

## Delayed versus Immediate In Situ Fixation of Stable Slipped Capital Femoral Epiphysis: A Retrospective Cohort Analysis of Radiographic Outcomes and Complications

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**Background:** Standard-of-care for slipped capital femoral epiphysis (SCFE) is direct admission with immediate in situ screw fixation upon radiographic confirmation of diagnosis.<sup>1</sup> The optimal timing of surgery is controversial,<sup>1,2</sup> and delayed management within 2-7 days is an alternative approach to immediate management within 24 hours that could decrease patient burden without increasing the risk of perioperative complications.

**Methods:** This retrospective cohort study included 173 adolescents (<18 years of age) diagnosed with SCFE at UNC Hospitals (Chapel Hill, NC) treated with in situ screw fixation between years 2004-2020. Perioperative complications, temporal classification, avascular necrosis, Southwick slip angle and epiphyseal-metaphyseal offset were used to clinically and radiographically compare immediate versus delayed management cohorts.

**Results:** We identified 51 stable SCFE hips that received immediate treatment at an average of 14.7 hours. We identified 82 stable SCFE hips that received delayed treatment at an average of 3.35 days (80.4 hours). Relative risk of avascular necrosis and complications per hip were lower with delayed treatment. Preoperative epiphyseal-metaphyseal offset was higher in the immediate treatment group. There were no other significant differences in Southwick slip angle or epiphyseal-metaphyseal offset at each preoperative/postoperative timepoint.

**Conclusion:** Delayed management of stable SCFE with in situ screw fixation within one week of diagnosis may be a safe alternative to immediate fixation without increasing risk of avascular necrosis or exacerbating slip severity.

**Importance:** Patients who follow non-weight-bearing protocols post-SCFE diagnosis may have additional time to prepare for major surgery, allowing for referral to an institution with pediatric orthopedic specialists with potential improvement of long-term outcomes.

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## HIV reservoir quantification using cross-subtype multiplex ddPCR

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**Background:** A reservoir of long-lived cells that harbors replication-competent HIV provirus persists despite uninterrupted antiretroviral therapy (ART) and is the preeminent barrier to a cure. A major obstacle to conducting HIV cure trials in populations in Africa, where the global HIV burden is the highest, is the lack of an accurate assay to quantify the replication-competent reservoir across the dominant global HIV-1 subtypes. Here, we developed a cross-subtype multiplex droplet digital PCR (ddPCR) assay that measures both intact and defective proviral HIV DNA, allowing for accurate estimation of replication-competent HIV reservoir size.

**Methods:** We analyzed sequence diversity across the primer and probe binding sites using alignments of 2,400 HIV sequences in the Los Alamos National Library database, including subtypes A (n=171), B (n=1179), C (n=719), D (n=71) and CRF01\_AE (n=292). For nucleotide positions with <90% sequence conservation, we altered our primers via sequence changes and use of degenerate bases to capture the diversity within these dominant global subtypes.

**Results:** We show that our 3-target cross-subtype assay reliably quantifies all 3 targets for all subtypes tested within an average of 1.2 fold (range 1-3.0), and is able to detect HIV DNA down to the single-copy level.

**Conclusion:** In longitudinal blood samples from Kenyan infants infected with subtypes A, C and D, we observe that intact HIV DNA levels follow similar dynamics to the patterns of HIV RNA and total HIV DNA (intact plus defective proviral genomes) levels over time during the first year of ART.

**Importance:** This high-throughput cross-subtype reservoir assay will be useful to facilitate the evaluation of future HIV cure strategies in areas of the world where HIV prevalence is highest.

## Evaluating cumulative radiation exposure in Subarachnoid Hemorrhage/Aneurysm patients at UNC Hospital

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**Background:** Patients presenting to the hospital system with subarachnoid hemorrhage/aneurysms require frequent exposure to ionizing radiation. Imaging modalities such as the CTs, CTAs, Digital Subtraction Angiography with and without coil embolization all contribute to a patient's cumulative radiation exposure. Cumulative radiation is a known cause of cancer development as well as other skin/eye related pathology [1,2,3]. As physicians we regularly weigh the benefit of a diagnostic imaging exam versus the harm that could arise from exposing patients to unnecessary radiation. Although this balance is a great consideration for many providers, there is a lack of published data on patients presenting with subarachnoid hemorrhage and/or aneurysm cumulative radiation dose institutionally at UNC and at the US national level versus places like Europe that have Diagnostic Reference Levels (DRLs) to compare trends of radiation treatment institutionally and nationally [4]. Increasing investigation on this topic institutionally and eventually nationally in the US could help guide providers when choosing imaging modalities and ultimately reduce radiation exposure for patients. In Europe the use of DRLs have decreased the excessive radiation dose of patients in general by 50% between the mid 1980s and 2005 [4]. The lack of literature however in the US has led to a wide variation of radiation exposure with patients from different institutions as well as patients within the same institution for similar pathology [5]. Due to the lack of this information there is a possibility that patients are receiving excessive radiation dosing than needed for diagnosis/treatment of SAH/aneurysm at UNC hospital. Our objective is to better characterize the cumulative radiation dose for our patient population at UNC hospital. Identifying the level of cumulative radiation exposure per SAH/aneurysm visit currently at UNC Hospital can help distinguish whether those patterns deviate from similar institutions in the country or internationally.

**Methods:** Retrospective Chart review of 34 subarachnoid patients in the UNC hospital system via EPIC was done in order to calculate the total cumulative radiation doses. Patient charts were reviewed for the total amount of radiation induced imaging from CTs, CTAs, Digital Subtraction Angiography with and without coil embolization, X-rays etc. Dosage was added together in Gys and averaged out per patient. Patients 18 or older were included in the study.

**Results:** Using JASP descriptive statistics analysis, the average total radiation dose for 34 patients with SAH/Aneurysm at UNC was 2.925 Gy. With patient dosing ranging from .05 Gy to 9.8Gy.

**Conclusion:** This study increases our understanding of cumulative radiation doses of patients presenting with subarachnoid hemorrhage in the UNC hospital system. This study furthers our awareness of radiation exposure in the UNC patient population and may potentially affect future imaging diagnostic guidelines at the institution. More data collection is required to apply the findings more broadly at the institutional, national, and international level.

**Importance:** The preliminary cumulative radiation average at UNC was higher when compared to the average of 2.76 Gy for 77 patients with SAH at the Brigham and Women's Hospital [5]. Internationally a study in Korea which attempted to calculate a DRL using data from 23 hospitals in Korea found their aneurysm patients (patient's more likely to need higher radiation dosing due to interventional techniques) to have an average of 1.847 Gy when diagnostic and interventional techniques were averaged out [6]. This indicates that techniques at UNC have the potential of being dropped by 37% when compared to Korean hospital techniques. In the future monitoring/recording this information continuously at UNC as well as other institutions all over the country can improve outcomes by allowing us to be aware of the current state of radiation levels and sure up uncertainties of where UNC compares to other institutions in the country or internationally on cumulative radiation dosing. From there we can address the multitude of issues that can lead to possible excessive cumulative radiation dosing if it is found that we are higher comparatively nationally and internationally. By developing a system like DRLs in Europe we have the opportunity to greatly decrease the exposure patients receive from radiation imaging in the country and ultimately decrease the chance of pathology development from those exposures [1,2,3,4].

