for all toe off classifiers was 1.8% [1.0%] for steady-state steps and 0% [0%] for transition steps.

CONCLUSIONS: We determined that most EMG signals from the second day contained changes in signal quality. Changes were likely caused by donning/doffing the prosthesis. These variations would normally cause classification errors, but using only mechanical sensors likely kept error rates low. Future work includes creating an adaptive system that can learn to reincorporate EMG.

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**TABLE I**

<table>
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<th>Classifier</th>
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<th>HC_RD</th>
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<th>MST_SD</th>
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</table>
Research Day Abstract

Presenting Author:* Laurie A. Chalifoux MD
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Position:* Assistant Professor
Abstract Category:* Clinical Research
Principal Investigator:* Laurie A. Chalifoux MD
Department:* Anesthesiology
Does this research involve women’s health?* Yes

Abstract Title:* A Randomized Controlled Trial Comparing Combined Spinal- Epidural Dosing Strategies for External Cephalic Version

Introduction: Breech presentation is a leading cause of cesarean delivery (CD). ACOG recommends that external cephalic version (ECV) should be offered whenever possible to facilitate vertex vaginal delivery, thus avoiding the morbidity associated with CD. Meta-analyses of RCTs suggest that neuraxial techniques employing higher doses of local anesthetic result in increased ECV success. Methods: We conducted a prospective, randomized trial to assess the impact of bupivacaine dose (2.5, 5, 7.5, 10 mg) with fentanyl 15 mcg as part of a combined spinal-epidural on the success rate of ECV for breech presentation. Patients and OBs were blinded to group assignment. Secondary outcomes included mode of delivery, patient pain scores and satisfaction, OB’s perceived abdominal relaxation, length of stay, incidence of complications, and hypotension requiring vasopressor treatment. Results: 229 subjects completed the study. ECVs were performed by 79 OB’s with median performed 2 [1 to 18]. There was no difference among groups in ECV success (P=0.99). (Table) The mode of delivery and indication for CD were similar among groups. One emergent CD occurred in each group temporally related to the ECV. Discussion: Our results do not support the hypothesis of a neuraxial dose-response effect on ECV success. Previous trials comparing neuraxial technique to nothing or to systemic opiate for ECV were limited by lack of patient and OB blinding. Our overall ECV success rate of 51% was comparable to our previously published rates, but lower than other studies using high dose neuraxial techniques. This may be related to institutional practice (e.g., technique, number of attempts, threshold to abort procedure). We conclude that escalating bupivacaine dose does not confer an increase in ECV success or NSVD, but does incur an increase in hypotension and prolong length of stay.

1: Effect of intrathecal bupivacaine dose on ECV outcomes (presented as n (%) or median IQR)

<table>
<thead>
<tr>
<th>Bupivacaine intrathecal dose (mg)</th>
<th>Version success n (%)</th>
<th>Vaginal delivery n (%)</th>
<th>CD: n(%)/Malposition</th>
<th>Arrest of labor</th>
<th>Non-reassuring</th>
<th>Abdom relax (0-100)</th>
<th>ECV pain(0-100)</th>
<th>Hypotension n (%)</th>
<th>Patient satisf (0-10)</th>
<th>Time: start to D/C (min)</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.5 (n=58)</td>
<td>29 (50)</td>
<td>24 (41)</td>
<td>27 (79)</td>
<td>3 (9)</td>
<td>78 (63-91)</td>
<td>12 (1-18)</td>
<td>27 (47)</td>
<td>10 (9 to 10)</td>
<td>209 (178-291)</td>
<td></td>
</tr>
<tr>
<td>5mg (n=56)</td>
<td>29 (52)</td>
<td>21 (38)</td>
<td>26 (75)</td>
<td>5 (14)</td>
<td>83 (71-92)</td>
<td>5 (1-19)</td>
<td>43 (77)</td>
<td>10 (9 to 10)</td>
<td>230 (180-258)</td>
<td></td>
</tr>
<tr>
<td>7.5mg(n=58)</td>
<td>30 (52)</td>
<td>27 (47)</td>
<td>25 (81)</td>
<td>4 (11)</td>
<td>84 (77-94)</td>
<td>4 (0-9)</td>
<td>53 (91)</td>
<td>10 (8 to 10)</td>
<td>286 (117-355)</td>
<td></td>
</tr>
<tr>
<td>10mg(n=57)</td>
<td>28 (49)</td>
<td>21 (37)</td>
<td>26 (72)</td>
<td>6 (17)</td>
<td>87 (72-95)</td>
<td>5 (0-10)</td>
<td>49 (86)</td>
<td></td>
<td>315 (241-363)</td>
<td></td>
</tr>
</tbody>
</table>

