Analysis of the NOTCH pathway in HNSCCC: A target with a wide prognostic and therapeutic potential.

WINNER 'Clinical & Translational' Category for 2023 Lifespan Research Day

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Abstract

Background: Notch1 mutations are the second most common mutations found in head and neck carcinoma (HNSCC), but their function remains unknown.

Methods: HNSCC (N=1576) patient tumors underwent DNA (592–gene or whole exome; N=1576) and RNA (whole transcriptome; N=799) sequencing at Caris Life Sciences. PD–L1+ expression was tested by IHC (22c3). NOTCHsig–High samples were defined as >2–fold median expression of HEY1, HES1, MYC, or CCND1, while NOTCHsig–Low samples had <2–fold median expression of each gene. Overall survival (OS) was calculated from insurance claim–based data using Kaplan–Meier estimate. Statistical significance was determined using Chi–square/Mann–Whitney U tests.

Results: NOTCH1 mutations were identified in 16.4% (N=258) of HNSCC patients, with increased prevalence in patients =60 years (19 vs 11% <60 years, p<0.001), primary tumors (19 vs 11% in metastases, p<0.001), and p16– patients (23 vs 11% p16+, p<0.001). Further stratification by PDL1 expression showed lower NOTCH1 mutations rates (12%) in PDL1– samples, while PDL1+ samples with low (Combined Positive Score, CPS 1–20) and high (CPS > 20) expression had similar rates (21 and 25%, respectively). NOTCH1 mutations were associated with worse OS (1.2 HR, 95% CI 1.0–1.4, p=0.03), and while no difference was observed in p16+ and p16– subgroups, p16– patients harboring NOTCH1 mutations were more frequently co–mutated with FAT1 (43 vs 19% in NOTCH1 WT, p<0.01) and PIK3CA (17 vs 9%, p<0.05). Among NOTCH1–WT patients, NOTCHsig–High was more common in p16– patients (56 vs 45% p16+, p<0.01), metastases (59 vs 51% in primary, p<0.05), and PDL1– patients (67 vs 53% PDL1+ low vs 47% PDL1+ high, p<0.05). NOTCHsig–High was associated with worse OS (1.2 HR, 95% CI 1.0–1.4, p=0.03), with no difference in OS observed in p16– subgroups, while p16+ NOTCHsig–High was associated with worse OS (1.6 HR, 95% CI 1.1–2.2, p<0.01).

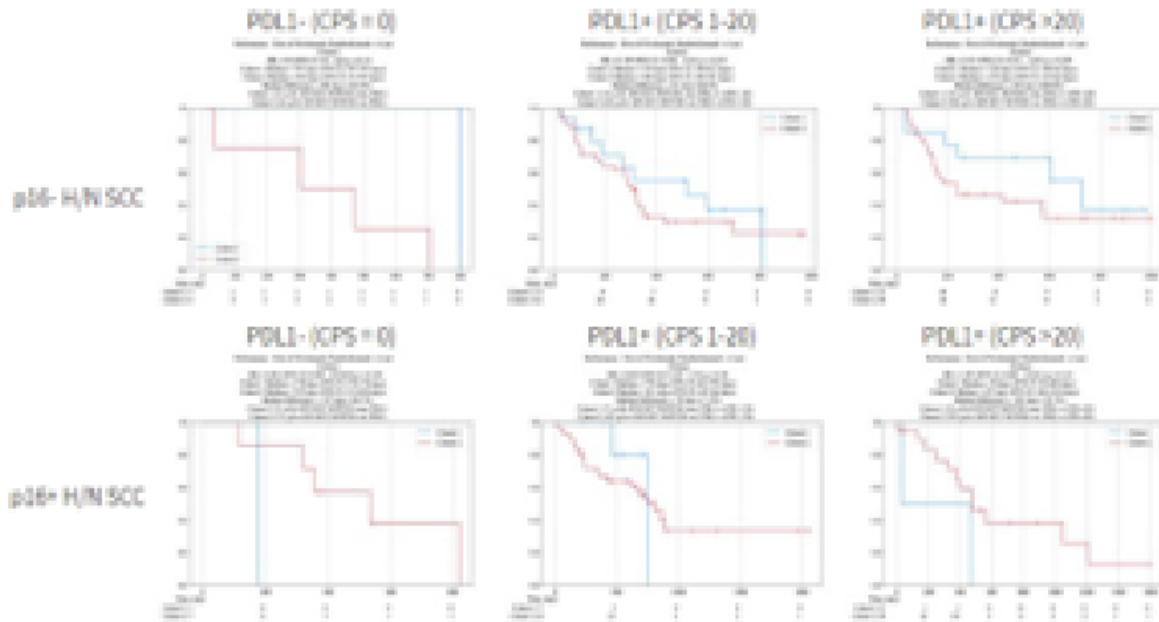**Conclusion:** Among the NOTCHsig genes, high expression of MYC was the strongest predictor of worse OS (1.8 HR 95% CI 1.2–2.7, p<0.01).