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## The Metabolic Cost Of Walking Balance Control and Adaption In Young Adults

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**Background:** Older adults consume oxygen at a faster rate during walking than young adults, accelerating fatigue and reducing independence. Despite its importance in governing independence and quality of life, the mechanisms responsible for this increased metabolic energy cost remain elusive. O'Connor et al. found that the metabolic cost of walking increases in the presence of optical flow perturbations designed to challenge balance via the visual perception of instability [1]. These data suggest that the act of preserving balance during walking exacts a metabolic penalty. However, prior work has focused on average outcomes after several minutes of responding to perturbations. We have shown that young and older adults respond to the onset of optical flow balance perturbations with generalized anticipatory control (i.e., shorter and wider steps [2,3]). This gives way to task-specific reactive control with prolonged exposure, in which step width and length return to baseline values despite persistent increases in step-to-step variability to orchestrate balance corrections. This adaption may be governed in part by metabolic costs associated with generalized anticipatory versus task-specific reactive control. Our aim was to quantify the role of metabolic energy cost in governing neuromuscular adaption to prolonged exposure to optical flow perturbations during walking in young adults. We first hypothesized that metabolic cost would increase at the onset of balance perturbations in a manner consistent with wider and shorter steps and increased step-to-step variability. We also hypothesized that metabolic cost would decrease with prolonged exposure in a manner consistent with a return of step width and step length to values seen during normal, unperturbed walking.

**Methods:** 18 healthy young adults (age:  $23.3 \pm 2.7$ , 10M/8F) walked for a total of 20 min at 1.2 m/s while watching a speed-matched virtual hallway projected on a semi-circular curved screen positioned in front of the treadmill. At the 5-min mark, we added side-to-side oscillations to the virtual hallway, prescribed as a summation of sine waves with a nominal amplitude of 0.35 m. After 10 minutes of responding to optical flow perturbations, subjects walked for 5 min without perturbations. We used three-dimensional motion capture to record the trajectories of markers placed on subjects' trunk, pelvis, and right and left legs. These were used to extract step kinematics, including step width, step length, and their respective variabilities. We also measured subjects' rates of oxygen consumption and carbon dioxide production using a portable indirect calorimetry system (Cosmed K5). We used standard procedures to estimate net metabolic power, reporting in W/kg. For all outcome measures, we computed average values during the following four time periods of interest: Pre (minutes 3-5), Early Perturbation (minutes 5-7), Late Perturbation (minutes 13-15), and Post (minutes 15-17). A repeated measures ANOVA tested for main effects of time, following by post-hoc pairwise comparisons.

**Results:** With the onset of perturbations, participants walked with 3% shorter, 17% wider, and 53-73% more variable steps ( $p\text{-values} \leq 0.001$ ). As hypothesized, these changes were accompanied by a significant 12% increase in net metabolic power compared to walking normally ( $p=0.001$ ). With prolonged exposure to perturbations, we found that step width and step length tended toward values seen during normal, unperturbed walking. Specifically, compared to those measured at the onset of perturbations, participants increased step length by 2% and decreased step width by 8% ( $p\text{-values} \leq 0.004$ ) following prolonged exposure.

**Conclusion:** Consistent with our previous work[2,3], these changes occurred despite continued or even modest increases in step width variability. We interpret those cumulative findings to suggest that participants responded to the onset of perturbations using generalized anticipatory control, but deprioritized that strategy in favor of task-specific, reactive control following prolonged exposure. As the most significant novel contribution of this study, we add here that these changes were accompanied by and may thereby be orchestrated to permit a statistically significant 5% reduction in net metabolic power compared to that at the onset of perturbations ( $p=0.005$ ).

**Importance:** Our findings suggest that metabolic energy cost may shape the strategies we use to regulate and adapt walking balance in response to perturbations. Planned studies will compare the metabolic cost of balance control and adaption between younger and older adults. Our findings may have important implications for the interaction between higher metabolic cost of walking, increased fatigability, and increased risk of falls in older adults.

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## Long-Term Speech Recognition in Younger and Older Adult Cochlear Implant Users

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**Background:** Despite substantial advancement, speech recognition outcomes among cochlear implant (CI) recipients remain highly variable with better performance described for younger adults compared to older adults. However, older adults may take longer to reach asymptotic performance compared younger adults. Currently, there is a paucity of data characterizing the relationship between age at implantation and long-term speech recognition in adult CI recipients, particularly beyond 1 year of CI use. The present study aimed to characterize long-term outcomes in younger and older adult CI recipients.

**Methods:** A retrospective review in which adult CI recipients with at least 5 years of device use were identified and stratified into younger (18-64 years, n=202) and older ( $\geq 65$  years, n=217) cohorts. Speech recognition, as measured with consonant-nucleus-consonant (CNC) words in quiet and AzBio sentences in noise (10 dB signal-to-noise ratio), was reviewed at 1, 5, and 10 years post-activation.

**Results:** Mean speech recognition scores were better for younger adults than older adults. Speech recognition was stable or continued to improve through 10 years of CI use for both cohorts, with no indication of more prolonged acclimatization in older adults. For the better performing CI recipients, the influence of age at implantation was apparent for sentence recognition in noise though not for word recognition in quiet.

**Conclusions:** Younger and older adults experience long-term speech recognition benefit with a CI, though younger adults demonstrated better performance overall. For older adult CI recipients, assessing performance in quiet and in noise may provide unique information and aid clinicians in determining when to counsel on listening strategies and assistive technologies to maximize CI performance in the presence of auditory aging.

**Importance:** This study further characterizes auditory acclimatization in younger and older adult cochlear implant users.

## Burn Injury, Characteristics, and Epidemiology in African American Children in North Carolina

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**Background:** Unintentional injuries, including burns, represent the leading cause of morbidity and mortality for children in the United States<sup>1</sup>. This study seeks to identify trends among African American pediatric burn patients compared to other races with regards to burn characteristics, hospital stay, and type of surgical intervention utilized.

**Methods:** This is a retrospective review of all admitted pediatric burn patients (< 18 years old) to a busy, tertiary burn center in North Carolina from 2009 through 2019. We used bivariate analysis to compare patients based on reported race, comparing African Americans to all other races. Modified Poisson regression was used to model the probability of undergoing autologous skin grafting based on African American race, adjusted for potential confounders. To estimate socioeconomic disadvantage, we used the Area Deprivation Index (ADI), which uses factors for the theoretical domains of income, education, employment, and housing quality to rank groups of geographical blocks from lowest level of disadvantage (1) to the highest (100)<sup>2</sup>.

**Results:** 4,227 children were admitted to UNC between 2009-2019. The median age was 3 years (IQR 1-8) with a male preponderance at 59.8% (n=2,529). The median TBSA was 2% (IQR 1-5). African American (AA) children were disproportionally represented among pediatric burn patients, comprising 33.7% of all patients, compared to an African American state population of 22.2%. AA patients were more likely to have scald burn injuries compared to other races at 68.5% (n=976) compared to 49.3% (1,382, p<0.001) with both fire and contact injuries less common in AA children. AA patients had a slightly larger TBSA with a median of 3% (IQR 1-6) compared to 2% (IQR 1-5, p<0.001). In the hospital, AA patients had a longer mean length of stay at 5.8 days (SD 13.6) versus 4.9 days (SD 13.8) but were not more likely to be admitted to the ICU with an admission prevalence of 17.1% (n=244) compared to 15.4% (n=430, p=0.13). Compared to other races, African American patients were more likely to have autologous skin grafting at their initial operation, with an adjusted RR of 1.49 (95% CI 1.22-1.82) when controlling for age, Area Deprivation Index (ADI) national rank, TBSA, and burn type.

**Conclusion:** African American children were disproportionately represented among pediatric burn patients, more likely to have scald burn injuries that were slightly bigger compared to patients of other races, had longer hospital stays, and were more likely to have autologous skin grafting upon initial surgical intervention.