*Abstracts longer than one page will not be accepted.
**Abstract Title:** Congenital Central Hypoventilation Syndrome (CCHS): Altered baroreflex responses to orthostatic stress

**Background:** CCHS patients demonstrate symptoms of hypoventilation and autonomic nervous system (ANS) dysfunction. Head-up tilt (HUT) is an effective tool to analyze baroreflex response to orthostatic stress. A prior report demonstrated altered baroreflex response in a small cohort (n=12) of 16-year-old clinically confirmed CCHS patients. The objective of this study is to evaluate and compare baroreflex responses in a larger and PHOX2B mutation-confirmed CCHS pediatric and young adult cohort and matched healthy controls.

**Methods:** 35 HUT tests performed in 22 unique CCHS patients (13 females/9 males) at a mean age of 13.25 ± 5.05 years were age- and gender-matched to 35 healthy controls. R-R intervals, systolic and diastolic blood pressure (BP-S and BP-D, respectively) were continuously recorded during HUT testing (20 min supine pre-HUT, 10 min HUT at 70° incline, 2 min supine for post-HUT). Mean values for the recorded variables were compared through paired sample t-tests (10-sec bins; significance p<0.05).

**Results:** Pre-HUT baseline measurements were significantly different in R-R intervals between CCHS patients and controls (91.1±2.4 SEM vs. 72.1±1.7 SEM, respectively)(p<0.001), whereas these measurements were not different in BP-S (102.2±3.1 SEM CCHS vs. 103.6±2.6 SEM controls) and BP-D (65.6±1.8 SEM CCHS vs. 65.2±1.4 SEM controls) measurements. BP-S and BP-D decrements during HUT (compared to pre-HUT) were exaggerated in CCHS patients vs. controls. But the R-R interval decrements during HUT (compared to pre-HUT) were dampened in CCHS patients vs. controls.

**Conclusions:** The exaggerated BP-S and BP-D reductions and diminished R-R interval changes in CCHS patients (compared to controls) confirm impaired baroreflex, and extend this finding throughout childhood and early adulthood in this cohort of PHOX2B mutation-confirmed CCHS patients. Despite the exaggerated BP response to HUT and the reduced ability to compensate with changes in R-R interval, most CCHS patients lack a behavioral perception to the orthostatic stress, preventing them from postural adaptation to expedite BP recovery. This may prove critical as CCHS patients are now surviving into adulthood, when baroreflex responses typically diminish. While these findings are interesting, differences in pre-HUT BP for these two groups must be considered. Further studies are indicated to determine if specific CCHS-causing PHOX2B mutations have a more or less profound effect on baroreflex and if these alterations extend into later adulthood.
Glioblastoma stem cells (GSCs) are recognized as the driving force behind the malignancy, invasiveness, chemo/radio therapy resistance, and aggressive recurrence in one of the most lethal solid tumors known to man, glioblastoma multiforme (GBM). Genetic stratification of GBM patients reveals signatures underlying their respective unique GSC phenotypes, such as the recently identified four master transcription factors (TFs), namely Sox2, Olig2, Sall2, and Pou3F2, as the core drivers of the Proneural subclass of GBM, one of the most aggressive and lethal subclass. The 4 master TFs have been shown to collectively dictate a GSC specific epigenetic state, whereas genetic knockdown of these TFs leads to epigenetically stable and differentiated states. In collaboration with MIT, we developed novel strategies to deliver siRNA encapsulated lipid polymeric nano particles (LPNPs) to counter the hyper activities of the 4 master TFs. Our hypothesis is that, targeted delivery of siRNAs encapsulated in LPNPs eliminates GSC phenotypes from the GBM cellular hierarchy, rendering more differentiated and therapeutically responsive tumor types with epigenetic fingerprints evident under super resolution imaging of the chromatin architecture. Inspired by the developments in super resolution microscopy technologies, such as photon localization microscopy (PLM) including stochastic optical reconstruction microscopy (STORM) and photo-activated localization microscopy (PALM), we have assembled a synergistic collaborative team between the Department of Neurological Surgery in the Feinberg School of Medicine and the Departments of Biomedical Engineering and Mechanical Engineering in the McCormick School of Engineering and Applied Sciences to pursue direct evidence at the chromatin level for the therapeutic benefits of anti-tumor nanomedicine. The pilot evaluation of GSC-targeting nanomedicine provides crucial evidence of therapeutic efficacy, and sets pace for personalized Precision Medicine with chromatin level validations.
Research Day Abstract

