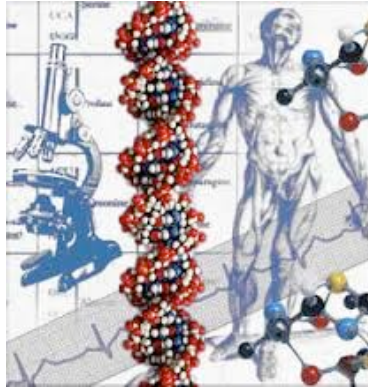


*East Carolina University
Brody School of Medicine
2016 Summer Scholars
Research Program*



Medical Student Research Day

August 8th, 2016
Brody Commons
Brody Medical Sciences Building

The Brody School of Medicine Summer Scholars Program would like to express its sincere gratitude to the following individuals and participating faculty of the following departments for their support of the 2016 Program. Those listed provided financial support for student stipends, research resources, administrative support and/or provisions for the 2016 Medical Student Research Day. These generous contributions make it possible for BSOM students to learn and make their own contributions to the field of medicine through scholarly pursuits.

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ABSTRACTS

ADJUVANT PERIOPERATIVE CHEMOTHERAPY VERSUS POSTOPERATIVE CHEMORADIO THERAPY IN TREATMENT OF GASTRIC ADENOCARCINOMA

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Background: Both perioperative chemotherapy and postoperative chemoradiotherapy have a significant survival advantage over surgery alone for the treatment of gastric cancer. However, the advantage of one regimen over the other has never been studied.

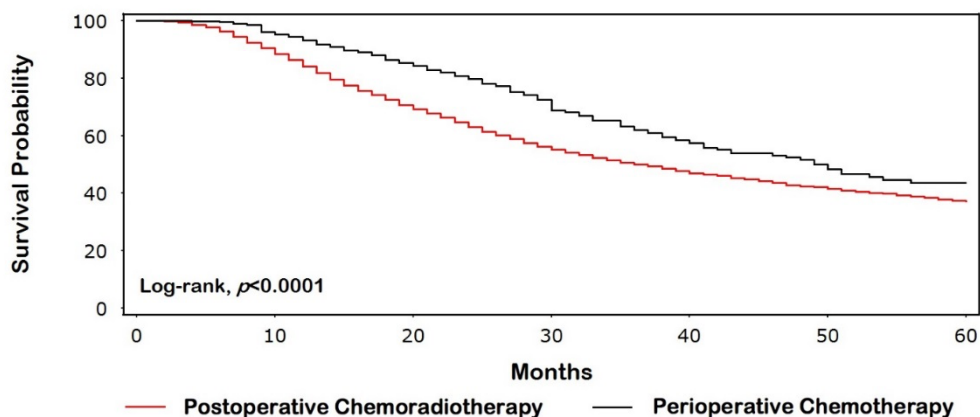
Objective: The purpose of this study is to determine the survival advantage of perioperative chemotherapy compared with postoperative chemoradiotherapy in the treatment of gastric and gastroesophageal adenocarcinoma.

Methods: Patients with resected stage II and III adenocarcinomas of the stomach or gastroesophageal junction (GEJ) from 2004-2013 were identified using the National Cancer Database.

Results: A total of 5,617 patients were identified. The majority were male (68%), white (66%), and with a Charlson Comorbidity Index (CCI) of <1 (74%). Adjusting for age, race, ethnicity, CCI, tumor size, stage, and grade, patients receiving perioperative chemotherapy survived significantly longer than those receiving postoperative chemoradiotherapy (HR=.56, 95%CI=.48-.65; $p<.0001$) (see figure). Similar results were observed when data were stratified by stage (stage II HR=.76, 95%CI=.61-.95, $p<.016$; stage III HR=.47, CI95%=.38-.58, $p<.0001$) and primary site (GEJ HR=.54, 95%CI=.44-.68, $p<.0001$).

Conclusions: In the largest series to date for stage II/III resectable gastric and gastroesophageal adenocarcinoma, from over 1,500 Commission on Cancer (CoC)-accredited facilities, perioperative chemotherapy was shown to have a significant survival advantage over postoperative chemoradiotherapy.

Figure 1: Overall survival for perioperative chemotherapy and postoperative chemoradiotherapy.



CHARACTERISTICS OF PATIENTS DIAGNOSED WITH CATASTROPHIC CUTANEOUS CARCINOMATOSIS

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Background: Catastrophic Cutaneous Carcinomatosis (CCC) is a dermatologic condition in which a non-organ transplant patient is diagnosed with ten or more nonmelanoma skin cancers in a one year period. We identified patients from a large skin cancer data base who had been diagnosed with at least ten nonmelanoma skin cancers in one year. We looked at characteristics of these patients and if they could be diagnosed with CCC.

Objective: We performed a retrospective chart review at the Brody School of Medicine of dermatology patients with 10 or more cases of nonmelanoma skin cancer in a one year period to identify characteristics of these patients.

Methods: Brody School of Medicine's EHR and paper charts were used to review patients diagnosed with 10 or more cases of basal cell carcinomas and/or squamous cell carcinomas in a one year period. The characteristics of the 37 patients eligible for the study were compiled and analyzed to determine correlations. One patient's chart was unable to be located.

Results: Of the 37 patients eligible for the study all were Caucasian with 78% of our patients being males. Approximately half (41%) of our patients were immunosuppressed. Hypertension was common with 70% of our patients having high blood pressure. Eight patients diagnosed with diabetes had a comorbidity of hypertension as well. Twenty-one of 37 patients (57%) were deceased. Of the patients who were deceased 5 (24%) died due to skin cancer. Patients who were immunosuppressed were younger at the onset of their first skin cancer by 15 years. This was a statistically significant difference. There was also a statistically significant difference in the number of basal cell carcinomas; immunocompetent patients had more basal cell carcinomas than immunocompromised patients. Patients who were immunosuppressed showed a greater number of squamous cell carcinomas, however this data was not statistically significant.

Conclusion: The data shows that the majority of patients diagnosed with Catastrophic Cutaneous Carcinomatosis will be Caucasian and male. Many CCC patients will have a comorbidity of hypertension. Differences in the rates of squamous cell carcinomas and basal cell carcinomas exist between patients who are immunosuppressed and immunocompetent. Patients with multiple skin cancers suffer significant morbidity and many die from their disease. Management requires a coordinated multispecialty approach.

IS CIRCULATING GLUTAMINE THE UNKNOWN FACTOR DRIVING α -CELL HYPERPLASIA IN GLUCAGON RECEPTOR-INACTIVATED ZEBRAFISH?

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There is a developing interest in identifying ways to interrupt glucagon signaling pathway as a potential treatment for diabetes. One method of interrupting glucagon signaling is by inactivating the glucagon receptor (*Gcgr*); however, significant α -cell hyperplasia is observed in *Gcgr*^{-/-} mice and zebrafish. The exact mechanism of the observed α -cell hyperplasia is unclear. It has been shown in mice that α -cell hyperplasia is driven via the mTOR signaling pathway by elevated serum amino acid levels. We analyzed blood samples from adult zebrafish and confirmed that serum amino acid levels are significantly higher in *gcgr*^{-/-} than in wt zebrafish. Culturing in medium containing amino acid levels similar to those in the serum of *Gcgr*^{-/-} mice induced rapid α -cell expansion in 7 day old wt larvae. Interestingly, we observed that α -cell expansion ceased with increasing amino acid concentrations in the absence of glutamine. Finally, CRISPR mutagenesis of the *slc38a5a&b* genes, which encode neutral amino acid transporters highly expressed in the pancreas, normalized α -cell number in *gcgr*^{-/-} zebrafish. Collectively, the data suggest that glutamine plays a significant role in promoting rapid α -cell expansion and long-term hyperplasia in *gcgr*^{-/-} zebrafish, however it may not be the only factor involved.