**Importance:** This research provides insight into the demographics of pediatric burn patients in North Carolina, as well as data on burn characteristics and medical interventions used for African American patients compared to other races. This information is necessary in order to



guide treatment decisions, inform prevention strategies, and accurately assess mortality risk in a vulnerable patient population.

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## CYP2C19 Genotype Impact on Intracranial Arterial Stenosis in Flow Diversion Treatment of Cerebral Aneurysms

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**Background:** Flow diversion treatment of cerebral aneurysms requires dual anti-platelet therapy (DAPT) to prevent thrombosis and intimal hyperplasia (stenosis). Clopidogrel is a first-line agent in many DAPT therapies, but not all patients respond to this treatment. Cytochrome P450 enzymes activate clopidogrel into a metabolite that decreases platelet aggregation. Genetic variation in this enzyme is believed to explain variable DAPT response and can be assessed using a CYP2C19 genetic screening assay. Results from this assay are often used to guide DAPT drug selection; however, little clinical data exists examining current practice guidelines in patients treated with a flow diverter.

**Methods:** CYP2C19 genotype, anatomic features, and demographic characteristics of aneurysms were reviewed retrospectively. The presence of stenosis was determined by review of a cerebral angiogram performed approximately six months post-flow diverter placement. Two independent providers reviewed each angiogram. A collaborative review of the angiogram was performed to reach a consensus if the initial interpretation differed between reviewers. CYP2C19 results were interpreted using established criteria that designates CYP\*17/\*17 as ultrarapid, \*1/\*17 as rapid, \*1/\*1 as normal, \*1/\*2 and \*2/\*17 as intermediate, and \*2/\*2 as poor metabolism.

**Results:** A comparison of CYP2C19 genotype versus rate of stenosis was calculated. 103 aneurysms were treated with a DAPT regimen containing clopidogrel. 1/2 (50%) of ultrarapid, 10/27 (37%) of rapid, 18/60 (30%) of normal, and 5/14 (36%) of intermediate metabolizers developed stenosis. No poor metabolizers received DAPT containing clopidogrel. 11/18 (61%) aneurysms treated with a DAPT regimen without clopidogrel developed stenosis.

**Conclusion:** In flow diversion patients who received CYP2C19 genotype testing and DAPT with clopidogrel, no statistically significant difference in the rate of stenosis was observed.

**Importance:** To our knowledge, this study represents the first results from a retrospective study comparing CYP2C19 genotype versus rate of stenosis in cerebral aneurysms treated with a flow diverter.

## Incorporating Medical Students into Telemedicine Visits in the Ambulatory Setting

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**Background:** As medical schools have reintroduced students into clinical rotations during the COVID-19 pandemic, preceptors and students have had to quickly adapt to telemedicine without guidelines of how to integrate students into these visits. Our study is a mixed-methods cross-sectional analysis aimed at elucidating what structures work best for telemedicine visits for both preceptor ease and medical student education.

**Methods:** Surveys were emailed to Community-Based Longitudinal Care (CBLC) preceptors, CBLC third-year medical students (MS3s), and fourth-year medical students (MS4s) at the University of North Carolina School of Medicine (UNC SOM) Charlotte Campus at Atrium Health. These surveys inquired about preceptor and MS3 experiences incorporating medical students in telemedicine visits and MS4 experiences in comparison to in-person rotations.

**Results:** 28 preceptors (17 who involved medical students in telemedicine), 13 MS3s, and 7 MS4s responded to the survey. Qualitatively, respondents preferred having visit pre-briefs and debriefs. Responses for who ran the visit varied for preceptors and MS3s, but 5/6 MS4s (83.3%) who responded preferred seeing the patient independently. 14/17 preceptors (82.4%) felt they were adequately able to teach via telemedicine, 10 of whom (58.8%) felt it was the same as in person. All MS4s were satisfied with learning via telemedicine, but only 8/12 MS3s (66.7%) were satisfied. The average comfort level of MS3s with telemedicine visits increased from 2.54 to 4.08 ( $p = 0.00058$ ) and the average comfort level of MS4s increased from 3.4 to 4.4 ( $p = 0.0341$ ).

**Conclusion:** Telemedicine is a feasible way of providing medical education, but the experience for new clinical learners must be improved, particularly in developing confidence, independence, and medical knowledge. Our study suggests guidelines divided into pre-visit, visit, and post-visit sections. Future areas of interest include investigating ways to ease the preceptor experience, particularly in pediatrics and OB/GYN.

**Importance:** This study presents novel qualitative data on medical education via telemedicine, a new medium of clinical learning that has not been extensively explored prior to the COVID-19 pandemic.

## Frailty Score as a Predictor of Prolonged Length of Stay

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**Background:** Characteristics associated with a prolonged hospital length of stay (LOS) for patients undergoing percutaneous coronary intervention (PCI) have not been well studied. More specifically, the Canadian Study on Health and Ageing (CSHA) Frailty Scale's value as an independent predictor of outcomes in the setting of PCI is unclear.

**Methods:** We performed a retrospective analysis of inpatient PCI admissions at UNC Hospitals between 1/2018 and 7/2019 using quality improvement database that combines EMR data points with National Cardiovascular Disease Registry (NCDR) output. Two cohorts were compared; patients with the longest LOS were assigned to the "long LOS" group, while patients with the shortest LOS were assigned to the "short LOS" group. Univariate analysis was performed comparing 55 unique patient variables between cohorts. Multivariate analysis was then performed to determine which variables were the strongest independent predictors for a prolonged LOS.

**Results:** 97 subjects were identified, with 49 assigned to "short LOS" and 48 to "long LOS." Comparison of the two groups is summarized in Table 1. Long LOS patients were more likely to be older, female, and frail. On index catheterization, radial access was more common in the short LOS group. Multivariate analysis revealed that increasing patient age and increasing CHSA frailty scale are the two variables most predictive of a prolonged LOS. The average age was  $62.14 \pm 9.81$  in the "short LOS" group and  $71.85 \pm 11.23$  in the "LOS group" ( $p > 0.001$ ). Additionally, the average CHSA frailty score was  $3.80 \pm 0.640$ , in the "short LOS group" and  $4.94 \pm 1.10$  in the "long LOS" group ( $p < 0.001$ ).

**Conclusion:** CHSA frailty scale is a strong independent predictor for a prolonged LOS.

**Importance:** This study presents novel quantitative data on CSHA frailty score as a predictor for readmission following PCI.

## Investigation of Post-Surgical Readmission Risk Factors of Head and Neck Surgery

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**Background:** With the majority of the readmissions resulting from preventable causes related to the initial surgery and admission, hospital readmissions within 30 days of discharge have become an important metric of quality of care and reducible cost by hospitals. Otolaryngology patients are one of the high-readmission-risk groups due to the complexity of surgery and high likelihood of postoperative complications. There exists a readmission risk calculation method; however, its efficacy is questionable. The purpose of this study was to identify factors that affect the readmission rates of otolaryngology patients after surgery and improve upon the current prediction system.

**Methods:** Data were collected for patients who were admitted and received otolaryngology surgery at University of North Carolina Hospital between March 2019 and February 2020 and met the U.S. Centers for Medicare & Medicaid Services Readmissions criteria. The patients were divided into two groups: those who were readmitted (n=21) and those who were not (n=344). Patient- and hospital-related factors were compared using uni- and multivariate regression analyses.

**Results:** Among the variables, prior chemotherapy or radiation (odds ratio (OR) = 5.1, 95% CI, 1.5 – 17.3, P = 0.009), lack of antibiotics (OR = 3.3, 95% CI, 1.1 – 9.7, P = 0.032), and active smoking (OR = 3.9, 95% CI, 1.3 – 11.3, P = 0.013) were found to have significant impacts on readmission. The nomogram showed an increase in the readmission likelihood from 0.03% to 4%, 16%, and 40% with the addition of each risk factor.