Presenting Author:* Matthew Adam Pilecki MD-MBA (In Progress)
E-mail:* m-pilecki@northwestern.edu
Position:* MD-MBA Candidate
Abstract Category:* Clinical Research and Public Health
Principal Investigator:* James C. Carr MD
Department:* Radiology

Does this research involve women’s health?* No

Abstract Title:* Cost Effectiveness Analysis of Radiological and EMB Monitoring Strategies in the First Year after Cardiac Transplantation

Introduction
Several modalities have emerged to monitor acute cardiac transplant patients for graft rejection (ACR). The established gold standard relies on a combination of frequent echocardiography, cardiac catheterization and endomyocardial biopsy (EMB). EMB is highly expensive and invasive test while newer modalities such as cardiovascular magnetic resonance imaging (CMR) offer alternative strategies for these patients. We assessed the cost effectiveness of CMR to EMB the definitive gold standard invasive strategy in the first year after cardiac transplantation.

Methods
We developed a Markov model using cost, utility of states, sensitivity and specificity of test parameters to assess the cost effectiveness and value per quality adjusted life year of various monitoring strategies. We modeled the efficacy based on the utility spent in each Markov state based on reports from literature review. Cost for procedures were estimated based on Medicare reimbursement and validated against internal institutional data.

Results
Approximately 37% of HT recipients will experience at least 1 episode of ACR in the first postoperative year at NMH. Approximately 80% to 85% of these rejection episodes respond to the initial corticosteroid regimen. The risk of infection death is highest in the first year after transplant (29% of deaths between 2 and 12 months). Nationally, there are very few instances of acute transplant rejection leading to re-transplantation in the first year post transplantation; 0.15% (n=19) and even less hyper-acute rejection episodes leading to re-transplantation 0.0014% (n=2). On average, at our institution 12.3 monitoring nodes occurred in the first year post transplant. At this level of monitoring, the average cost of invasive monitoring per patient per year is estimated to be $239,000 with effectiveness of 306.45 QALDs. The most cost effective option is CMR only; $69,229.60 with effectiveness of 308.05 QALDs.

Conclusions
A strategy of CMR with invasive monitoring is not only cost saving but effective in improving utility of life post-transplant in the first year. Further sensitivity analysis and dedicated randomized control trials may be able to identify an optimized combined protocol which is equally effective, less invasive and less costly. In the setting of increasing health care costs, potential reduction can result in significant savings for Medicare.

*Abstracts longer than one page will not be accepted.
Research Day Abstract

Presenting Author:* Chelsea M. Gustafson, PharmD
E-mail:* cgustafs@nm.org
Position:* PGY2 Oncology Pharmacy Resident
Abstract Category:* Clinical Research
Principal Investigator:* Chelsea M. Gustafson, PharmD
Department:* Pharmacology

Does this research involve women’s health?* No

Abstract Title: * Effect of Vitamin D Levels on Mobilization and Engraftment in Autologous Stem Cell Transplant Patients

Background:
Vitamin D is a steroid hormone that plays a vital role in many biological functions including immune and inflammatory modulation and mediation of the balance of calcium and phosphate. One-third of the United States population has been found to have insufficient vitamin D levels however this number has been reported up to 89% in allogeneic stem cell transplant (SCT) patients prior to transplantation. The rate of hypovitaminosis D has not been reported specifically for the autologous SCT population.