PERCEPTION OF AGE AS AN INDICATOR OF COMPLIANCE IN PURCHASING ALCOHOL

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Background: The North Carolina Alcohol Beverage Control Law prohibits the sale of alcohol to anyone under the age of 21. Unlike the state law for tobacco demanding proof of identification; laws regarding the purchase of alcohol does not specifically demand proof of identification for everyone. Statutory language allows retailers to use their own perception of the purchaser's age to determine if the purchaser is of required age.

Objective: To examine the effectiveness of using age perception as an indicator of compliance for purchasing alcohol in retail outlets located in an eastern North Carolina county.

Method: A randomized survey of retail outlets selling alcohol in an eastern county was conducted in partnership with a community based coalition. A surveyor was selected who appeared to be near the age of 21. This individual attempted to purchase alcohol without proper identification from convenient, grocery, drug and liquor stores in an eastern North Carolina county. Compliance was assessed based upon results of purchase attempt.

Results: The total sample size was 91; of which 57 attempts to purchase alcohol without proper identification were successful, resulting in an overall compliance rate of 37%. It was determined that convenient stores had the least compliance rate at 28% while grocery stores had the highest at 64%. When considering store clerk characteristics, results indicate male clerks were least likely to ask for identification.

Conclusion: The practice of using perception of age by retail outlets for the purchase of alcohol can result in non-adherence with North Carolina law. Study results indicate the need for future studies with a larger sample size for generalizing results to broader populations.

PROFILING PATIENTS RECEIVING CANCER DIAGNOSES THROUGH THE EMERGENCY DEPARTMENT

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Background: Cancer management and therapeutic intervention is most beneficial if detected during early stages of disease, which highlights the importance of effective screening procedures and routine health care visits to evaluate early symptomatology. Nevertheless, diagnosing cancer as a direct result of emergency department visits is not uncommon. As such, efforts to stratify patients at high-risk for delayed diagnosis may allow clinicians to improve morbidity and mortality related to cancer.

Hypothesis: We hypothesized that patients receiving their initial cancer diagnosis through the ED will have more advanced diseases as well as more comorbidities determined via calculated Charlson Comorbidity Indexes (CCIs).

Methods: Data was obtained from emergency department visits at Vidant Medical Center in Pitt County made during 2014-2015 that were associated with an oncological related ICD-9 code. A retrospective review was conducted and statistical analyses were performed using JMP 12 software.

Results: Diagnosis by Emergency Department was recorded in 21.1% of patients analyzed (n=64/303). Survival time following diagnosis was significantly lower in individuals diagnosed in the ED (72 months vs. 5 months, $p < .0001$) indicating that these patients had more advanced diseases than their counterparts. Compared to patients not diagnosed in the ED, patients were of older age, predominately male, had higher CCIs, and most commonly identified as African-American.

Conclusion: Identified high-risk groups may benefit from interventions to reduce delayed diagnoses. Further studies should be conducted to profile patients receiving initial cancer diagnoses via the ED in other regions of the country. In addition, efforts should be made to understand how emergency presentations of cancer arise.

COMPARING LUNG INFLAMMATORY RESPONSES IN C57 MICE WITH PPAR γ -KO MICE AFTER INSTILLING WITH MULTIWALL CARBON NANOTUBES AND ESAT-6

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Background: Prior research in this lab has shown that mice instilled with multiwall carbon nanotubes (MWCNT) develop chronic granulomatous disease. ESAT-6 is a T cell activator that is associated with sarcoidosis and tuberculosis. Mice instilled with MWCNT and ESAT-6 develop more extensive lung granulomas with fibrosis, than with MWCNT alone. Macrophage specific PPAR γ KO mice have more extensive granulomatous disease than C57 (wildtype) mice.

Hypothesis: PPAR γ KO mice instilled with MWCNT and ESAT-6 by an oropharyngeal route will have increased granuloma formation compared with C57 mice given the same treatment.

Methods: Lungs were surgically removed from mice and frozen in OCT. Using a cryostat, 7 μ m sections were placed onto glass slides. Sections were stained with antibodies for CD11c (dendritic cell and macrophage/ monocyte marker) and Siglec F (macrophage marker) and imaged using confocal microscopy. A previously established scoring system was utilized to compare the sizes of granulomas in the different mice strains in the modified Wright's stain images.

Results: Granulomas in PPAR γ KO mice were increased in frequency and size compared to C57 mice when instilled with MWCNT and MWCNT + ESAT-6. CD11c is not changed in alveolar macrophages, whereas Siglec F is increased in PPAR γ KO mice. PPAR γ KO mice lungs had increased binding of CD11c and Siglec F compared to C57 mice. Additionally, both PPAR γ KO and C57 lungs displayed more severe granulomatous pathology when instilled with MWCNT + ESAT-6, rather than MWCNT alone.

Conclusion: The increased granulomatous disease in PPAR γ KO mice compared to C57 mice supports the hypothesis that PPAR γ and its mediated pathways have a role in preventing granuloma formation. The exacerbated granulomas seen in MWCNT + ESAT-6 versus those seen in lungs instilled with MWCNT alone further demonstrate that ESAT-6, when combined with MWCNT causes increased granuloma formation. Macrophage specific PPAR γ KO mice instilled with MWCNT and ESAT-6 could be a potential model to study human sarcoid disease, a chronic inflammatory lung disease of unknown etiology that mainly effects the lungs.

ASTHMA-OBESITY STUDY: MICRORNA 155 AS A POTENTIAL PRIMING FACTOR FOR ASTHMA IN OBESE PATIENTS

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Background: Epidemiologic studies have shown that obesity is positively correlated with asthma. Recent work has demonstrated that microRNA (miR-155) is significantly increased in alveolar macrophages from obese patients when compared to lean patients, and the clinical significance of this miR-155 elevation has not been investigated. Most adults living with obesity-associated asthma have Th2-low (non-allergic) asthma and do not see improvements in their symptoms with standard steroid therapy. This lack of effective treatment for Th2-low asthma patients represents a major clinical problem and miR-155 is being investigated as a therapeutic target or biomarker.

Hypothesis: microRNA, miR-155, is a priming factor for exacerbated inflammatory dysfunction observed in adult patients with obesity-associated asthma.

Methods: Patients from ECU Severe Asthma Clinic who had been seen by Arjun Mohan, MD were screened to see if they met inclusion criteria for this study. Once all the subjects have been recruited, they will undergo a bronchoscopy. Alveolar macrophages and airway epithelial cells will then be assayed for miR-155, TNF α , and PPAR γ .

Results: At this time, there are no results, as the study is ongoing. This study is currently in the subject recruitment phase.

Conclusion: Currently, 144 asthma patients have been screened. Out of those patients, there are eight possible candidates. The goal is to recruit five subjects for each group of the study.

AUTOPSY MORTALITY REVIEW PROVIDES CLINICALLY IMPORTANT INFORMATION THAT CAN IMPROVE PATIENT CARE

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Background: The Institute of Medicine Report on improving diagnosis in healthcare promotes development and deployment of approaches to "identify, learn from, and reduce diagnostic errors and near misses in clinical practice". Autopsies are a historically validated and presently underutilized method that can address Institute of Medicine recommendations.

Objective: To determine whether certain types of death, such as unexpected deaths and death within 48 hours of admission, are associated with more quality issues than other types of deaths, and if death related to specific organ systems are more likely to be associated with more quality issues.

Methods: A form was created based on a review of methods used to determine the UHC mortality index and mortality and peer review being conducted nationally by hospitals. The one-page Mortality Review Form (see Figure 4) was completed by three board-certified, forensic pathologists based on their initial autopsy findings and medical record review for 48 autopsy cases performed from 01/06/15 to 07/05/16. Responses were then collated and statistical significance determined using chi-squared analysis at $p < 0.05$. Categories were also analyzed by organ system responsible for primary cause of death based on review of 40 adult, final autopsy reports and statistical significance determined.