NOTCH1 mutations and high expression of NOTCH–regulated genes in NOTCH1–WT patients were associated with p16– status and poor clinical outcomes. These data highlight NOTCH prognostic value and potential targetability.

Clinical Implications: Further evaluation is warranted to determine whether NOTCH signaling influences treatment response and investigate its use in clinical trials.

Clinical outcomes – Immunotherapy by p16/PDL1

COVID–19 Data Analysis: Harnessing Artificial Intelligence, IoT, and Social Network Analysis to Combat the Global Pandemic and its Societal Impact

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: This study intends to analyze COVID–19 data and examine how it affects social life in people. The study includes a variety of COVID–19 data analysis topics, such as the cooperative use of AI, ML, deep learning, and the Internet of Things (IoT) in the COVID–19 eradication effort. Additionally, the project investigates how artificial intelligence and Internet of Things (IoT) techniques might be used to forecast, identify, and diagnose patients with the novel coronavirus. Using social network analysis and sentiment analysis techniques, the project will also look into how false information, corrupted data, and conspiracy theories are spread on social media sites like Twitter. Existing approaches are assessed through a thorough comparative examination. In the end, the study will offer various data analysis methods, identify areas for future research, and offer broad guidelines for successfully controlling the coronavirus and adjusting to the shifting work and living circumstances.

Methods: The study used a thorough and methodical way to look into several COVID–19 data analysis issues. The survey report starts out by introducing the novel virus and exploring the historical background of earlier pandemics. The research also examines the function of social media and online activism in the communication of COVID–19–related information. The study primarily looks at how social media sites affect the propagation of false information and fabricated virus–related data. The project also examines the application of machine learning, artificial intelligence, and Internet of Things (IoT) strategies to attack COVID–19.

Results: The comprehensive survey on COVID–19 data analysis yielded significant findings across various research areas. Firstly, the study highlighted the emergence of the novel coronavirus and provided insights into previous pandemics of the last century, establishing a contextual foundation for understanding the current crisis. The role of social media platforms in the dissemination of information related to COVID–19 was thoroughly examined. It was observed that social media played a crucial role in the spread of fake news and manipulated results concerning the virus. The study delved into the application of artificial intelligence (AI), machine learning (ML), and Internet of Things (IoT) techniques in the fight against COVID–19. AI techniques also demonstrated promise in detecting, predicting, and diagnosing COVID–19 infections.

Conclusion:

Clinical Implications: This research offers a thorough analysis of the COVID–19 epidemic, covering a variety of topics. The study also covers how to analyze data linked to the epidemic and how to fight it using AI, ML, IoT, social media, and social network analysis. The authors give future prospects for research as well as a taxonomy of disciplines and how they are used in COVID–19 data processing.

COBRE Center for Stress, Trauma, and Resilience
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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--- Abstract ---

Background: There is increasing evidence for a profound and persistent impact of adverse childhood experiences (ACEs) on psychological and physical health outcomes over the lifespan. In 2021, we established a Center of Biomedical Research Excellence (COBRE) for Stress, Trauma, and Resilience (STAR) at The Miriam Hospital. The STAR COBRE supports transformative research to understand how stress and trauma impact mental and physical health and to develop novel approaches to interventions that will promote resilience across the lifespan.

Methods: The STAR COBRE is unified by a mission to create a vibrant regional and national hub for transformative research into stress, trauma, and resilience. The STAR COBRE community is highly collaborative, dedicated to diversity and equity in all forms, and to creating an inclusive environment where the contributions of all are recognized and valued. The COBRE incorporates a life course approach, with an emphasis on sensitive periods of development—pregnancy, childhood, adolescence, aging.