A retrospective study evaluated the impact of vitamin D levels on several outcomes in pediatric allogeneic SCT patients with and without sufficient vitamin D levels. In patients with sufficient vitamin D levels, the study found a significant increase in overall survival and relapse free survival as well as a trend towards more rapid neutrophil recovery in the 3 months post-transplant. The role of vitamin D on mobilization was studied in mice by assessing response to granulocyte colony stimulating factor (G-CSF) in vitamin D receptor (VDR) deficient subjects as compared to historical controls. Mice deficient in VDR showed virtually no mobilization response to G-CSF.

The effect of low vitamin D levels on hematopoietic stem cell mobilization and engraftment in the adult autologous SCT population has yet to be reported in the literature.

Objective:
The primary objective of this study is to evaluate the association of vitamin D levels with the number of CD34+ cells collected during mobilization and time to neutrophil engraftment in autologous hematopoietic stem cell transplant patients.

Methods:
This is a retrospective, single-center, cohort study in multiple myeloma patients receiving autologous stem cell transplants. Patients at least 18 years of age undergoing both mobilization and autologous stem cell reinfusion at the study site who have had a vitamin D level drawn prior to stem cell reinfusion will be included in the study. These vitamin D levels along with baseline characteristics and outcomes data including number of apheresis session, use of plerixafor, days to engraftment, and others will be collected. Patients will be classified based on baseline vitamin D levels as being either deficient or sufficient for evaluation. All information will be obtained through retrospective chart review.

Results:
To be presented at the 2016 Research Day
Abstract Title: Characterization of Biphasic Reaction in Pediatric Patients with Anaphylaxis

Authors: C Cochran, Z Pittsenbarger, B Smith, M Yarbrough, R Gupta, J Trainor

Background: Biphasic reaction (BR) is defined as the second occurrence of anaphylaxis symptoms following the complete resolution of initial symptoms. These reactions can be life threatening, yet literature on BR in pediatric patients is limited. Variable incidence rates have been reported from 6–15%.

Objective: Determine rate of BR in pediatric patients. A secondary aim is to identify factors associated with higher odds of BR.

Methods: Retrospective chart review of patients with anaphylaxis (per 2006 NAIAD definition) aged 0 – 18 years from 9/9/09 – 2/28/14 presenting to a tertiary care emergency department (ED). We excluded patients with chronic idiopathic anaphylaxis, transfers from outside facility, and patients developing symptoms more than 4 hours after exposure. Data extracted from the medical record included: demographics, symptoms by history, physical exam findings, pre-arrival medications, ED-administered medications, time intervals between exposure to treatment, and occurrence of BR. We used chi-square tests, Fisher’s exact test, and multiple logistic regression to examine the association between patient characteristics and BR.

Results: 528 anaphylaxis encounters were identified for analysis. 39 patients (7.5%) developed BR. There were no statistical differences in gender, age, race, or medical history between the anaphylaxis group and the biphasic group. Univariate analysis of factors showed that patients with BR were more likely to present with cardiovascular symptoms (10.3% v 2.9%, p < 0.05), GI symptoms (76.9% v 56.1%, p < 0.05), and neurologic symptoms (23.1% v 8.6%, p < 0.05). After adjusting for these characteristics, patients with GI symptoms had higher odds of BR (OR=3.6, 95% CI: 1.3 – 9.9). Patients with BR were more likely to receive diphenhydramine prior to ED arrival (74% v 55%, P, 0.05) and require albuterol in the ED (39% v 23%, p < 0.05). 24% of patients with uniphasic anaphylaxis received epinephrine prior to arrival, compared to 31% of BR patients (not significant). There were no significant differences in allergen exposure or mean time from exposure to epinephrine in either group. Mean time from exposure to BR was 182 minutes.