**Conclusion:** Within our study population, nearly 75% of the readmitted patients came back for potentially preventable surgery-related complications. By determining the risk factors and creating a nomogram, we hope to identify and proactively intervene on “at risk” patients during the perioperative timeframe, reduce complications and morbidities that result readmission, and thereby improve the overall quality of care delivered.

**Importance:** The current readmission risk determination method at the University of North Carolina is inaccurate in predicting the likelihood of readmission, and many still come back for potentially preventable complications. Both the hospital and patient would benefit from the development of an improved prediction method and appropriate perioperative management.

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## Nasal Airway Obstruction: Cartilage Analysis

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**Background:** Nasal airway obstruction (NAO) is one of the most common sources of referral to otolaryngologist. Appropriate surgical treatment is commonly offered to improve symptoms. Common autologous graft choices during rhinoplasty are harvested from the nasal septum and conchal cartilages. To better understand graft properties, our study aims to identify histological changes in the nasal and auricular cartilage.

**Methods:** Specifically, we investigated three different cartilages: quadrangular, dorsal septal articulation with the upper lateral cartilage, and auricular. Seventy-three eligible patients ages greater than 18 were prospectively recruited to the study. Any excess cartilage during patients’ nasal/rhinoplasty surgery were collected.

**Results:** Data showed that cartilage cell count decreases with age in all three specimens. Overall, auricular cartilage had the highest median cell count among three cartilages. Special stains also showed that glycosaminoglycans, and collagen content decrease with age for dorsal and quadrangular. Elastin content also decreased with age specifically for auricular cartilage.

**Conclusion:** Age related cell count decline may stem from cellular apoptosis, impaired response from extracellular stimuli, and cellular senescence. Glycosaminoglycans (GAG), elastin, and collagen content decreased with age independent of mechanical loading. Decreased of these cellular content may indicate stiffen and more fibrous tissues, which are more susceptible to collapse upon compression.

**Importance:** Our study results provide insight into age-related histological changes in septal and conchal cartilages and may also provide insight into the pathophysiology of NAO.

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## T<sub>1</sub>ρ MRI as a Predictor of Symptoms Related to Posttraumatic Osteoarthritis

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**Background:** Anterior crucial ligament (ACL) injury is a common non-contact sports injury which is associated with an increased risk of osteoarthritis (OA).<sup>4</sup> Given the high prevalence among young people<sup>3</sup> and risk for OA, ACL injury presents a significant source of morbidity. Loss of proteoglycans may be an early change in the cartilage extracellular matrix reversible via gait altering interventions to improve optimal loading. Proteoglycan density can be estimated via T<sub>1</sub>ρ relaxation times<sup>2</sup>, which increase with a decline in proteoglycan density. Therefore, we aimed to identify associations of between limb femoral condylar proteoglycan density and self-reported knee symptoms in individuals 12 months following ACL reconstruction (ACLR) surgery.

**Methods:** 29 Individuals ages 18-35 underwent ACLR surgery. 12 months later, they were administered the Knee Osteoarthritis Outcome Score (KOOS) questionnaire and identified as symptomatic or asymptomatic based on their KOOS scores using a classification created by the Multicenter Orthopedic Outcome Network<sup>5</sup>. Magnetic resonance imaging was used to collect T<sub>1</sub>ρ relaxation times in the lateral and medial femoral condyles (LFC and MFC), which were further segmented into the weightbearing regions. T<sub>1</sub>ρ relaxation times in the surgical limb were divided by the non-surgical limb to calculate interlimb T<sub>1</sub>ρ ratios. T-tests were used to compare lateral and medial femoral condyle interlimb T<sub>1</sub>ρ relaxation times between symptomatic and asymptomatic individuals. We also conducted an ROC Curve analysis to calculated odds ratios and determine whether a critical T<sub>1</sub>ρ ratio could predict whether an individual has significant knee symptoms.

**Results:** Individuals with significant knee symptoms had significantly higher ( $p=.01$ ) LFC T<sub>1</sub>ρ ratios than individuals without significant knee symptoms, and this association remained when only the weight bearing portions were considered ( $p=.04$ ). The association approached significance for the MFC ( $p=.132$ ). Furthermore, ROC curve analysis revealed that individuals who have an LFC T<sub>1</sub>ρ ratio  $>1.11$  have a 12.6 times greater risk of developing symptomatic knee discomfort. When analysis was limited to the weight bearing portion of the LFC, the risk ratio was 8.5.

**Conclusion:** This study provides evidence that decreased proteoglycan density based on T<sub>1</sub>ρ MRI is linked to an increased likelihood of developing symptoms related to OA at 12-months following surgery.

**Importance:** These proteoglycan changes precede articular cartilage loss and may be reversible via gait alterations to optimize loading, which would reduce the burden of osteoarthritis following ACL injury.

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## Clinical Concussion Outcomes at Preseason Baseline in Contact and Non-Contact Sports

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*This research was funded in part by the Carolina Medical Student Research Program (CMSRP) and the Medical Alumni Association*

**Background:** Baseline concussion testing not only provides data to instruct clinicians on injury severity and return-to-play protocol, but may also provide useful data on pre-season deficits that 1) may be an indicator of subsequent injury risk or intervention need and 2) may be targeted by specific training and rehabilitation. **Aims:** To examine differences in contact sport student-athletes' baseline performance on clinical concussion measures compared to non-contact/limited-contact student-athletes. To explore differences specifically between volleyball student-athletes' baseline performance and non-volleyball student-athletes.

**Methods:** This was a retrospective, cross-sectional study utilizing data from a large clinical research program. Collegiate varsity athletes ( $n=550$ ; mean age  $18.5 \pm .85$  years) participating in ongoing research who completed baseline concussion assessments [demographic questionnaire, graded symptom checklist, neurocognitive assessment, and the Sensory Organization Test (SOT)] were included in the study. Multiple linear regression models with contact sport (yes/no) as the explanatory variable, controlling for concussion history and sex, were conducted for each outcome. To compare preseason baseline performance between volleyball and a similar sport, separate independent samples t-test, with volleyball as primary sport vs. cross-country/track as the independent variable and each concussion measure outcome as the dependent variables were utilized.

**Results:** When controlling for sex and concussion history, contact sport participation was associated with lower raw psychomotor and lower raw processing speed scores at preseason baseline ( $p=0.006$  and  $0.008$ , respectively) indicating poorer performance in these domains. However, the models used explained only a minimal amount of the variance in the outcomes ( $R^2=0.02$  and  $0.003$ ). No significant differences in symptom, SOT, or other cognitive outcomes at baseline were found. Volleyball and cross-country/track athletes did not differ on any outcomes at baseline.

**Conclusion:** Minimal differences in baseline testing performance were observed between contact and noncontact sport athletes. Future investigations should consider these relationships after injury.

**Importance:** Identification of deficits at baseline may help clinicians provide individualized care to student-athletes before and following concussion.

## Investigating the Therapeutic Role of Retinoic Acid-Related Orphan Receptor Alpha (RORα) in Heart Failure

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**Background:** More than 6 million Americans have heart failure (HF), and up to 80% of HF patients are over the age of 65. It is critical to understand the pathophysiology of HF in the aging adult population. Retinoic Acid-Related Orphan Receptor Alpha (RORα) is downregulated in failing heart compared to non-failing heart, but its cardioprotective mechanism is unknown. We hypothesize that RORα provides energy for the failing heart by regulating fatty acid oxidation (FAO) and lipid droplet formation (LDF), two critical pathways of generating ATP in the body. The aims of this study are to investigate (1) how RORα expression alters FAO and LDF in HF and (2) how age impacts FAO and LDF in the presence/absence of RORα.