Results: 31 deaths were expected and 17 unexpected. Quality issues were identified in 7 deaths; 4 of these were attributed to a system or process issue, 2 to both a system or process issue and a physician issue, and 1 to neither. Specific issue identification included patient evaluation/data acquisition (3), clinical decision making (3), performing a treatment or procedure (2), and communication and coordination (2). Statistical analysis showed that there were significantly more quality issues associated with unexpected deaths ($p = 0.003$), death associated with an adverse event or drug reaction ($p = 0.008$), death where the diagnostic workup was inadequate ($p = 0.009$), death where abnormal findings were not addressed ($p = 0.022$), death associated with diagnostic failure ($p = 0.009$), and death within 48 hours of a procedure ($p = 0.0001$). When primary cause of death by organ system was analyzed, death within 48 hours of admission was found to be more often associated with cardiac deaths ($p = 0.018$).

Conclusion: A structured mortality review form can provide important information to improve patient care, identifying subsets of patients where the autopsy is more likely to reveal quality issues, and enabling hospitals and physicians to focus on improving processes that will potentially reduce unexpected deaths.

ENHANCEMENT OF OPIOID-INDUCED MECHANICAL ANALGESIA VIA ACTIVATION OF D3 DOPAMINE RECEPTOR FOLLOWING SPINAL CORD INJURY

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Background: Of the 23 per million individuals worldwide who have sustained traumatic spinal cord injuries (SCI), one-third experience chronic neuropathic pain. Neuropathic pain is commonly treated with opioids, but long-term opioid use can result in tolerance and addiction. Recent studies suggest that the addition of a Dopamine D3 receptor (D3R) agonist may improve the clinical efficacy of opioid use in SCI.

Objective: To determine the effect of D3 agonist paired with morphine by intraperitoneal injection on mechanical and thermal pain thresholds, addictive potential, and spinal cord D3R and MOR expression levels in rats after traumatic SCI vs. sham surgery.

Methods: Von Frey and Hargreaves tests were performed after SCI or sham surgery in the absence of drug, after administration of morphine (2.5 mg/kg or 1.0 mg/kg), and after administration of morphine in combination with the D3R agonist pramipexole. Conditioned Place Preference (CPP) was used to assess the addictive potential of the drug treatment. ELISA and Western Blot analyses were used to determine protein levels of D3R and MOR.

Results: SCI reduced mechanical and thermal thresholds compared to the sham rats. The addition of pramipexole to 1.0mg/kg morphine increased mechanical thresholds in the sham rats, but had no significant effect in SCI rats. The addition of pramipexole to 1.0mg/kg morphine provided greater analgesia to mechanical stimulation for sham rats than 2.5mg/kg of morphine alone. SCI rats treated with 1.0mg/kg or 2.5mg/kg of morphine in combination with pramipexole showed significant increases in mechanical pain thresholds when compared to 2.5mg/kg morphine alone. The addition of pramipexole to 1.0mg/kg and 2.5mg/kg morphine dosages showed no significant thermal analgesic benefit in sham rats. The highest dose of morphine alone provided better thermal analgesia than any other drug dose or combination and showed no added analgesia when pramipexole. Conditioned placement preference (CPP) showed that sham rats treated with 2.5mg/kg morphine and 2.5mg/kg morphine + pramipexole developed the same degree of preference for the drugs. After SCI, a greater proportion of MOR receptors were phosphorylated compared to sham animals. ELISA assay of D3R showed no significant change in D3R in SCI rats compared to sham rats.

Conclusion: Our data suggest that activation of the D3R may enhance opioid-induced mechanical analgesia, but not thermal analgesia. This effect is different in sham vs. SCI animals. Additionally, lower doses of morphine may provide more analgesia for neuropathic pain after SCI.

SELF-REPORTED NUTRITION BEHAVIORS IMPROVE AS A RESULT OF MATCH OBESITY INTERVENTION IN MIDDLE SCHOOL STUDENTS

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Background: Childhood obesity is a major public health concern worldwide. Motivating Adolescents with Technology to CHOOSE Health™ (MATCH) is an intervention program implemented within public schools' core curriculum aimed to promote healthy behavior changes among 7th grade students. During the 2015-16 school year, new validated nutrition assessment questions were added to a Sleeping, Eating, Activity, and Technology (SEAT) survey used to describe student health behaviors pre- and post-MATCH. When delivering interventions, effectiveness often is related to increased fidelity of program implementation and participant "stage of change" (SOC), which can be characterized into "action" versus "pre-action" categories demonstrating greater readiness for behavior change.

Hypothesis: When comparing groups, greater change in self-reported nutrition behaviors will be seen for students at higher fidelity schools and students that self-report in an action SOC category.

Methods: Students participating in MATCH in 2015-16 completed pre- and post-MATCH SEAT surveys. Questions assessed self-reported nutrition behaviors and SOC. Analyses were conducted to examine for change in behaviors from pre- to post-MATCH and whether level of fidelity (measured by number of lessons taught) or SOC were associated with a greater degree of change. Wilcoxon rank sum was used for significance.

Results: Students (N=2,355) from 32 schools (28 in NC, 4 in SC) completed a pre- and post-SEAT survey and were included in this study. Mean change in reported frequency of intake was significantly lower post-MATCH for sugar-sweetened beverages (SSB) (1.1 times/week; p=0.0137), total snacks (3.0 times/week; p=0.0023), and fruits (1.1 times/week; p=0.0006). High fidelity schools did not show greater reduction in consumption compared to low fidelity schools. For example, SSB consumption reduced by 1.2 times/week (p=0.0468) in high fidelity schools, but reduced by 4.8 times/week (p=0.0653) in low fidelity schools. Students in a pre-action SOC category had a greater mean change in reported frequency of intake with a significant reduction in snacks (7.2 times/week) compared to students in an action SOC that increased their consumption by 1.0 times/week (p=0.0055).

Conclusion: Results from the validated nutrition questions demonstrated that after MATCH participation, students self-reported nutrition behaviors improved significantly, supporting program effectiveness. However, a higher level of fidelity and SOC were not associated with greater change. More analyses are needed to understand how fidelity of schools and/or SOC may play roles in nutrition behavior change.

HIF1- α IS SUFFICIENT TO STABILIZE VEGF mRNA UNDER HYPOXIA IN HEK293T CELLS

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Background: Hypoxia is involved in a number of pathological conditions, such as heart disease, stroke, and cancer angiogenesis. Under hypoxic conditions, cells alter both the transcriptional and post-transcriptional response in order to adapt to their environment.

Objective or Hypothesis: To determine if HIF transcriptional activity is necessary and/or sufficient for the stabilization of VEGF or MYC mRNA in HEK293T cells under hypoxia.

Methods: HEK293T cells were placed in 1g/L DMEM and treated with siRNA, HIF1- α plasmid, HIF2- α plasmid, hypoxia mimetics, and/or were placed in a Ruskin InVivo400 Hypoxic Incubator. After 24 hours treatment mRNA half-life was determined via Actinomycin D decay.

Results: Treatment of HEK293T cells with hypoxic mimetics had no significant effect on VEGF or MYC mRNA half-life. Overexpression of HIF1- α showed an increase in VEGF mRNA half-life, whereas there was no increase in MYC mRNA half-life. HIF2- α overexpression showed no increase in the half-life for either VEGF or MYC, but there was a significant increase in the amount of VEGF protein in comparison to the other conditions. VEGF mRNA half-life results from the knockdown of HIF1- α with siRNA plasmid were inconclusive. Knockdown of ARNT1 by siRNA was inconclusive, suggesting that ARNT2 may be compensating.

Conclusion: Overexpression of HIF1- α is sufficient to stabilize VEGF mRNA under normoxic conditions in HEK293T cells, whereas HIF2- α appears to play no role in mRNA stabilization but does increase VEGF protein translation significantly. Neither HIF1- α nor HIF2- α play any role in the stabilization of MYC mRNA. Further research is needed to determine if HIF1- α is absolutely necessary for the stabilization of VEGF mRNA and what is stabilizing MYC mRNA under hypoxia.