Conclusions: The overall rate of BR is low (7%). Patients with BR are more likely to present with GI symptoms. Time from exposure to epinephrine was not associated with increased likelihood of BR.
Research Day Abstract

Presenting Author:* Neil S. Kalsi, MD
E-mail:* nkalsi@eriefamilyhealth.org
Position:* Family Medicine Resident
Abstract Category:* Clinical Research
Principal Investigator:* Mary R. Talen, Ph.D.
Department:* Family Medicine
Does this research involve women’s health?* No

Abstract Title:* An analysis of pre-quit therapy for smoking cessation in an underserved minority population

Purpose: This is a project to evaluate the effectiveness of pre-quit treatment on smoking cessation and nicotine dependence, a novel method which uses a variation of the standard of care. Pre-quit therapy can be an effective approach for smoking cessation, smoking reduction and reduction of nicotine dependence in this low income, minority population.

Background: Tobacco use remains a significant public health issue despite a significant decline in the number of smokers. From 1965 to 2010 cigarette use prevalence has decreased from 42.4% to 19.3% (Asman). Recent studies have demonstrated the effectiveness of using nicotine replacement therapy (NRT), varenicline and bupropion in a novel way, called pre-quit treatment, to enhance patient’s smoking cessation. In a recent meta-analysis that compared physician advice alone to physician advice plus medications, regardless of a patient’s motivation to quit, patients who were prescribed medication had a significant increase in quit attempts and abstinence rates.

Goal: This project is designed to evaluate if patients who are smokers but prescribed pre-quit medications have an effective on patients’ smoking status. The goal of this retrospective study is to evaluate the effectiveness of pre-quit therapy in a predominately urban, underserved patient population in a federally qualified health center. The project was approved by the Erie Family health Center review committee.

Method: This is a retrospective cohort study evaluating the differences in smoking status and dependence between patients who are current smokers and received pre-treatment medications to patients who are current smokers and did not receive pre-treatment medications (e.g. varenicline or bupropion). There are approximately 500 patients who have been identified as smokers in this cohort at the Erie Humboldt Park Healthcenter. Pregnant women will be excluded in the study.

Subjects: Adult patients (18-65) who are current smokers and seen by a primary care provider in the past two years (2014-2016). Patients will be active patients at Erie Family Health Center Humboldt Park in Chicago, IL.

Outcomes: The analysis will include an evaluation of the differences of smoking status (packs per day) and readiness to quit between patients who received pre-quit treatments and patient who did not.

*Abstracts longer than one page will not be accepted.
Research Day Abstract

Presenting Author:* Michael Blanco, MD  
E-mail:* michael.blanco@northwestern.edu  
Position:* Resident  
Abstract Category:* Clinical Research  
Principal Investigator:* Monique Hinchcliff, MD  
Department:* Medicine  

Abstract Title:* Esophageal Dilation and Health Related Quality of Life in Systemic Sclerosis

**Background:** Esophageal dysmotility has been found in ~90% of patients with systemic sclerosis (SSc). Neuronal dysfunction, vascular perturbations, smooth muscle atrophy and fibrosis likely underlie the disease. Study results suggest that there is an association between esophageal dysmotility and interstitial lung disease. The study goals were to determine if widened esophageal diameter ( surrogate for esophageal dysmotility) on high-resolution computed tomography (HRCT) is associated with decreased health-related quality of life in patients with SSc ( surrogate for ILD).

**Materials and Methods:** One hundred fifty-one patients with SSc with HRCT and patient-reported outcome (PRO) questionnaires within 6 months of clinic visit were studied. Widest esophageal diameter (WED) was defined as the largest of the following three supine HRCT supine esophageal diameter measurements: (1) top of the aortic arch, (2) between the right inferior pulmonary vein and the aortic arch, and (3) between the diaphragmatic hiatus and the right inferior pulmonary vein. The following validated PRO measures were administered: Patient Reported Outcome Measure Information System (PROMIS)-29, Functional Assessment of Chronic Illness Therapy (FACT)-Dyspnea, Scleroderma Health Assessment Questionnaire (SHAQ), UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT 2.0) and Modified Medical Research Council (MMRC) Dyspnea Scale. The association between WED and PRO instruments was assessed using linear regression models adjusted for age, sex, race, BMI, SSc duration and subtype and smoking status.