Results: The STAR COBRE currently supports a diverse group of scholars including 3 Research Project Leaders, 2 Research Scientist Recruits, and 8 Pilot Project Leaders. STAR investigators are supported by: the Community Collaborative (CC) Core—supports community partnerships, recruitment/retention of marginalized & minoritized populations, and social justice initiatives; the Technology, Assessment, Data and Analysis (TADA) Core—supports methods harnessing cutting-edge technology, data management and statistics; and the Administrative Core—provides expert mentorship, networking and career development opportunities to catalyze career trajectories and R01 submissions.

Conclusion: The STAR COBRE serves as the only research center in Rhode Island focused on stress, trauma and resilience—a focus that is urgently needed to address adversity-related health disparities, particularly in the wake of the COVID-19 pandemic. We encourage early career investigators in RI who are interested in or curious about STAR-related research to apply for pilot funding and to join our STAR community. Visit starcobre.org to learn more.

Clinical Implications: The STAR COBRE Center offers many avenues for supporting clinical research at The Miriam Hospital, Lifespan, and across RI: (1) pilot funding for early career faculty, (2) support for novel technologies, biomarkers, measures, & (3) developing and sustaining community partnerships.

Asthma Control and Sleep Outcomes in Urban School–Age Children
2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Urban children are at increased risk for asthma morbidity. Urban children with asthma are more vulnerable to experiencing disrupted sleep when their asthma is in poor control. In this study, we used objective methods to assess the extent to which the sleep period is disrupted in urban children with asthma compared to healthy peers. Specifically, we examined the average frequency and duration of awakenings during the sleep period in both groups of urban children. We also compared the number and length of awakenings in children with well controlled asthma to those with poorly controlled asthma and examined these associations by ethnic group status.

Methods: Data are from Project NAPS (Nocturnal Asthma and Performance in School), an NICHD–funded longitudinal study of asthma, sleep, and academic outcomes in urban, ethnically diverse children (age 7–9; R01HD057220; Koinis Mitchell, PI). This study includes data from participants with asthma during the fall/winter 4–week monitoring period. Asthma control was assessed by validated questionnaire, and asthma symptoms via daily diary. Objective nighttime awakenings were assessed via actigraphy.

Results: This study included 346 children, aged 7–9 year–old (M=8.3, SD=0.86) from Latino (45%), Black/AA (34%) and NLW (21%) backgrounds and their caregivers. 62% of the study population had asthma and 80% were on controller medications. Among children with asthma, 64.4% had well controlled asthma. Children with asthma had a higher number of awakenings compared to healthy controls (b=2.21, SE=.06, p=.05). There was no difference in average length of awakenings between the two groups (p=.54). Children with not well/poorly controlled asthma had significantly higher number of awakenings (b=2.40, SE=1.07, p=.03) and slept fewer minutes overall (b=–19.03, SE=8.37, p=. 02) compared to children with well–controlled asthma.

Conclusion: Urban children with asthma have a higher risk of disrupted sleep compared to children without asthma. Challenges with asthma control can also lead to awakenings during the night. Latino children in the sample were more vulnerable to sleep disruptions during the monitoring period.

Clinical Implications: To our knowledge, this is the first study showing the impact of asthma and asthma control on sleep by using objective methods and assessing the impact of ethnicity in this vulnerable group of children.

Survey of prescribers' interest in and understanding of pharmacogenomics
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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--- Abstract ---

Background: The promise of pharmacogenomics (PGx) to improve medication safety and effectiveness is consistently demonstrated in the literature, ushering in the early majority of adopters. Successful uptake hinges on clinicians involved in patient care. Surveys of primary care providers found most lack formal training in PGx and are unprepared to utilize it. The relevance of PGx extends beyond primary care, so there is a need to assess prescriber preparedness across relevant specialties as PGx programs expand. As the profession leading PGx implementation, it's important for pharmacists to recognize where their expertise can supplement their physician and advanced practice provider colleagues. The aim of this study is to collect the experience and perception of PGx for prescribers across eleven specialties at an integrated academic health system.

Methods: This is a cross–sectional, quantitative online survey. A link to the survey was emailed to physicians and advanced practice providers at an integrated, academic health system in Rhode Island and practicing in one of eleven relevant specialties. Survey format included multiple choice, Likert–type, and Likert scale questions on respondent demographics, education on PGx, utilization of PGx, comfort with PGx, and beliefs on PGx utility.