SKILLED NURSING FACILITY RESIDENCE DOES NOT APPEAR TO INCREASE RISK OF DVT

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Background: Proximal lower extremity deep vein thrombosis (LE DVT) lead to pulmonary emboli (PE) in up to 50 percent of patients, resulting in up to 300,000 deaths annually¹. While recognized risk factors include prolonged physical inactivity, vessel injury, and coagulopathy, the decreased mobility accompanying skilled nursing facility (SNF) residence has not been evaluated to determine if these patients presenting to the ED experience a higher risk of developing DVT than the general population.

Hypothesis: Due to reduced mobility in SNFs and the increased risk of DVT associated with reduced mobility, SNF residents experience an increased risk of DVT.

Methods: Through a cross-sectional convenience sample, we identified patients presenting from a SNF to the Vidant Medical Center Level 1 Trauma ED with chief complaints unrelated to a DVT from June 1, 2016 to July 27, 2016. Patients were identified using EHR-Epic and then approached for consent. Demographic and medical history information were obtained from the consented patient, the patient's family, and the patient's medical record. A bedside focused LE DVT ultrasound was then performed.

Results: The DVT incidence among enrolled participants was 0. Twenty-two patients were approached; 3 were excluded based on study criteria, 4 refused participation, and 2 were removed due to a consent process issue leaving 13 enrolled patients (9 long-term and 4 short-term residents). Males (3) had an average age of 82 years (range 72-89) and females (10) had an average age of 77.5 years (range 65-89). SNF admission diagnoses included cognitive impairment (1), CVA (1), failure to thrive (6), and other ailments (5). With regard to mobility status, no patient enrolled was completely bedbound or was fully independently mobile whereas 4 relied on a walker/cane and 9 relied on a wheel chair. Five were on daily antiplatelet therapy, 2 were on daily anti-coagulant therapy, 1 was on daily combined therapy, and 5 received no daily therapy. Only 2 presented with prior DVT/PE history but neither reported current DVT symptoms. Of 11 without prior DVT history, 1 reported leg swelling and 1 reported both leg pain/swelling. Only 2 had amputations.

Conclusions: Although limited by the number of patients enrolled, we could not identify any subset of SNF residents in this sample who were at an increased risk of DVT compared to the general population. There was no measurable correlation of increased risk of DVT in SNF residents to any of the demographic or medical history factors examined.

References

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PATIENTS PRESENTING TO THE MINOR EMERGENCY DEPARTMENT AT VIDANT
MEDICAL CENTER ARE AT AN INCREASED RISK FOR UNINTENDED PREGNANCY
COMPARED TO THE NATIONAL AVERAGE

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Background: The Emergency Department (ED) is a common site of provision of non-emergent care or care that could be provided by family practice physicians. A previous study has attributed this to the ED's mandate to see patients regardless of ability to pay, patients lack of main health care provider and health insurance. Because of this, female patients presenting to the ED may be at a higher risk of unintended pregnancy; the ED may represent a viable location for provision of contraceptives.

Hypothesis: Women in the minor ED are at an increased risk of pregnancy compared to the general population due to higher rates of uninsured patients and low income patients.

Methods: Using an 18-question, anonymous, self-reported survey of female patients ages 18-49 presenting to the minor Emergency Department (ED) of Vidant Medical Center we determined the risk of pregnancy compared to the general population. Patients who were already pregnant, previously had a hysterectomy, or were being transferred up to the main Emergency Department were excluded from the study. Patients were identified as being at risk of unintended pregnancy if they were not trying to get pregnant, did not use any contraception in their last sexual encounter, used withdrawal as their primary method of contraception, or reported "sometimes" using condoms and no other method of pregnancy prevention.

Results: Of 101 patients surveyed, 31 (30.7%) were at risk for unintended pregnancy; this is statistically higher than the national average of 5.2% ($p < 0.0001$). More data is required to assign correlation between various demographic factors included in the survey.

Conclusion: These data support previous studies that patients in the ED are at a higher risk of unintended pregnancy than the national average. Women of childbearing age in the ED may benefit from contraceptives provided in this setting.

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COMPARATIVE EFFECTIVENESS OF SLEEVE GASTRECTOMY AND GASTRIC BYPASS IN THE ELDERLY POPULATION

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Background: Bariatric surgery in the elderly population remains a controversial but important issue. At least one third of American adults over age 65 suffer from obesity, with the prevalence expected to increase as the population ages. Currently, laparoscopic sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (GB) are the most commonly used bariatric procedures. The objective of this study is to compare perioperative safety, weight loss, and comorbidity reduction after SG and GB in elderly patients aged 65 years and older.

Methods: The Bariatrics Outcomes Longitudinal Database from 2007-2012 was used to identify patients ≥ 65 years of age that underwent non-revisional laparoscopic SG or GB. Propensity matching adjusted for differences in age, BMI, gender, American Society of Anesthesiologists (ASA) classification, and pre-operative comorbidities. Odds ratios (OR) with 95% confidence intervals (CI) are reported as indicated.

Results: We identified 7,958 patients with ages ranging from 65 to 86 years that underwent SG or GB in the defined study period. Our propensity matched cohorts consisted of 841 SG patients and 841 GB patients, with small differences in age (67.5 ± 2.8 vs 67.6 ± 2.5 , $p=0.032$, $OR=1.01$, 95% CI 0.97- 1.04) and BMI (44.4 ± 7.4 vs 45.1 ± 6.7 , $p=0.001$, $OR=1.02$, 95% CI 1.00- 1.03), but no differences in male gender (36.4% vs 37.2%, $p=0.723$, $OR=1.04$, 95% CI 0.85- 1.26) or ASA >2 (79.0% vs 80.4%, $p=0.467$, $OR=1.09$, 95% CI 0.86- 1.39). Results are summarized in the table below. There were no significant differences in pre-operative comorbidities. SG patients had lower rates of 30-day complication, re-operation, and readmission compared to GB patients, but also experienced less %TWL at 12 months. There were no significant differences in 12-month resolution rates of diabetes mellitus, hypertension, hyperlipidemia, or obstructive sleep apnea in SG and GB patients, respectively.

	Sleeve Gastrectomy	Roux-en-Y Gastric Bypass	p-value	OR	95% CI
30-day complication rate	6.7%	12.4%	<0.001	1.98	1.41-2.78
Re-operation rate	1.1%	2.5%	0.027	2.37	1.08-5.20
Readmission	2.9%	5.8%	0.003	2.11	1.28-3.47
% TWL at 12 months	26.2 ± 8.0	31.1 ± 8.8	<0.001	1.07	1.05-1.10
12 month resolution rate of comorbidities:					
Diabetes mellitus	48.5%	50.3%	0.777	1.07	0.65-1.77
Hypertension	28.4%	32.5%	0.383	1.22	0.78-1.89
Hyperlipidemia	28.3%	33.5%	0.328	1.27	0.78-2.07
Obstructive sleep apnea	41.0%	48.9%	0.208	1.38	0.88-2.26

Conclusion: After controlling for baseline patient characteristics in a propensity-matched analysis, elderly patients undergoing SG experienced less post-operative morbidity, but had similar 12-month comorbidity resolution rates, compared with GB patients. Our findings favor performance of SG in the elderly population.

CONDITIONAL LONG-TERM SURVIVAL OF PATIENTS DIAGNOSED WITH PANCREATIC ADENOCARCINOMA

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Background: Conditional survival, by accounting for time already survived, provides a more accurate measure of future survival than conventional estimates computed at the time of surgery.

Objective: Create a postoperative risk calculator and nomogram for physicians to better evaluate conditional long-term survival in patients who undergo surgical resection of pancreatic adenocarcinoma.

Methods: Patients diagnosed with pancreatic adenocarcinoma, from 2004 through 2013, identified from the American College of Surgeon National Cancer Data Base (NCDB), were included. A conditional risk-stratification matrix was constructed including histopathologic factors and use of adjuvant therapy for those who survive 90 days beyond surgery.