**Results:** The mean patient age (82% female) was 51y (range 18-84). The mean SSc disease duration from the first non-Raynaud phenomenon symptom was 7y (range 0-42). Limited (51%) and diffuse cutaneous (49%) SSc subtypes were equally represented. Means and standard deviations of PRO measures are shown in Table 1. The mean scores for PROMIS-29 and FACT-Dyspnea domains were not statistically significant (range -0.112 to 0.060, P-value range 0.25 to 0.91) per WED mm increase. Pearson correlation coefficients between WED and SHAQ domains (intestinal problems, breathing problems and disease severity) (range 0.0154 to 0.0653), UCLA SCTC GIT 2.0 (total GIT score) (0.0665), and MMRC (0.1152) were low.

**Table 1. Summary Statistics of PRO measures and WED.**

<table>
<thead>
<tr>
<th>PRO measures</th>
<th>N</th>
<th>Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PROMIS-29 General Health Index (T-score)</td>
<td>151</td>
<td>51.64 (9.23)</td>
</tr>
<tr>
<td>• Anxiety</td>
<td>151</td>
<td>50.35 (9.24)</td>
</tr>
<tr>
<td>• Depression</td>
<td>151</td>
<td>53.75 (10.82)</td>
</tr>
<tr>
<td>• Pain</td>
<td>151</td>
<td>55.34 (10.08)</td>
</tr>
<tr>
<td></td>
<td>151</td>
<td>44.64 (8.43)</td>
</tr>
<tr>
<td>• Social Roles and Activity</td>
<td>151</td>
<td>46.82 (10.74)</td>
</tr>
<tr>
<td>• Sleep Disturbance</td>
<td>151</td>
<td>51.88 (8.91)</td>
</tr>
<tr>
<td>FACIT Dyspnea Score (T-score)</td>
<td>145</td>
<td>42.11 (9.07)</td>
</tr>
<tr>
<td>• Functional Limitation Score</td>
<td>144</td>
<td>42.44 (9.7)</td>
</tr>
<tr>
<td>WED (mm)</td>
<td>151</td>
<td>18.91 (8.78)</td>
</tr>
</tbody>
</table>

**Conclusion:** There were no significant associations between WED on HRCT and health-related quality of life as assessed by PRO measures in patients with SSc. Methodological issues including imprecise PRO measures (FACT-Dyspnea was developed and validated in COPD patients), an imprecise WED predictor variable (fed state may affect WED) or an imprecise exposure (WED is not important in SSc-ILD or we did not measure it accurately). Additionally, our results may have been influenced by other unmeasured confounders. Another possibility is that our hypothesis may be incorrect, and there is no association between esophageal dilatation and SSc symptoms. Future studies should be designed to account for fed state when assessing WED.
Lymphoma affects many young women of childbearing age. The American Society of Clinical Oncology recommends early discussion regarding the reproductive risks of cancer treatment and referral to fertility preservation (FP) specialists when appropriate. In spite of this recommendation, rates of physician-documented discussions and referral remain low. Reasons for low referral rates include fear of treatment delay. To date, the real-life treatment delay and its effect on treatment outcomes among female lymphoma patients attempting fertility preservation has not been reported. We performed a retrospective analysis of female lymphoma patients who completed fertility preservation (FP) at our institution. Our primary objective was to assess the median treatment delay associated with FP. Our secondary objective was to assess relapse free survival (RFS). Time to treatment (TTT) was defined as the time from the initial hematology consult until the initiation of therapy. Relapse free survival (RFS), which was defined as time from date of treatment until relapse or death, as determined by either date of biopsy or imaging, if no biopsy was performed. Of 128 subjects, 50 controls and 33 women who underwent FP were analyzed. Median time to treatment among FP patients was 28 days (range: 18-76) versus 15.5 days (range: 0-74) for controls, resulting in a median delay of 12.5 days (p<0.001). There was no difference in relapse free survival (RFS) between groups (Table 1: Controls: 1 year RFS=93.5%, 5 year RFS=84.6%; FP: 1 year RFS=83.6%, 5 year RFS = 73.5%, p=0.23). Factors other than fertility preservation led to treatment delays prior to and after fertility preservation. Among FP patients, the median time from hematology consult until first estradiol draw was 10 days (range 0-22), and there was a median of 7.5 days additional delay after oocyte retrieval (range 0-22). The median number of days to complete stimulation protocol was 11 (range: 5-14). A median of 14 (range: 0-37) oocytes were retrieved per patient. In 2 women, no oocytes could be successfully retrieved. Five women achieved pregnancy following fertility preservation. Of these, 3 were spontaneous, and 2 required reproductive assistance; one from frozen embryos and one from frozen oocytes. Of three women returning to use their frozen gametes, 2 were successful, and one was unsuccessful. Overall this study shows that fertility preservation is feasible and results in a small delay in therapy for women of childbearing age with lymphoma. This approach does not appear to affect outcomes in our study.