**Methods:** In the HF model, WT (n=13) and RORα KO (n=10) mice were fasted to simulate the energy deficits of HF. In the aging model, WT (n=16) and RORα KO (n=15) mice were sacrificed at young (5 mo) and old (17 mo) age. In both models, FAO/LDF activity in mouse hearts were measured using qPCR, microarray, and Western blot and analyzed using two-way ANOVA with Tukey's post hoc analysis.

**Results:** When HF was simulated, decreased RORα expression correlated with decreased ( $p \leq 0.05$ ) compensatory increases in FAO activity and expression of FAO and LDF genes. Increased age correlated with decreased ( $p \leq 0.05$ ) expression of key FAO/LDF genes in both WT and RORα KO groups. RORα expression decreased four-fold ( $p \leq 0.0001$ ) with aging alone in the WT group.

**Conclusion:** Our findings suggest that RORα plays a key role in regulating FAO and LDF activity. Furthermore, the decreased expression of RORα with aging has not yet been reported. The consequent downregulation of FAO/LDF genes in the aging heart may contribute to the susceptibility to HF in the geriatric population. Future clinical studies need to further investigate the cardioprotective role of RORα in aging patients.

**Importance:** RORα has tremendous potential as a gene therapy target in the treatment of HF. By upregulating this single gene, many downstream effects can be achieved to protect the heart. In addition, RORα can potentially be utilized as a clinical marker for predicting responsiveness to current HF treatments.

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## Regional Analysis of Lung Structure, Ventilation, and Mucociliary Clearance by MRI and Scintigraphy Before and After Elexacaftor/Tezacaftor/Ivacaftor Treatment in Cystic Fibrosis

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**Background:** CF lung disease progresses heterogeneously over time. The development of imaging methods that sensitively detect lung disease and spatially relates structure and function abnormalities is expected to provide important tools for clinical care and therapeutic development efforts. In this project, we sought to develop the tools required to co-register and analyze multiple imaging modalities, including  $^1\text{H}$ -UTE-MRI for lung structure,  $^{19}\text{F}$ -MRI with inhaled perfluoropropane gas for ventilation imaging, and gamma scintigraphy with inhaled  $^{99\text{m}}\text{Tc}$ -sulfur colloid particles for mucociliary clearance (MCC).

**Methods:**  $^1\text{H}$ -UTE-MRI,  $^{19}\text{F}$ -MRI, and MCC images obtained in 7 subjects before and after treatment with elexacaftor/tezacaftor/ivacaftor were used for method development. A MIMVista (MIM Software) protocol was developed to co-register scans from these three imaging modalities. After co-registration, lung regions were created to divide the lung into four quadrants. In each quadrant, structural abnormalities were scored and validated. Multiple ventilation parameters and MCC rates were also calculated on a per quadrant basis. Several regression models were used to analyze these data.

**Results:** Total structure and mucus plugging scores improved with treatment ( $p=0.37$  and  $0.15$ , respectively) whereas bronchiectasis score did not change. Ventilation parameters, particularly the fraction of quadrant volume occupied by slowly ventilating voxels ( $\text{FQV}_{\text{slow}}$ ) significantly varied by quadrant location ( $p=0.012$ ) and improved with treatment ( $p=0.036$ ). MCC analyses are ongoing.

**Conclusion:** Structure and functional imaging with MRI revealed clear disease heterogeneity and was able to capture treatment responses in a small population. Ventilation and structural abnormalities were not significantly related, suggesting that these modalities may provide complementary data.

**Importance:** These methods allow us to co-register multiple 2D and 3D image types, including  $^{57}\text{Co}$  transmission scans,  $^{99\text{m}}\text{Tc}$  deposition scans, UTE  $^1\text{H}$ -MRI, and  $^{19}\text{F}$ -MRI. Selection of quadrants or other regions of interest allows an integrated evaluation of lung structure and ventilation that captures regional heterogeneity across the lung.

## An Analysis of the Patient Experience Through Oral History Interviews

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**Background:** A novel approach to delivering patient-centered care is to turn to the descriptive personal accounts about health, illness and medical care found in oral history interviews. Oral histories are a powerful research methodology for furthering understanding of the complex values and needs of individuals, and for learning how the individual's experience can be understood in the larger context of their community (Tsui & Starecheski, 2018). In this research project, oral history interviews collected from Yancey and Mitchell counties in western North Carolina were studied in an effort to empower the patient perspective and gain a deeper understanding of what patients value in their relationships with medical providers.

**Methods:** I studied fourteen oral history interviews collected from Yancey and Mitchell counties in western North Carolina using narrative analysis techniques. First, we looked at individual interviews and identified themes that related to the patient experience. Next, we identified common themes across multiple interviews in order to characterize shared patient values.

**Results:** Many of the oral histories revealed common themes about power dynamics and patient identity. Specifically, the interviews revealed how medical systems create power imbalances that contribute to patients' feelings of a loss of control and self-identity; however, the oral histories also illustrated how narrators fight this loss of agency. On an individual level, narrators reject the limitations set on them by the medical system and restructure their identity in their own terms. On a collective level, narrators turn to their communities for strength and support at times when their identity or agency feels threatened by disease or medical treatment.

**Conclusion:** The close-reading and narrative analysis skills utilized in this project provide important insight into complex aspects of the patient experience and illustrate the importance of carefully attending to the patient perspective. Giving patients the space to share their own experiences allows them to construct their story in a way that reflects how they would like to be seen – instead of how the medical community depicts them.

**Importance:** These skills could be brought into medical education to enrich how medical students think about and understand the patient experience and to encourage closer clinician-patient communication.

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## Increasing Rates of Depression Screening in a Rural Federal Qualified Health Center in North Carolina

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**Background:** The identification of patients at risk for major depressive disorder (MDD) is crucial to initiating treatment and connecting patients with behavioral health resources. Screening for MDD with the Patient Health Questionnaire 9 (PHQ-9) is commonly used to identify patients requiring additional follow-up. This quality improvement intervention aimed to increase documented PHQ-9 depression screening rates and increase referral rates to behavioral health services at Prospect Hill Community Clinic (PHCC) in Prospect Hill, NC.

**Methods:** Three PDSA cycles were completed over the course of three months from July – September 2019. The first cycle consisted of verbal reminders about existing workflow. The second involved administering reusable PHQ-9s to all patients older than 12 years old upon rooming. The third modified the questionnaires to incorporate substance abuse screening and designated room numbers for each document. Rates of PHQ-9 documentation and behavioral health encounters were collected from the electronic health record (EHR). Paired t-tests were used to compare pre-intervention rates in the 6-month period prior to the first PDSA cycle to the 6-month period after the first cycle.

**Results:** A sample of 1,392 patients without recent PHQ-9s visited PHCC from July 1st 2019 to Sept 23rd, 2019. Patients' mean age was 45 (SD 20), ranging from 12 to 98 years old. Sixty-four percent were White, 33% were Black/African-American, and 40% had sliding fee scale insurance. There was a significant increase in rates of depression screening with follow-up and behavioral health encounters post-intervention (mean difference 11%, 95% CI=8.95, 12.38  $p<0.00005$  and mean difference 39 visits/month, 95% CI=23, 55  $p=0.0016$  respectively).

**Conclusion:** Expanding criteria for who is screened along with reusing questionnaire documents may improve rates of PHQ-9 documentation and behavioral health referrals. Overlapping significant increases in behavioral health visits suggest PHQ-9s may serve as an entry point to mental health services.