Results: A total of 44,560 patients (51% male, 54% >65 years of age) presented with pancreatic cancer. A majority of patients had tumors > 2cm size (76%), grade I/II (65%), lymphovascular invasion (63%), and positive margins (67%), $p < 0.0001$. These factors and the addition of adjuvant therapy were associated with three and five year survival on univariate and multivariate analysis. The figure represents the risk matrix for patients < 65 yo with neoplasms < 2 cm in size. As an example, patient ≤ 65 years of age, with early stage cancer (Size ≤ 2 cm, Grade I/II, - LN, - Margins), who received adjuvant therapy had a 62% probability of surviving beyond 3 years (95% CI=61%-64%) In comparison, if adjuvant treatment was not received, this patient's conditional survival probability decreased to 51% (95% CI=50%-53%).

Conclusions: These results provide surgeons and their patients with more accurate information regarding long-term survival, as well as the benefit of adjuvant therapy after pancreatic surgery.

SYSTEMIC CASPASE ACTIVITY IN PATIENTS WITH A LEFT VENTRICULAR ASSIST DEVICE

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Background: The caspase family of cysteine proteases has a clearly identified and essential role in the signaling pathways associated with apoptosis and inflammation both as part of natural cell processes as well as part of pathogenic processes. Caspase activity has been associated with the pathogenesis, disease progression, and prognosis of a variety of disease states, including experimentally induced traumatic brain injury in rats, human prostate cancer, cerebrovascular accident (CVA), multiple sclerosis, squamous cell cancer of the head and neck, and others. Additionally, a growing body of evidence suggests that caspase activity may serve as a valuable biomarker for the assessment of myocardial damage following acute myocardial infarction (AMI) and associated cardiovascular diseases; however, little is known about the caspase profiles of patients with a Left Ventricular Assist Device (LVAD) implant.

Objectives: The purpose of this study was to examine the levels of caspase activity in patients with a LVAD implant in an effort to identify any correlation between caspase activity and LVAD patient outcomes and to provide a foundation of knowledge for caspase activity present in the systemic circulation of LVAD patients.

Methods: 246 plasma samples from 49 patients with a LVAD implant and 20 plasma samples from 8 healthy volunteers were studied, with each LVAD patient sample corresponding to certain pre- or post-LVAD implantation time points. Caspase-like activity was measured using a luminometer and commercially available bioluminescent assay kits from Promega. Fold changes from baseline (pre-LVAD) samples were determined and used for statistical analysis. Within each assay, samples were grouped according to significant clinical events.

Results: The mean fold change from baseline caspase-like activity in LVAD patients was significantly higher than the healthy control caspase activities in the following groups of outcomes: death ($p=0.0075$), CVA ($p=0.0083$), and thrombosis ($p=0.0043$), while no significant difference was observed between the control and patients with no recorded post-VAD clinical event. The mean of the samples that corresponded to time points that fell in the range of 3 to 12 days post-VAD was significantly higher than the control for LVAD patients who experienced post-VAD CVA ($p=0.0085$) and pump thrombosis ($p=0.0132$).

Conclusion: Caspase activity positively correlates with LVAD patient clinical events and has the potential to be an important biomarker for LVAD patient outcomes.

COR-KNOT™ DEVICE REDUCES OPERATIVE TIMES IN ROBOTICALLY MITRAL VALVE REPAIR (RMVP)

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Background: Increased operative time is a potential problem associated with robotic cardiac procedures when compared to median sternotomy procedures, which can limit robotic candidates to healthier patients with less complex valve pathology. Annuloplasty is performed in all Robotically-Assisted Mitral Valve Repair (RMVP) procedures and is therefore a portion of the operation to target in order to reduce operative time. The Cor-Knot™ device (LSI Solutions, Inc., Victor, NY) is a titanium fastening tool that avoids the need for intra-cardiac robotic knot tying during annuloplasty band placement, potentially reducing operative times.

Hypothesis: The additive technology of the Cor-Knot™ device reduces suture placement, knot securement, and annuloplasty band placement (ABP) times in RMVP procedures, thus leading to reduced aortic cross clamp (XC) and cardiopulmonary bypass (CPB) times.

Methods: A review of annuloplasty intraoperative video footage was performed for RMVP procedures completed at our institution from 2006 to 2016. 366 procedures were evaluated and a Student's T-Test was used to compare procedures using Cor-Knot™ to those using robotic knot-tying techniques. Variables compared included individual suture placement and knot securement times, as well as overall ABP, XC, and CPB times.

Results: Suture placement* and knot securement* times were reduced using the Cor-Knot™ device. In addition, reduction in ABP*, CPB, and XC* was also observed. Results are summarized in table 1.

Conclusion: The Cor-Knot™ device reduced annuloplasty band placement times in RMVP resulting in a decrease in operative times. Furthermore, this reduction in time decreased both cardiac arrest and cardiopulmonary bypass times. This reduction in time could be beneficial to patients and could allow sicker patients with more complex valve pathology to be candidates for RMVP.

Table 1.

	Group A (Cor-Knot™)	Group B (Knot-tying)
Robotic Cases	193	173
Sutures Placed	1930	1900
Suture Placement (sec)	70.73±42.29*	75.19±47.29
Knot Securement (sec)	53.49±23.50*	63.57±28.13
ABP (min)	31.53±9.14*	34.83±9.79
CPB (min)	157.54±47.85	164.54±35.22
XC (min)	101.83±30.36*	117.99±27.68

* Denotes statistical significance, $p < 0.02$

END-TIDAL CO₂ MEASUREMENTS IN PEDIATRIC PATIENTS SHOW AGREEMENT BETWEEN ADULT/PEDIATRIC AND INFANT/NEONATE CO₂ SAMPLING LINES

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Background: Waveform capnography has been described extensively for its role in identifying correct endotracheal (ET) tube placement and predicting return of spontaneous circulation during resuscitation. Two devices are currently being used to measure end-tidal CO₂ (EtCO₂) in intubated patients: an adult/pediatric (Et_ACO₂) and an infant/neonate (Et_NCO₂) CO₂ sampling line, recommended by manufacturer Covidien for ET tube sizes ≥5.0 mm and ≤4.5 mm, respectively. A comparison of the two sampling lines in a pediatric population is needed since many prehospital providers do not carry the Et_NCO₂ line.

Hypothesis: We hypothesized that the difference in adapter dead space between the Et_ACO₂ and Et_NCO₂ sampling line (<6.6 cc and <0.5 cc, respectively) would alter the measured EtCO₂ in pediatric patients intubated with ET tube sizes ≤4.5 mm.

Methods: A prospective study was performed on patients in the PICU who were intubated with an ET tube size ≤4.5 mm, on mechanical ventilation, and having EtCO₂ monitored with an Et_NCO₂ sampling line. The intervention involved replacing the Et_NCO₂ line with an Et_ACO₂ line for about 30 seconds, then switching back to the Et_NCO₂ line. EtCO₂ and SpO₂ were recorded prior to, during, and after the intervention. Ventilator settings, temperature, and arterial blood gases were among the independent variables recorded. A repeated measures ANOVA was used to assess any difference in mean EtCO₂ between the lines and two Bland-Altman plots were used to measure agreement between measurements from the two lines.

Results: No statistically-significant difference in mean measured EtCO₂ between the Et_NCO₂ and Et_ACO₂ line has been demonstrated (current n=17, pre-Et_NCO₂=41.7±4.7 mmHg, Et_ACO₂=42.2± 6.6 mmHg, post-Et_NCO₂=42.1±4.4 mmHg; p=0.96). For the Bland-Altman plot, the limits of agreement (LOA) between the pre-Et_NCO₂ and Et_ACO₂ line (-6.2 to 7.1 mmHg; bias=0.47) and between the Et_ACO₂ and post-Et_NCO₂ line (-6.1 to 6.2 mmHg; bias=0.06) provide a 95% CI of the difference in measurements between the lines.

Conclusions: Final conclusions are pending further data collection. Though we have not demonstrated a statistically-significant difference in mean measured EtCO₂ between the two lines, the LOA (±6-7 mmHg) may constitute clinical significance for some providers if those differences are sufficient to alter clinical decision-making. If the final data analysis concludes no clinically-significant difference between the two devices, it may be both accurate and cost-effective for providers to employ only the Et_ACO₂ device.