Results: The response rate was 3.7% (60/1614) and represented eight specialties. Majority were physicians (70%) and had been practicing for either 20+ years (32%) or were currently a trainee (22%). Over 70% had no education in PGx but 77% were interested in receiving some. The mean PGx comfort score was 10 out of a possible 40. 85% agreed genetics can influence response to medications and 53% agreed they prescribe medications influenced by PGx. When asked if their patients would benefit from PGx, 22% agreed and 55% were neutral.

Conclusion: Almost all respondents had little to no experience with PGx, but were willing to learn more. There is significant opportunity to improve prescribers' comfort with using PGx in practice.

Clinical Implications: Incorporating PGx results into prescribing decisions has been shown to reduce risk of side effects, improve time to effective therapy, reduce hospital admissions, and reduce costs for patients and health institutions. Without prescribers' willingness and ability to adopt PGx, patients will miss out on these benefits.

Use of a validated tool to assess transition readiness to adult care of adolescents living with HIV in Rwanda

2023 Lifespan Research Day Abstract Submission Contest

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Febronie Mushimiyimana, MD, University Teaching Hospital of Kigali. Dept of Pathology & Laboratory Medicine

Juliette Unyuzumutima, RN, University Teaching Hospital of Kigali. Dept of Pediatrics

Lisine Tuyisenge, MD, University Teaching Hospital of Kigali. Dept of Pediatrics

Rami Kantor, MD, Professor, The Miriam Hospital. Dept of Medicine

Abstract

Background: Recent African studies report that only 11–60% of transitioned adolescents living with HIV (ALHIV) were successfully retained in care after healthcare transition (HCT) from pediatric to adult care settings. HCT without adequate pre–transition preparation can result in loss of follow–up and poor treatment adherence. Transition guidelines recommend longitudinal transition readiness assessment using an objective measure, a practice not routinely implemented.

Methods: During March–April 2023, HCT readiness was assessed in a cross–sectional study of Rwandan ALHIV age = 18 years attending the University Teaching Hospital of Kigali pediatric HIV clinic and about to transition to adult care. Transition readiness was assessed using the validated Transition Assessment Readiness Questionnaire (TRAQ 5.0), consisting of 20 questions in five subscales: Appointment Keeping; Tracking Health Issues; Managing Medications; Talking with Providers; and Managing Daily Activities. Responses were graded on a Likert scale of 1–5 (1 being 'No, I do not know how' and 5 being 'Yes, I always do this when I need to'). Scores less than 4 indicate need for education.

Results: In 32 perinatally–infected ALHIV, mean age at diagnosis was 3.7 years (SD 2.7) and at antiretroviral therapy initiation 5.2 years (SD 3.3). Mean number of clinic visits in the prior 12 months was 4 (S.D 0.48, range 3–6). Half were still in high school, and most (88%) lived with their biological parents. The mean TRAQ scores were Appointment Keeping 3.82 (SD 0.61); Tracking Health Issues 3.43 (SD 0.93); Managing Medications 4.56 (SD 0.59); Talking with Providers 4.71 (SD 0.4); and Managing Daily Activities 4.52 (SD 0.46).

Conclusion: In a first–of–its–kind study in East Africa, a validated HCT assessment in Rwandan ALHIV suggests overall readiness in managing medications, daily living tasks and communication with providers. Needs for further education in tracking health issues and keeping appointments were identified, which are important for independent self–management of chronic disease. Longitudinal follow–up and comparison to other populations (now feasible due to using a validated tool) are needed, to develop and further evaluate the impact of needed interventions on post–transition outcomes.

Clinical Implications: The validated transition readiness assessment tool can be used successfully in this setting. Future studies will assess implementation in clinical practice.

Effect of Heart Failure Take Home Kit on 30 day Readmission Rate for Heart Failure Patients.

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Heart failure (HF) is a chronic condition requiring management of symptoms with medication, device, and lifestyle changes. Despite improvements in treatments for HF, over time symptoms worsen, making HF the most common cause for hospital readmission. The cost of HF hospitalizations was more than $20 billion in 2012 and is expected to reach over 50 billion by 2030. Readmissions can be avoided by monitoring weight daily, maintaining healthy blood pressure, adhering to a low sodium diet, medication compliance, and daily exercise. We aimed to reduce 30–day readmission rate and improve patients' health by employing self–monitoring strategies for early indications of HF exacerbations.