**Importance:** The reusable questionnaires are low-cost, environmentally friendly, and accessible to patients in a rural setting as well as those who may have limited technological proficiency.

## Factors Impacting Patient Radiation Exposure During Prostatic Artery Embolization

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**Background:** PAE is a challenging procedure potentially resulting in high radiation doses. The purpose of this study was to identify which patient and procedural factors most impact a patient's radiation dose during PAE.

**Methods:** This study consisted of a retrospective analysis of PAEs performed by a single interventional radiologist between May 2014 and August 2019 (n = 232). Univariate and multivariate analyses with a stepwise selection model building strategy were used to test significance.

**Results:** Increased body mass index (BMI), fluoroscopy time, and total procedural time are associated with increased patient radiation dose ( $p < 0.0001$  for all), while BMI explains the most variance in patient radiation dose ( $R^2 = 0.255$ ). The effect of BMI on radiation dose depends on fluoroscopy unit; a unit increase in BMI is associated with an increase in dose of 119-190 mGy, depending on the fluoroscopy unit ( $p < 0.0001$ ). There is also a significant positive association between iliac artery tortuosity and radiation dose ( $p = 0.00046$ ).

**Conclusion:** These results indicate that increased patient BMI, iliac artery tortuosity, procedural fluoroscopy time, and total procedural time are positively associated with increased radiation doses. Among these factors, patient BMI explains the most variance in radiation dose during PAE.

**Importance:** Better understanding of which patient and procedural factors most impact a patient's radiation dose during PAE can help counsel patients on the most appropriate BPH treatment. Overweight patients in particular considering PAE can be better informed of their risk for radiation exposure. This research will help guide informed patient decision making and peri-procedural planning.

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## Anxiety Levels and COVID-19 Preparedness in High-Risk Populations

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**Background:** UNC WakeBrook Primary Care is a clinic that provides primary care to patients with serious mental illness and/or substance use disorders. UNC Center for Latino Health (CELAH) facilitates coordinated bilingual care for Latino patients at UNC. Both clinics serve high-risk populations. Our goal was to gain an understanding of these subsets of patients, including comparative anxiety levels, knowledge about COVID-19, and proximity to people who have tested positive in order to better direct care and education about future public health crises.

**Methods:** A standardized survey with nine open-ended questions (Spanish and English) was administered over the phone over the course of three months (June-August) to patients at Wakebrook and CELAH. Demographic and survey results were analyzed with simple averages and percentages. STATA statistical software was used to perform 2 sample T testing.

**Results:** There were a total of 95 CELAH and 68 WakeBrook patients. Wakebrook patients reported significantly higher anxiety compared to CELAH patients ( $p=.003$ ). Women in both populations reported higher anxiety levels than men ( $p=.01$ ), and women with a mental health diagnosis reported the highest levels of anxiety overall.

**Conclusion:** Wakebrook patients indicated higher anxiety levels compared to CELAH patients, despite being less likely to report working somewhere COVID-19 had been detected or knowing someone diagnosed with coronavirus. Women, particularly those with a mental health diagnosis, may require more education and emotional support during a pandemic. Most patients from both groups were able to identify >2 symptoms. A majority at both clinics were also taking the basic precautions recommended by the CDC, indicating success of early public messaging about symptoms and protective measures.

**Importance:** This research gives us an understanding of how at-risk populations are responding to COVID-19 and a better sense of how to approach these two at-risk populations in both clinical settings and for public health planning.



## MT1-MMP in Thoracic Aortic Aneurysms in the setting of Marfan Syndrome

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**Background:** Thoracic aortic aneurysm (TAA) development in Marfan syndrome occurs through dysregulated remodeling of vascular extracellular matrix<sup>1,2</sup>. Membrane-bound type-1 MMP (MT1-MMP) is a key mediator of TAA formation through pericellular proteolysis, activation of other MMPs such as MMP2, and intracellular Transforming Growth Factor (TGF)- $\beta$  signaling<sup>3,4</sup>. This study tested the hypothesis that elevated MT1-MMP in aortic tissue correlates with development of TAA in Marfan patients.

**Methods:** Aortic tissue was homogenized in PBS + inhibitor and analyzed for total protein using BCA. Ten  $\mu$ g of total protein was loaded onto the 4-15% bis-tris mini gel and separated by electrophoresis. Even loading was confirmed with activation, and the gel was transferred to a nitrocellulose membrane for immunoblotting analysis. The membrane was incubated in antisera specific for MT1-MMP (1:2000; Cat#ab38971, Abcam, 5% bovine serum albumin (BSA)/PBS). A secondary peroxidase-conjugated antibody was applied (1:5000, 5% BSA/PBS) and signals were detected with a chemiluminescent substrate and recorded using a dedicated imager. Band intensity was quantified using ImageJ. Total protein was quantified using total lane density analysis in ImageJ from the nitrocellulose membrane after gel transfer.

**Results:** Abundance of MT1-MMP was measured in aortic tissue from patients with TAAs in the setting of Marfan syndrome (n=7) and compared to Idiopathic TAA (n=8). The MT1-MMP relative protein abundance in TAA in the setting of Marfan syndrome ( $1.85 \pm 0.78$ ,  $p < .01$ ) as compared to Idiopathic TAA ( $1 \pm 0$ ).

**Conclusion:** MT1-MMP relative protein abundance is greater in TAA in the setting of Marfan syndrome as compared to idiopathic TAA. This suggests an increased role of MT1-MMP in aneurysm formation in Marfan patients compared to Idiopathic TAA.

**Importance:** Knowledge of MT1-MMP and TIMP in thoracic aortic aneurysm in the setting of Marfan syndrome will allow for the development of targeted diagnosis, surveillance, and treatment.

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## Clinical Outcomes after Delayed Treatment of Stable Slipped Capital Femoral Epiphysis: A Retrospective Cohort Study

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**Background:** There is controversy on the optimal timing of surgical stabilization of stable slipped capital femoral epiphysis (S-SCFE), a condition that mainly affects obese adolescents<sup>1</sup>. Current standard-of-care for SCFE is direct admission preceding urgent in situ fixation (ISF) within 48 hours<sup>2</sup>. This is limited by geographic, socioeconomic, or transportation factors. Delayed treatment within 2 to 7 days is an alternative approach<sup>2</sup> and may decrease patient burden without increasing risk of post-operative complications or long-term outcomes, mainly avascular necrosis (AVN) of the femoral head.

**Methods:** This retrospective cohort study included 173 SCFE patients <18y age at time of ISF, under CPT code 27176 at UNC Hospital. Patient demographics, date of diagnosis and surgery, and post-operative complications were recorded. Each SCFE was classified radiographically by Tönnis arthritis grade<sup>3</sup> at last follow-up. Post-op complications including infection, hardware failures/revisions, or AVN were classified by the Clavien-Dindo-Sink (CDS)<sup>4</sup> grading system for comparison between cohorts.

**Results:** We identified 183 S-SCFE hips that underwent ISF at UNC Hospital from 2004-2020. Of these, 58 were treated on a delayed basis (average 100.0 hrs), and 75 within 48 hours (average 20.6 hrs). At most recent follow up, there were 20 hips with 31 total post-operative complications and 13 hips with 27 total post-operative complications in the Immediate and Delayed cohorts respectively, with 4 confirmed instances of AVN in each cohort. There was no significant difference between cohorts for complication incidence ( $p = 0.76$ ), Tönnis grade ( $p = 0.89$ ) at last follow-up, or CDS grade per hip with complication ( $p = 0.28$ ). Patient-reported-outcomes (PROs) are lacking.