Acknowledgements: A special thanks to the Vidant PICU staff, ECU Division of EMS, Dr. Kori Brewer, and the Brody Summer Scholars Program.

NEUROMUSCULAR BLOCKING AGENT- VERSUS SEDATION-FACILITATED INTUBATION FOR EMERGENT PHARMACOLOGICALLY-ASSISTED ENDOTRACHEAL INTUBATION IN HOSPITALIZED ADULTS

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Introduction: Equipoise exists among practitioners regarding the optimal strategy for emergent pharmacologically-assisted intubation (PAI) of critically-ill hospitalized patients. We hypothesized that first-attempt neuromuscular blocking agent-facilitated intubation (NMBA-FI) results in decreased incidence of new hypotension (primary outcome) and in-hospital mortality/hospice when compared to a purely sedation-facilitated intubation (SFI) strategy.

Methods: We used our 960-bed Level 1 trauma center's Respiratory Therapy database to randomly identify adults (age>18) intubated in intensive care units or in-patient wards from January 2014-July 2015. Subjects who did not receive PAI (n=68) or lacked recorded vitals signs (VS) within 1 hour pre- and post-PAI (n=7) were excluded.

Hemodynamic measures and demographic and clinical covariables previously demonstrated to be predictive of difficult or complicated intubation were extracted from the medical record. Hypotension was defined as a new mean arterial pressure (MAP) <65, a >25% post-PAI reduction in MAP, or a new or >50% increase in pressors within 30 minutes post-PAI, or cardiac arrest within 1 hour.

We estimated the adjusted incident rate ratio for 46 covariates using a poisson family generalized linear model with log link and robust standard error in STATA 14.1.

Results: 158 subjects were eligible for inclusion in the primary analysis. 54 subjects received NMBA-FI, 65 subjects developed hypotension, and 64 died. The SFI and NMBA-FI groups were unbalanced on proportion of surgical patients (6% vs 48%, respectively). The SFI group had higher observed baseline Shock Indices (SI = heart rate/ systolic blood pressure), and the SFI group received more sedating drugs ($p < 0.0001$) than the NMBA-FI group (median 3 agents vs 1, respectively). The groups otherwise were statistically balanced on important measured pre-intubation and care-process covariates.

Subjects receiving NMBA-FI had a lower risk of hypotension (crude risk ratio (RR), 0.44; 95% CI 0.26-0.74) (adjusted RR 0.41, 95% CI 0.18-0.94) and death (crude risk ratio (RR), 0.59; 95% CI 0.33-0.88) (adjusted RR 0.41, 95% CI 0.21-0.79). The crude absolute reduction in mortality risk was -22% (95% CI -37- -0.07) for subjects receiving NMBA-FI.

Results were statistically similar in sensitivity analyses excluding surgical patients and when patients excluded for missing VS were included in the mortality analyses.

Conclusion: Use of emergent sedation-facilitated intubation is associated with higher incidence of hypotension and in-hospital death when compared to NMBA-facilitated intubation.

INFLUENCE OF TECHNICAL DIFFICULTY ON PATIENT OUTCOMES IN THORACOSCOPIC LOBECTOMIES

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Background: Previously, it was thought that factors leading to more complicated surgical dissection resulted in worse outcomes for patients undergoing lung resections for cancer ¹. Some studies have demonstrated both open and thoracoscopic lobectomies to be safe and effective in complicated patients ^{2,3}. However, other studies of different patient populations and using different surgical techniques continue to show conflicting results with respect to morbidity and mortality ⁴⁻⁶.

Objective or Hypothesis: To determine if patient outcomes are affected by the technical difficulty of thoracoscopic lobectomy and, if so, which outcomes are affected and which aspects of technical difficulty contribute to the difference in outcome.

Methods: Patients who underwent thoracoscopic lobectomy between April 2014 and May 2016 were included for retrospective chart review of preoperative history, perioperative notes, and postoperative course. Patients were categorized as either "routine" or "complicated" based on operative notes. A two tailed T test of unequal variance was performed to determine significance of results.

Results: 66 total patients were included in the study: 41 patients were classified as "routine" and 25 were classified as "complicated". When comparing the following variables, none were found to be significantly different: length of hospital stay (5.3 vs. 4.2), length of ICU stay (0.59 vs. 0.12), chest tube duration (5.9 vs. 4.3), duration of air leak (2.8 vs. 2.4), readmission rate (0.12 vs. 0.12) and postoperative complication rate (0.46 vs. 0.28) ($P>0.05$). There were no mortalities in the "complicated" patient group and 1 mortality in the "routine" patient group.

Conclusion: No statistical difference in postoperative course or outcome was found when comparing patients whose operative course was technically difficult versus those whose operative course was routine. Thus, it cannot be concluded that technically difficult thoracoscopic lobectomies are predictive of a challenging postoperative course.

EFFECT OF PRE-PRANDIAL OLIVE OIL AS A LINER NEUROENDOCRINE CELLS OF THE GUT ON DIABETES

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Background: Bariatric surgery results in full and durable remission of T2DM. Although the exact mechanism is not clear, it is directly related with decreased contact between food and the walls of the gut. This effect is also seen with insertion of duodeno-jejunal liners in rodents and humans. Population studies have also demonstrated an inverse relation between strict adherence to Mediterranean diet rich in olive oil and risk of type 2 diabetes. This study is designed to evaluate the effect of pre-prandial olive oil, by itself rather than as a component of the Mediterranean diet, on serum glucose and insulin levels following a meal.

Hypothesis: Pre-prandial olive oil interferes with intestinal signaling lowering blood glucose and insulin levels improving type 2 diabetes.

Methods: Two phased mixed meal challenge with subsequent glucose, insulin and lactate serum levels will be conducted on 6 type 2 diabetic patients 12 days apart. The first set of mixed meal challenges provides baseline levels for participants, the second test is performed after each participant consumes 15mL of olive oil.

Results: Expected results, to be collected after pending IRB approval, should show significant decrease of serum glucose and insulin levels during the second set of mixed meal challenge compared to baselines obtained during the first test.

Possible Conclusion: Data to be collected would highlight the role of olive oil on lowering blood glucose after a meal. Positive results would suggest that that olive oil interfere with intestinal signaling cascades decreasing the contact between food and the gut. Similar to gastric bypass surgery and duodeno-jejunal, olive oil might result in improved diabetes management through coating the walls of the gut. Unlike other procedures, preprandial olive oil consumption is a more affordable and less invasive method to mediate diabetes. Further study can be done on what signaling mechanism so immediately affects blood levels of glucose, lactate, and insulin.

COLLABORATION TO IMPROVE BLOOD PRESSURE IN THE US BLACK BELT:
ADDRESSING THE TRIPLE THREAT

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Cardiovascular disease (CVD) is one of the leading causes of death in the United States and although the disease has shown some decline in the last few decades, there is still a noteworthy relationship of uncontrolled hypertension-related mortality with the African American (AA) populations. The southeast U.S. has a >60% occurrence of hypertension and also is geographically associated with the "Black Belt" region. The Black Belt region is known for increased poverty, largely minority (AA) Population, the notable "color of the soil" and rural scenery. This project was created to target AA patients from this region that have uncontrolled blood pressure in hopes of finding motivating and educational techniques that would help reduce these large racial disparities within hypertension/CVD. 80 Practices from North Carolina and Alabama are being recruited and then 25 AA patients within each practice will be given motivational techniques in addition to standard hypertension care and their blood pressures are recorded over a year. The data collected thus far has been for practice demographics and practice readiness to commence this study. All practices currently selected have demonstrated that they were ready to implement the changes into their care and are motivated to make sure their patients succeeded. There was a small difference in response between nurses, physicians, and administrators showing that the latter are more confident in implementing changes. The practices recruited into the study include community health centers, private practices, and a free clinic. Their AA patient population varies from 6-80% and uninsured/Medicaid/medicare patients varies from 5-100%.