Methods: The study was a single center, prospective, randomized, controlled trial. We enrolled 40 subjects during admission Patients were randomized in a 1:1 ratio into treatment group (TG): (HF kit, inpatient education, telephone follow up) or control group (CG) (inpatient education, telephone follow up). All patients were followed for 6 months.

Results: In the first 3 months of the study no patient in the TG was readmitted to the hospital. Seven patients in the CG were readmitted to the hospital. Three of those patients were readmitted in the first 30 days. In the 3–6 month period 3 patients in the TG group and 5 patients in the CG were admitted. At the end of the study 3 patients in the TG had readmissions and 12 patients in the CG were readmitted. Four patients passed away during the follow up period. Those patients were not considered in the final analysis. Two were in the TG and 2 were in the CG.

Conclusion: Individual patients in the TG had fewer readmissions than the CG during the follow up (8% vs 33%). Thirty day readmissions for the study cohort were far less than the average for HF patients which is about 25% according to the AHA. Limitations include small sample size and short follow up. Because of the pandemic patients waited to go to the hospital until they were sicker. Results may have been different if we enrolled patients earlier on in HF exacerbation.

Clinical Implications: Providing HF patients with self–monitoring tools may decrease readmissions.

Sexual Victimization and Sexual Health among College Women: A Systematic Review

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Sexual violence is a major public health concern, especially for college women. Sexual victimization is associated with numerous negative consequences, including difficulties relating to sexual functioning. The current systematic review aimed to synthesize the existing research literature examining the association between sexual violence on sexual functioning among college women.
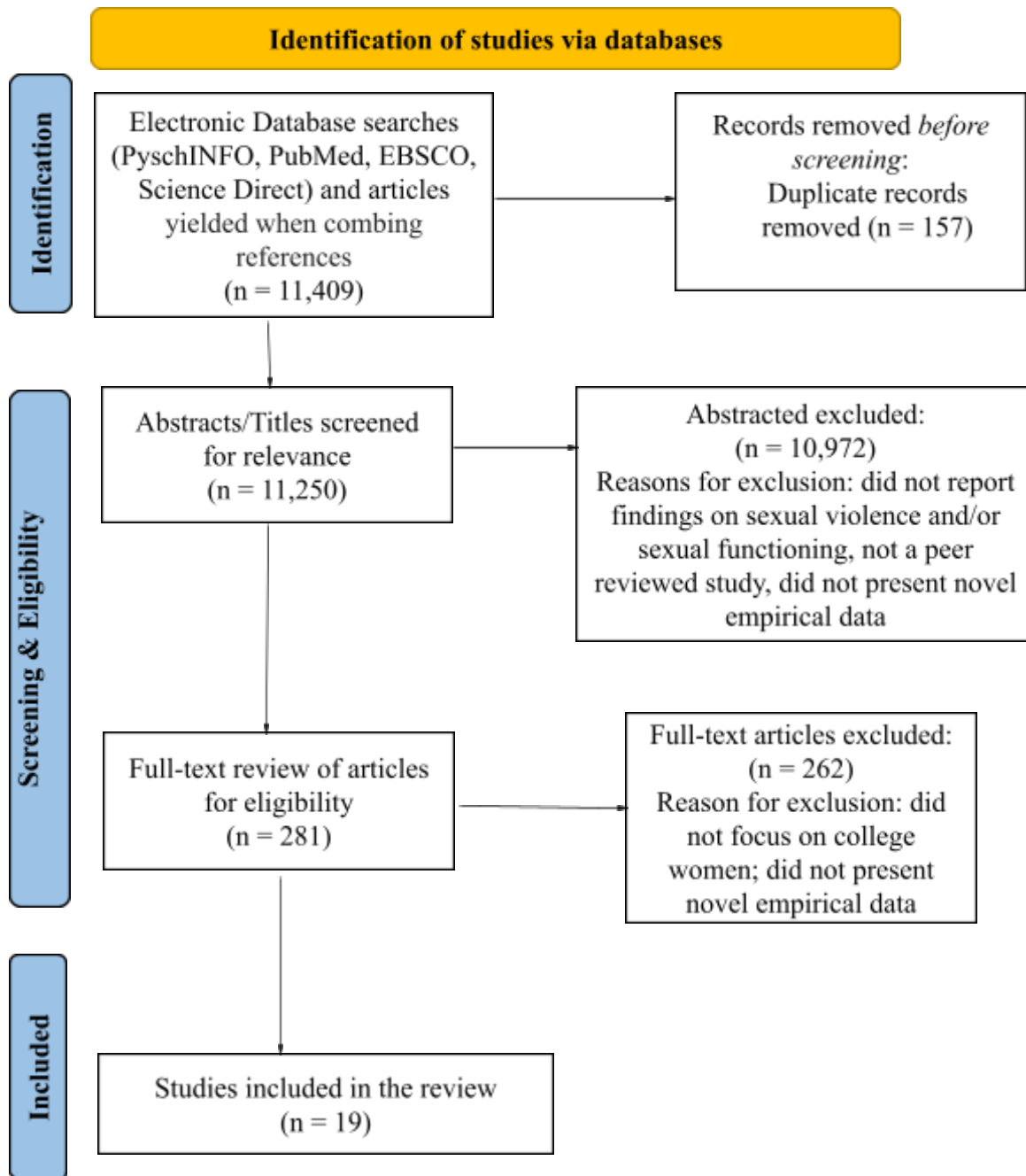
Methods: Only peer–reviewed articles reporting original data and written in English, which assessed for sexual functioning and sexual victimization among a sample of college women, were include in the review. Articles were included if the research study assessed sexual victimization occurring in childhood, adolescence, or adulthood.