**Conclusion:** Delayed surgery of S-SCFE within 7 days of diagnosis may be a safe alternative to immediate treatment, without increased risk of post-operative complications or development of AVN. PRO data and multi-center collaboration are needed to increase the validation of our findings.

**Importance:** Insight into the efficacy of Delayed ISF for S-SCFE as a safe alternative in patients with limiting factors, who follow non-weight-bearing protocols post-SCFE diagnosis, may allow additional time to refer patients to appropriate institutions with Pediatric Orthopaedists, with potentially improved long-term outcomes and PROs.

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## Surface Reconstruction of the Spine Using Depth Calibration and Edge Detection for Low-dose Tomosynthesis

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**Background:** Digital tomosynthesis could provide an alternative to computed tomography for low-dose 3-D x-ray imaging in scoliosis and trauma imaging of the spine. In tomosynthesis, x-ray projections over limited angles are digitally reconstructed to render a stack of images (Dobbins and Godfrey 2003). However, image stacks in tomosynthesis do not contain calibrated depth information, making this method unsuitable in its current implementation for surface visualization or volumetric reconstruction as needed for scoliosis (Kim *et al.* 2010) and traumatic spine imaging.

**Methods:** We tested an edge detection-based segmentation algorithm on chest tomosynthesis data to extract the osseous boundaries of the spine from the false edges of objects not in the plane of the image. We then generated a point cloud from the contours of segmentation and fitted a surface of elemental triangles to visualize the vertebrae. For edge detection, we used the Canny algorithm (Canny 1986) which is widely used in the field of computer vision to extract useful structural information from different vision objects including diagnostic images. After identifying the discernible vertebral bodies from the segmented image stack and generating a point cloud of the contours of segmentation, we applied Delaunay triangulation (Amenta *et al.* 1998) which fits a surface of elemental triangles using all possible 3-element combination of the points in the cloud such that the hypersphere of each triangle does not contain any other point in the cloud.

**Results:** Despite that no one threshold could be identified empirically to categorize the edges of the vertebral column as being strong against the artifactual edges of other structures not in the plane of the image, the proposed tomosynthesis post-processing protocol was able to visualize the surface of 3 lumbar vertebrae of which anatomical landmarks like the vertebral body, spinous process, and the intervertebral space were identifiable.

**Conclusion:** Segmentation of the tomosynthesis dataset proved to be the rate-limiting step in this work. While the Canny edge detection-based segmentation method was able to extract 3 lumbar vertebrae in a chest tomosynthesis data, the algorithm was not robust enough to outline the entire vertebral column and suppress all false edges for Cobb angle calculation and fracture detection. Due to the novel nature of this project, it is challenging to know what algorithm of segmentation is well-suited for this task, but we believe that semantic segmentation (Lessmann

*et al* 2019) using convolutional neural network could be the way forward despite that it is both labor and resource intensive to implement.

**Importance:** This work implements a novel imaging protocol for 3-D digital tomosynthesis surface rendering and can be easily applied to existing clinical tomosynthesis systems, providing a safe and accurate alternative for assessment of vertebral positioning in pediatric scoliosis and fractures in trauma imaging.

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## Context Matters: Parent Language during Play and Snack in Infants at Varying Likelihood of Autism

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**Background:** Mealtimes are one of the earliest and frequently occurring opportunities for children to engage in reciprocal social communication, enabling attention, elicitation of back-and-forth responses, and vocabulary learning (Fiese & Schwartz, 2008). For young children, mealtimes encourage the use of eye contact, facial expressions, and vocalizations - precursors to skills like joint attention and gaze and gesture following (Harding et al., 2013; Tomasello et al., 2007). Additionally, mealtimes fit well with routines-based early intervention, in which parents and caregivers (hereto referred to as parents), are coached to create a language-rich environment across family routines.

Traditional parent language research examines play interactions with little research examining mealtimes. Studies that have examined mealtimes have noted distinctive language characteristics in this context, such as more lexical diversity during mealtime as compared to play in typically developing infants (Zimmerman et al., 2019). In contrast, children with complex communication needs hear less diverse vocabulary and fewer advanced topics and concepts during mealtimes from parents (Ferm et al., 2005). Given mealtimes are an important context for developing early language skills, understanding whether they are underutilized in providing language input may be important for children at elevated likelihood of Autism Spectrum Disorder (ASD).

This study examined how parent language differs in play and snack contexts among groups of infants at lower and elevated likelihood of ASD with the long-term goal of identifying potential early intervention targets within family routines.

Aim 1 - To determine if parent language differs between mealtime and free-play.

Aim 2 - To determine if parent language during mealtime differs in children with lower and elevated likelihood of ASD.

Aim 3 - To determine the relationship between child variables (language, sensory, and fine motor skills) and parent language during feeding and play interactions.

**Methods:** Data were collected through the Parent and Infants Engaged (PIE) project. Children were recruited from the community and asked to complete the First Years Inventory-Lite 3.1b (FYI), a screener for early detection of likelihood of developing ASD (Baranek et al., 2014). Children were placed into two groups based on FYI scores: elevated likelihood of ASD (ELASD)



or lower likelihood of ASD (LLASD). All families who completed the FYI were invited to participate in an assessment at the campus laboratory. The 72 children analyzed for this study had complete audio/video data for play and snack where the parent spoke English (n=40 ELASD, 32 LLASD).

To analyze the semantics and structure of parent language, the audio/video from the parent-child play and snack vignettes (each 5 minutes) were independently transcribed by two reliable research assistants. Then, the transcripts were combined using the audio/video to ensure accuracy. Transcripts were entered into Systematic Analysis of Language Transcription (SALT) software and analyzed. Using SALT, the following metrics were extracted: proportions of total nouns, verbs, and adjectives, number of utterances, mean length of utterance, type token ratio, number of different words, words per minute.

Child expressive/receptive language and fine motor skills were measured by the Mullen Scales of Early Learning (MSEL), which was administered by a trained research assistant. The MSEL T-score for each domain was used in analysis.

**Results:** Children were a mean age of 14.26 months ( $\pm 1.653$ ) and 66.7% were male. The majority of children were White (80.6%), not Hispanic or Latino (86.1%), and had a household income of more than \$60,000 (74.58%). The highest education level of the child's parents was most commonly a college degree or higher (93.65%).

#### *Aim 1*

Parent language inclusive of both groups was analyzed. There were significant differences between play and snack contexts in words per minute,  $t(71)=3.102$ ,  $p=.003$ . Parents used more words per minute during play compared to snack. Additionally, there was a significant difference in the proportion of verbs  $t(71)=2.808$ ,  $p=.006$  (more during play) and proportion of adjectives used  $t(71)=-4.257$ ,  $p<.001$  (more during snack).

#### *Aim 2*

Parent language was not significantly different based on likelihood group during play or snack.

#### *Aim 3*

Child expressive language skills were significantly correlated with the proportion of verbs parents used during snack  $r(72)=-.242$ ,  $p=.041$ .

There was a significant, positive relationship between child receptive language scores and words per minute in play  $r(72)=.301$ ,  $p=.010$ . There existed significant, negative relationships between child receptive language and the proportion of verbs during both play  $r(72)=-.293$ ,  $p=.013$  and snack  $r(72)=-.250$ ,  $p=.034$ .

There was a significant negative relationship between child fine motor score and the utterances per minute during snack  $r(71)=-.327$ ,  $p=.005$ . Additionally, there was a significant negative relationship between child fine motor score and the number of different words used per minute during snack  $r(71)=-.317$ ,  $p=.007$ , as well as words per minute during snack  $r(71)=-.268$ ,  $p=.024$ .