OBESE MALE PRIMARY BODY SHAPE CORRELATES WITH METABOLIC DISEASE

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Background: Obesity is a very costly illness, often co-presenting with metabolic diseases. Body-mass index (BMI) values, the most commonly used metric for measuring obesity, can be misleading or inaccurate in terms of predicting metabolic health and quantifying obesity. More accurate shape quantifiers of metabolic disease are being sought. Three-dimensional body scanners can be used to obtain volume and surface area measurements of patients, including primary body shape ratios.

Objective or Hypothesis: Primary body shape ratios will more strongly correlate to metabolic diseases compared to BMI.

Methods: Retrospective review of scanner data from 110 preoperative bariatric male patients were analyzed along with their comorbidities. Primary body shape, BMI, and total volume over surface area values were calculated. P values < .05 were considered significant.

Results: Primary body shape values showed the strongest correlation with metabolic disease compared to other values obtained. Primary body shape values closer to .5 are more correlated to metabolic disease than measurements closer to 1.

Conclusion: The data supports the hypothesis that primary body shape will correlate with metabolic disease. Using a three-dimensional scanner to obtain body volume values from patients may be more accurate in terms of predicating metabolic health.

VACCINIA VIRUS VIRULENCE FACTOR A35 ALTERS LEUKOCYTE SUBPOPULATIONS IN THE LUNG

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Background: Vaccinia virus is used as the live virus vaccine for smallpox and monkeypox and can be used as a recombinant vaccine platform for other infectious diseases and cancer. However, its virulence makes it contraindicated in approximately 25% of the population. Removing virulence genes from Vaccinia virus will aid in the development of safer vaccines that can effectively protect a wider range of the population. Our lab is studying Vaccinia virus virulence. The Vaccinia virus gene A35R is highly conserved, and we have shown it increases virulence by inhibiting the body's anti-viral immune response. The deletion of the A35R gene attenuates the virus and creates a deletion mutant (A35 Δ). However, we do not fully understand how A35R functions in mammals. Understanding which immune cells are recruited or retained in the lung if A35R is present in the virus will give us a better understanding of its mechanism of action in increasing disease.

Objective: To determine how the Vaccinia virus gene A35R effects the elicitation, proliferation, or retention of leukocyte populations in mouse lung.

Methods: C57BL/6 mice were infected intranasally (respiratory) with either WR (wild type Vaccinia virus), A35 Δ , or mock infected with phosphate-buffered saline (PBS). Lungs were harvested and processed at day 3 or day 6 post infection and leukocyte cell populations were stained with several different colored fluorescently labeled primary antibodies and quantified using multiparameter flow cytometry analysis.

Results: Data collected on day 3 suggest infection with Vaccinia virus (WR and A35R Δ) may increase CD11b and B220 positive cells and slightly decrease CD8 positive cells in lungs. In the presence of the A35 gene (WR), there are decreases in the percentages of CD4 and CD11c positive cells, Ly6 granulocytes, F4/80 macrophages, TCR $\gamma\Delta$ T cells, and DX5 NK cells in the lungs. In the mice infected with A35R Δ , there was no statistically significant change in the number of leukocytes harvested from the lungs compared to mice infected with WR. Little difference was seen on day 6 between WR and Δ A35R infected mice.

Conclusion: The preliminary data suggest that Vaccinia virus infections alter lung leukocyte populations and that A35 may increase virulence by blocking infiltration or retention of immune cells into the site of infection during early infection. Further repeats of the experiment as well as additional experiments looking at the kinetics of cell responses will be required to confirm findings in order to better understand how A35R causes immunosuppression and increases virulence in mammals.

ADVANCED DIRECTIVE KNOWLEDGE AND PREFERENCES AMONG PATIENTS AND PROVIDERS

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Background: Many seriously ill patients are treated using unwanted and potentially futile treatments. Advanced directives and End of Life (EOL) health care planning are measures advocated to administer of EOL care that is more consistent with previously stated patient treatment preferences and goals. In 2015, Medicare introduced payments for practitioners providing EOL care planning, incentivizing practitioners to discuss EOL care with their patients.

Objective: The purpose of this study is to survey and compare family medicine, geriatrics and cardiology patients' perceptions and knowledge of advance directives and EOL care. This study also surveys and compares family medicine and cardiology providers' perceptions of advance directives and EOL care. This study also aspires to increase patient awareness of forms of advance directives and to access barriers to creating advance directives.

Methods: Patients 65 and older were recruited at an academic outpatient Family Medicine clinic and Cardiology clinic in North Carolina to complete a 23-question survey on patient attitudes and knowledge of advance directives and EOL care. Patients were briefly educated by a medical student about advanced directives and EOL care. Providers were surveyed with a 5-question survey on discussing advanced directives with patients and perceived barriers to these discussions.

Results: Preliminary results for survey of patients: of 121 survey participants, 68% were females, 53% were white, 25% were 81 years old or older. While 96% and 84% of patients were familiar with Health Care Power of Attorney (HCPOA) and Do Not Resuscitate forms, respectively, only 24% of participants were familiar with the NC MOST form. Upon completing the survey, 32% of participants were interested in discussing advance directives or completing a MOST form.

Preliminary results for survey of providers: of 36 providers surveyed, 36% were attending physicians, 78% believed they could learn more when asked. 49% of participants believed time was the greatest barrier to discussing advance directives with patients. 72% of providers believed patients lack of knowledge was a barrier to discussing advance directives.

Conclusion: Majority of patients were unaware of NC MOST form. Further analysis will investigate whether knowledge of EOL care and knowledge of advanced directives is related to health care decisions. Physicians describe lack of time and lack of patient knowledge as a barrier to discussing advance directives. These results may identify an unmet demand for patient education in regards to advanced directives and EOL care.

STUDY ON INCREASING COGNITION ADMINISTRATION ORDER FLEXIBILITY

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Background:

Cognition is a computerized neurocognitive test that consists of 15 unique versions (batteries) that contain 10 subtests. Currently, all the batteries are taken in a specific order (i.e., version 1, version 2, ..., version 15) and this was the case for the 19 astronauts, astronaut candidates, and mission controllers at JSC. The purpose of keeping the same order was to minimize practice effects and stimulus set difficulty that are reflected in the normative data. Two problems have arisen due to this strict approach. 1) The administration order of versions 1-15 is often broken due to technical or logistical issues. For example, technical problems cause users to switch to a different laptop or iPad and often cause users to start at version 1 again. 2) BHP Ops hope to administer subset of tests and thus gain a greater flexibility in the administration of the test. These situations produce test sequences that are out of order and differ between individual tests. It is unclear how test administration rate affect practice effects.

Objective/Hypothesis:

The study will disentangle the practice effects and the stimulus set difficulty effects, provide data on the effects of administration rate on practice effects, and potentially find a correlation between Cognition performance and 6df space docking performance. This study will ultimately enable the administration of Cognition to be more flexible.

Methods:

The design of the experiment includes 30 participants with a master's degree or higher who will perform all 15 batteries of the 10 subtests in a randomized administration order with the addition of another battery 3 at the end. Fifteen of the participants will perform consecutive batteries at an interval of 5 days or less whereas the other fifteen participants will perform consecutive batteries at an interval of 10 days or more. After the completion of each battery, all participants will perform the 6df tasks. Multivariable mixed effects regression models with indicator variables for battery number, administration number, and administration frequency group will be performed. The correlation between Cognition speed and accuracy outcomes and 6df docking simulation performance will be investigated.

Conclusion: The overall purpose of this experiment is to provide regression estimates that can adjust for administration order effects and practice effects of Cognition along with finding a possible correlation between Cognition performance and 6df space docking simulator performance. These three findings will ultimately enable Cognition to be utilized in a more versatile manner along with potentially predicting space docking performance.