**Table 1.** Median TTT in days (range) and RFS

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>All (range)</th>
<th>Frontline (range)</th>
<th>R/R (range)</th>
<th>1 yr (%)</th>
<th>5 yr (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FP</td>
<td>33</td>
<td>28 (18-76)</td>
<td>28 (18-47)</td>
<td>27.5 (22-76)</td>
<td>83.5</td>
<td>73.5</td>
</tr>
<tr>
<td>Control</td>
<td>50</td>
<td>16 (0-74)</td>
<td>15 (3-74)</td>
<td>17 (0-55)</td>
<td>93.5</td>
<td>84.6</td>
</tr>
<tr>
<td>p value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>0.05</td>
<td>0.23</td>
<td>0.23</td>
<td></td>
</tr>
</tbody>
</table>

**Figure 1. Median Time to Treatment**

Time to initiation of lymphoma therapy in patients who underwent fertility preservation compared to controls. Fertility preservation resulted in a median treatment delay of 12.5 days (p<0.001).
Objective:
To assess the increased utilization of multiparametric magnetic resonance imaging (mpMRI) and fusion biopsy of the prostate, we compared prostate cancer detection rates among a) men undergoing MR-US fusion biopsy, b) mpMRI cognitive-registration biopsy and c) conventional transrectal ultrasound-guided biopsy for the detection of prostate cancer.

Methods: Retrospective review of consecutive patients undergoing mpMRI of the prostate with subsequent prostate biopsy from October 2013 to September 2015. Lesions concerning for prostate cancer visualized on mpMRI were targeted with cognitive-registration or MR-US fusion biopsies. A cohort of men undergoing conventional prostate biopsy was utilized for comparison. Rates of cancer detection were compared among the three cohorts.

Results: 231 patients underwent mpMRI-targeted biopsy (81 fusion, 150 cognitive). There was no difference in PSA, mpMRI-defined PIRADS score or number of lesions, or history of prostate cancer among cohorts. The overall detection rate of cancer was significantly higher in the fusion cohort (48.1%) compared to both the cognitive (34.6% p=0.04) and conventional (32.0%, p=0.03) cohorts. Cancer detection rates were comparable in the MRI-cognitive and TRUS biopsy groups (34.6% vs. 32%). MR-fusion detected significantly more Gleason > 7 cancer (61.5 vs. 37.5%, p=0.04) and significantly less Gleason 6 cancer (38.5 vs. 62.5%, p=0.04) compared to conventional biopsy.

Conclusions:
Targeted biopsy of the prostate using MR-US fusion increased the cancer detection rate compared to both cognitive registration and conventional biopsy and was associated with detection of higher-grade cancer compared to conventional biopsy.

Table 1: Biopsy results of convention 12-core extended sextant transrectal biopsy vs. magnetic resonance-ultrasound fusion transrectal biopsy

<table>
<thead>
<tr>
<th></th>
<th>Conventional</th>
<th>MR-US Fusion</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of cores (IQR)</td>
<td>12.1 (11.5-13)</td>
<td>15.2 (13-18)</td>
<td>0.54</td>
</tr>
<tr>
<td>Prostate cancer detection</td>
<td>32% (32/100)</td>
<td>48.1% (39/81)</td>
<td>0.03</td>
</tr>
<tr>
<td>Gleason score 6</td>
<td>62.5% (20)</td>
<td>38.5% (15)</td>
<td>0.12</td>
</tr>
<tr>
<td>7 or higher</td>
<td>37.5% (12)</td>
<td>61.5% (24)</td>
<td>0.04</td>
</tr>
</tbody>
</table>