**Conclusion:** Overall, we found that parents used significantly less language during mealtimes as compared to play regardless of likelihood status. Additionally, contrary to our hypothesis, children's fine motor skills were negatively associated with several parent language metrics, where less advanced fine motor skills were associated with more parent language. This may reflect parents providing more coaching to children with less advanced fine motor skills. Overall, these results point to an opportunity for SLPs in early intervention to coach families on providing more language input during mealtimes regardless of the child's diagnosis. Additionally, SLPs may consider how child fine motor skills impact the type and frequency of language input, which emphasizes the importance of collaboration with occupational therapists when working with young children with early signs of ASD.

**Importance:** This research highlights differences in parent language during mealtime compared to play and relative to their child's developmental skills in young children with developmental delays. Parent coaching on how to increase language input during mealtimes, particularly for children with strong fine motor skills, could be beneficial in routines based early intervention.

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## Characteristics of Treated Glaucoma Suspect and Ocular Hypertensives in an Academic Center

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**Background:** Glaucoma is one of the leading causes of blindness in individuals over 60, yet there is a lack of a consensus in the definition of glaucoma. This results in variability in practice, which poses a serious problem for glaucoma suspect patients who possess clinical findings or risk factors that indicate an increased likelihood of developing glaucoma, such as elevated intraocular pressure (IOP), suspicious-appearing optic nerves, and/or abnormal visual fields. This retrospective cohort study aimed to determine what factors play a role in treating glaucoma suspect and ocular hypertensive patients in clinical ophthalmology practice.

**Methods:** A list of patients with a diagnosis code of glaucoma suspect or ocular hypertension was acquired and 600 patient charts were randomly selected for review. From these, patients meeting inclusion criteria with 3 or more sets of IOP values and no diagnosis of glaucoma were reviewed for age, living status, race, ethnicity, family history, IOP, central corneal thickness (CCT), retinal nerve fiber layer (RNFL) thickness, RNFL symmetry, and visual field mean deviation (MD).

**Results:** Average IOP was significantly higher in treated patients ( $p = 0.0145$  OD,  $p = 0.0146$  OS). Average RNFL thickness was significantly lower in the treated group ( $p = 0.00562$  OD,  $p = 0.0171$  OS) as was RNFL symmetry ( $p = 0.016$ ). There was no statistical difference in age, current living status, race, ethnicity, family history of glaucoma, CCT, and MD on 24-2 between treated and non-treated patients.

**Conclusion:** Of the factors assessed, IOP and RNFL thickness/symmetry were the most important factors in the decision to treat a glaucoma suspect or ocular hypertensive patient.

**Importance:** This study is an important step in better defining glaucoma and glaucoma suspect.

### Funding

1. This research was supported by NIA 2-T35-AG038047 - UNC Chapel Hill National Training Center MSTAR Program.
2. Editorial assistance from NC Translational and Clinical Sciences Institute, which is supported by the National Center for Advancing Translational Sciences, National Institutes of Health, through Grant Award Number UL1TR002489.

## Modeling Chordoma Combination Immunotherapy with Natural Killer Cells and IL-15

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**Background:** Chordoma is a rare bone tumor derived from notochord remnants that has demonstrated resistance to treatment modalities such as cytotoxic chemotherapy, radiotherapy, and surgical resection. Previous work has shown that chordoma tumors express PD-L1 and EGFR to varying degrees, rendering them targetable by therapeutic antibodies against PD-L1 (N-601) and EGFR (cetuximab). N-601 and cetuximab are humanized IgG1 monoclonal antibodies that mediate antibody dependent cellular cytotoxicity (ADCC) with natural killer (NK) cells, further enabling their antitumor activity. N-803 is a clinical grade IL-15 superagonist that stimulates and expands T cells and NK cells with proven clinical efficacy against solid tumors. No studies have explored the potential role of N-601, N-803, or combinatory approaches with NK cell-mediated immunotherapies in chordoma.

**Methods:** Healthy donor and chordoma patient NK cells were used as effectors against chordoma cell lines treated with N-601 or cetuximab for *in vitro* ADCC killing. Healthy donor and chordoma patient NK cells were also treated overnight with N-803 before being used as effectors. PD-L1 chimeric antigen receptor (CAR) engineered NK cells were evaluated as effectors against chordoma cells that were treated or untreated with IFN $\gamma$  to upregulate PD-L1.

**Results:** 6/6 chordoma cell lines (3 clival, 3 sacral) expressed PD-L1 and EGFR. Treatment of chordoma cell lines with anti-PD-L1 or anti-EGFR therapeutic antibodies increased tumor cell sensitivity to killing by healthy donor and chordoma patient NK cells via ADCC. Lysis of chordoma cell lines was further enhanced by treatment of NK cells with N-803. PD-L1 CAR engineered NK cells were effective against chordoma cell lines, which was enhanced by upregulation of PD-L1 on tumor cells by IFN $\gamma$ .

**Conclusion:** N-601 and cetuximab enhance NK cell killing of chordoma cells *in vitro* through ADCC, and this is further enhanced by treatment of NK cells with N-803. PD-L1 CAR engineered NK cells are cytotoxic against chordoma cells in a PD-L1-dependent manner. These data demonstrate the anti-tumor activity of N-601, cetuximab, N-803, and PD-L1 t-haNK cells in preclinical models of chordoma and support further evaluation in clinical studies.



**Importance:** Chordoma is a deadly malignancy with a dismal prognosis and no FDA-approved agents for treatment. This work will be used to support drafting of the first ever neoadjuvant clinical trial for chordoma patients.

## Optic Nerve Appearance in Patients Diagnosed with Chronic Progressive External Ophthalmoplegia

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**Background:** Chronic progressive external ophthalmoplegia (CPEO) is a mitochondrial disease involving limited ocular movements. CPEO is characterized by bilateral ptosis, limited ocular movements, and limb and bulbar muscle involvement<sup>1</sup>.

Glymphatics is a mechanism by which the brain clears toxic metabolites that have accumulated within its parenchyma. These waste products enter the cerebral spinal fluid (CSF) for clearance. The perioptic subarachnoid space is a unique environment that requires eye movement for CSF clearance<sup>2</sup>.

A recent study reveals the tendency for CSF within the optic nerve space to be gravitationally dependent, especially in the absence of eye movement. The study demonstrated that contrast flow in the perioptic subarachnoid space is slow in the absence of eye movement<sup>3</sup>.

We suspect that reduced eye movement in CPEO decreases CSF clearance from the optic nerve, likely preventing normal circulation necessary for optic nerve cleansing via glymphatics. Therefore, this would be an additional insult to the optic nerve apart from the mitochondrial dysfunction. The aim of this case series was to characterize patients with CPEO who develop optic atrophy.

**Methods:** The study design is a retrospective case series study. The study population included all individuals diagnosed with chronic progressive external ophthalmoplegia at UNC Health systems since January 1, 2010. Data on age, clinical diagnoses, and ophthalmic exam findings were collected.

**Results:** From the 13 patients with diagnosis of chronic progressive external ophthalmoplegia, two of them presented with optic disc pallor, either in one or both eyes. For both patients, their ocular movements were limited. The two patients were 75 and 82 years old. The median age for the patients in this study was 46.

**Conclusion:** It is possible that advanced age is an important association for optic disc pallor in patients with CPEO. We suspect that the atrophy is due to the chronicity of accumulated metabolic waste products due to limitation of orbital CSF clearance.

Further studies including longitudinal retinal nerve fiber layer imaging and glymphatic flow in CPEO patients could provide greater insight into if impaired glymphatic flow directly causes ocular pathologies.

**Importance:** Impaired glymphatic flow due to decreased eye movement could potentially be a direct cause of ocular pathologies.

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