COMBINED HIGH FIELD INTRAOPERATIVE MAGNETIC RESONANCE IMAGING AND BRAINPATH TECHNIQUE FOR RESECTION OF DEEP SEATED LESIONS

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Background: Neurosurgery has been revolutionized with the advancement of technology and surgical instrumentation. Limitations in neurosurgery have been addressed by new technology with the aim of resulting in the most optimal outcomes with minimal damage to brain tissue

Objective: To assess the feasibility of combining a minimally invasive tubular brain retraction system (Brain Path™) with high field intraoperative magnetic resonance imaging (iMRI) to maximize safe resection of intrinsic brain tumors and to minimize surgical morbidity

Method: A prospective multicenter database (the IMRIS iMRI Neurosurgery Database, I-MiND) was used to identify brain tumor resections that were performed using a combination of the MRI compatible Brain Path™ tubular brain retraction system placed during small craniotomies and iMRI to assess the feasibility of this technique and its impact upon the extent of resection and patient outcomes.

Results: 7 patients were identified that underwent surgical resection using the combination of the Brain Path™ technique and iMRI. The mean age was 51.2 years (range: 37-61). The lesions addressed using this method included 3 glioblastomas, a renal cell carcinoma brain metastasis, a large deep frontal breast carcinoma brain metastasis, a deep left temporal World Health Organization (WHO) grade I tumor (an angiocentric glioma), and an intraventricular WHO grade III tumor (an anaplastic astrocytoma). Mean tumor diameter was 2.95 cm (range: 1.2-4.4). Intraoperative MRI demonstrated complete resection in 3 of the 7 cases (43%). Additional resection was performed after iMRI in 3 of 7 cases (43%) leading ultimately to gross total resection in two of the three cases. In 1 of the 7 cases the tubular retraction system was left in place during acquisition of the iMRI. There were no intraoperative complications. Immediately postoperatively, neurological function was stable in 5 cases (71%) and improved in 2 (28%) cases. The median length of stay postoperatively was 2 days (range: 1-4).

Conclusion: Combining an MRI compatible minimally invasive tubular brain retraction system (Brain Path™) with high field iMRI as a novel strategy to facilitate maximal safe resection of intrinsic brain tumors is feasible, may decrease surgical morbidity, and merits further investigation.

ADAPTABILITY OF PEDIATRIC TUMORS POST RADIATION THERAPY: A PROSPECTIVE STUDY

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Background: The rate of cure for children and adolescents with central nervous system tumors (CNS) has increased to 75% over recent years. This is attributed to the successful utilization of multimodal therapy including neurosurgery, radiation therapy (RT) and chemotherapy. However, the very therapies that are associated with high overall survival rates also come with high rates of adverse long-term effects on the patient's health and psychosocial well-being. This has led to the development of new RTs that decrease normal tissue exposure, in order to increase efficacy while simultaneously decreasing toxicity. Proton beam radiation therapy (PBRT) is an example of one of these new treatments. Unlike conventional RT, protons have less exit dose radiation leading to a significant decrease in hippocampal, temporal lobe and mean brain dose. Hypothetically, PBRT should decrease radiation toxicity and the rate of side effects compared to conventional RT. However, because this therapy is in its infancy, there is little long-term data to support this hypothesis.

Objective: In order to address the deficit in PBRT prospective data and proof of efficacy, this project will cultivate data on acute toxicity, survival and long-term health outcomes by administering a series of computer-based neurocognitive tests, health questionnaires, vision tests, quality of life reports and psychosocial reports, repeatedly, over time.

Methods: Using the National Institutes of Health toolbox of tests, this project will show the effects of PBRT on neurocognitive functions. This battery consists of tests that assess executive function, attention, episodic memory, language, processing speed and working memory. General wellbeing, vision, quality of life and psychosocial status will be monitored via questionnaires and reports from the patient and/or family. Currently, there are 28 patients in this study who have been monitored over one to three years. This project will continue to monitor these patients, and others who are identified at Siteman Cancer Center, to look for trends and themes over time.

VITAMIN D, PARATHYROID HORMONE, AND DAIRY INTAKE IN OBESE CHILDREN AND ADOLESCENTS

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Background: The majority of children and adolescents seeking obesity treatment are vitamin D deficient (25(OH)D < 20 ng/mL). However, it is not yet known if low serum vitamin D levels in obese individuals reflect true vitamin D status.

Objective: Our first objective is to study parathyroid hormone (PTH) levels in obese pediatric patients to determine if serum 25(OH)D concentration reflects vitamin D status. A second objective is to evaluate the role of dairy consumption, the major source of vitamin D and calcium intake, in measured 25(OH)D levels and PTH levels.

Methods: Retrospective chart review of children and adolescents evaluated in a comprehensive obesity clinic between 2012 and 2016 (n = 125). Demographic data, past medical history, drink habits, height, weight, 25(OH)D, PTH, and other fasting laboratory values were extracted from the EHR. Pearson's or Spearman's rho correlation coefficient, chi-square tests, independent samples t-tests and one-way ANOVA will be employed where appropriate.

Results: There was a weak negative relationship between vitamin D and PTH, a weak positive relationship between dairy intake and vitamin D, and a weak negative relationship between dairy intake and PTH. However, in contrast to what was expected, of the 80 individuals with vitamin D deficiency (< 20 ng/mL), 20 individuals had highly suppressed levels of PTH (\leq 16 pg/mL). Only 10 of the 96 individuals who provided dietary recall received the recommended amount of approximately 24 ounces of milk per day. Surprisingly, of these 10 individuals, 5 had insufficient vitamin D (< 30 ng/mL) and 5 had deficient vitamin D (< 20 ng/mL). Of the 86 individuals who reported inadequate dairy intake, 26 had highly suppressed levels of PTH (\leq 16 pg/mL) while only 2 had appropriately elevated PTH (> 65 pg/mL).

Conclusion: Vitamin D levels were not as strongly predictive of PTH levels as they were in healthy weight adults. Dairy consumption was not predictive of vitamin D concentrations. Low levels of dairy consumption were paradoxically associated with low levels of PTH.

A NOVEL MITOCHONDRIA-TARGETING COMPOUND DELAYS PERMEABILITY TRANSITION PORES IN MITOCHONDRIA ISOLATED FROM LEFT VENTRICLES OF RATS

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Background: Mitochondrial Permeability Transition Pores (mPTP) are non-specific pores residing in the mitochondrial inner membrane. They open due to calcium overload caused by oxidative stress. The opening of mPTP cascades into the rupture of the outer mitochondrial membrane and the release of signaling molecules for cellular apoptosis. Extensive research has determined that mPTP play an essential role in many pathophysiological conditions. Several pharmacological approaches are currently being tested for their ability to improve mitochondrial function, yet almost none of the leading candidates specifically target mitochondria. SBT-61 is an idebenone conjugate designed to target mitochondria and delay the opening of mPTP. Thus, this drug is postulated to have a superior effect in protecting heart cells from damage during ischemic-reperfusion conditions (e.g. heart attacks).

Objective/Hypothesis: SBT-61 is hypothesized to have superior biological efficacy on mitochondria compared to idebenone by delaying the opening of mPTP and increasing the Calcium Retention Capacity (CRC) of mitochondria isolated from the left ventricles of rats.

Methods: Mitochondria were isolated from a rat's left ventricle using Mitochondria Isolation Medium (MIM) and Bovine Serum Albumin (BSA). The mitochondria were treated with different drugs of interests (Idebenone, reduced Idebenone, SBT-61, and reduced SBT-61) and exposed to freeze-thaw stress treatment to mimic an ischemic attack. A CRC Assay was conducted to measure the sensitivity of the mitochondria to calcium-induced mPTP opening.

Results: Our data suggested that, after freeze-thaw treatment, the reduced SBT-61 increased CRC and delayed the opening of mPTP while the reduced Idebenone did not. No significant results were found in the oxidized forms of Idebenone and SBT-61 compared to the control. No CRC was calculated for DTT because mPTP opening was never observed after freeze-thaw treatment.

Conclusion: This data supports the hypothesis that SBT-61 shows a superior protective mechanism on mitochondria compared to Idebenone, but only when considering the reduced versions of the drugs. We were able to conclude that when drugs are oxidized, they lose their biological efficacy. Although the complete mechanism of action of SBT-61 is unknown, this result is most likely due to its intrinsic property of being able to target mitochondria specifically. This data has important implications for the efficacy of SBT-61 on mitochondrial function in heart cells.