Results: A total of 19 articles met these inclusion criteria and were included in the synthesis of the literature. In studies of college women, sexual victimization occurring in adulthood was associated with worse sexual health outcomes among college women in 7 of the 19 studies. Findings were mixed regarding the association between childhood sexual abuse and sexual functioning among college women. Further, in 3 studies, psychological symptoms (e.g., depression, anxiety) mediated the association between sexual victimization in adulthood and worse sexual functioning among college women. Studies varied in what domains of sexual functioning were assessed, and as a result, a limited number of studies included assessments of the same domain of sexual functioning. Further, some studies did not assess sexual victimization at multiple points in development (i.e., childhood, adolescence, adulthood).

Conclusion: Future studies with longitudinal designs and a wider range of sexual functioning outcomes are needed, including studies focused on women attending 2–year and technical colleges.

Clinical Implications: Future studies should consider using diagnostic clinical interviews for female sexual dysfunction disorders and include all relevant diagnostic criteria to improve the accuracy and specificity of prevalence of sexual dysfunction in this overlooked population.

Figure 1. PRISMA flow diagram. Systematic identification of studies that evaluated sexual

health in college women who experienced sexual violence. PRISMA = Preferred Reporting Items

for Systematic Reviews and Meta-Analyses.

Identification of studies via databases

Identification

Electronic Database searches
(PyschINFO, PubMed, EBSCO,
Science Direct) and articles
yielded when combing
references
(n = 11,409)

Records removed *before
screening*:
Duplicate records
removed (n = 157)

Screening & Eligibility

Abstracts/Titles screened
for relevance
(n = 11,250)

Abstracted excluded:
(n = 10,972)
Reasons for exclusion: did not report
findings on sexual violence and/or
sexual functioning, not a peer
reviewed study, did not present novel
empirical data

Full-text review of articles
for eligibility
(n = 281)

Full-text articles excluded:
(n = 262)
Reason for exclusion: did
not focus on college
women; did not present
novel empirical data

Included

Studies included in the review
(n = 19)

Physical Therapists and medical providers aren't clearing the spine in patients with vertigo and dizziness

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational
Primary Research Location: Southeastern New England
Funded By: none

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Abstract

Background: To describe current practice trends of medical providers in assessing the cervical spine in those with complaints of dizziness and vertigo (D/V), benign paroxysmal positional vertigo (BPPV) or concussion (CON).

Methods: Online survey assessed if providers assessed the cervical spine in patients with complaints of DV, BPPV or CON.

Results: Survey data of Rhode Island and Massachusetts medical providers demonstrated a statistically significant result (P < 0.01) for practitioners who see patients with DV, BPPV or CON. 11.1% of PTs, 50% MDs & 52.9% of PA/NPs do not assess the neck as part of the examination for these patients. 16.7% MDs & 11.8% of PA/NPs only assess the neck if pain is present. The craniocervical flexion (CCFT) tests was used rarely/never to assess these patients by: PTs 45.7%, 86% MD, DO 48%, PA/NP 100% of the time. Smooth pursuit (SP) was rated as being used rarely/never: PTs 54.3%, MD 90.2%, DO 80%, PA/NP 93.75% of the time. Supine cervical flexion rotation test (SCFRT) was rated as being used rarely/never: PTs 42.5%, MD 88.2%, DO 36%, PA/NP 81.25% of the time. 86.9% of PTs, 38% of MDs, 88.5% of DOs and 62.5% of PA/NP reported that they used active cervical ROM (CROM) to screen the neck in these patients.

Conclusion: Despite the high prevalence of cervical involvement in patients referred for the treatment of DV, BPPV or CON, the vast majority of referring providers reported not assessing the neck as a point of origin for the patient's symptoms. The percentage of medical providers using evidence-based techniques to identify cervical involvement such as the CCFT, SP, SCFRT was even worse. CROM was used by the majority of medical providers despite its lack of validity in assessing upper cervical spine mobility.

Clinical Implications: Given the high prevalence of cervical involvement, Physical Therapists and referring providers must do a better job of screening the cervical spine in patients with DV, BPPV and CON. The continued used of CROM as a mechanism for screening patients for cervical involvement must stop as it has been shown unable to assess upper cervical mobility.

Distal–less homeobox 5 (DLX5) knockdown inhibits Osteoarthritis pathway networks while inciting cartilage repair networks in mesenchymal lineage cells

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Knee Osteoarthritis (OA) is a leading cause of disability and functional impairment in the United States. As the articular cartilage is regularly exposed to biomechanical forces from joint impact, focal cartilage are common. There is a need to develop effective strategies to restore damaged cartilage tissue. Bone–marrow–derived mesenchymal stromal cells (BM–MSCs) have been extensively researched in preclinical models of cartilage restoration. However, BM–MSCs have certain limitations. During late–stage chondrogenesis, BM–MSCs exhibit increased gene expression of common cartilage hypertrophy–ossification markers. DLX5, a bone–morphogenic protein 2 (BMP–2) inducible transcription factor and hypertrophy markers, is significantly upregulated in BM–MSCs and in the chondrocytes isolated from OA patients. The objective of this study is to investigate the therapeutic efficacy of using DLX5 knock–down BM–MSCs as a cell based therapy for attenuating OA.

Methods: BM–MSCs were stabilized with pRetro–E2–SV40 to ensure phenotypic stability during culture expansion. DLX5 knock–down was performed using lentivirus bearing shDLX5. DLX5 knockdown was confirmed by westernblot. RNAseq was performed and the resulting large data set was analyzed using ingenuity pathway analysis (IPA) software to determine affected gene networks. shDLX5 cells, non–targeting controls (NTC) or saline were administered via intraarticular injection into the knees of athymic rats following medial meniscus destabilization by partial tearing. Knees were isolated for histological analysis using Toluidine Blue stain 48 days post–injury.

Results: DLX5 knockdown(Fig.1A) does not affect the viability of the cells(Fig.1B). RNAseq analysis of these cells revealed that DLX5 knockdown inhibits osteoarthritits pathway and activated woundhealing pathways(Fig.2). DLX5 knockdown BM–MSCs significantly promoted the cartilage repair in the rats in vivo as compared to NTC and saline controls(Fig.3).

Conclusion: We investigated the therapeutic capability of using DLX5 knockdown BM–MSCs for cartilage injury repair and OA prevention. BM–MSCs did not show significant cell death upon DLX5 knockdown. Further, RNAseq suggested vital changes in the gene expression of DLX5 knockdown cells indicating the inhibition of OA pathway and the activation of cartilage injury repair pathways. Our in–vivo study demonstrates that DLX5 knockdown BM–MSC treatment results in significantly improved cartilage health.

Clinical Implications: These findings suggest that DLX5 is a potential theraputic target for stimulating cartilage repair and post–traumatic OA prevention.
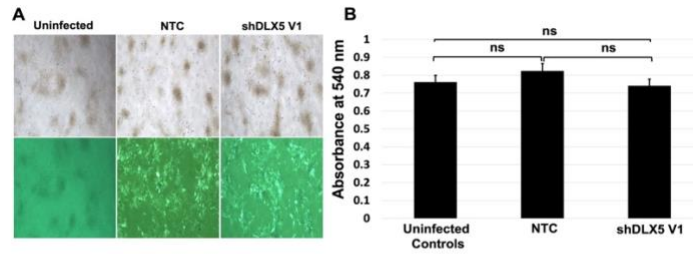
Fig - 1: DLX5 knockdown does not affect viability of the cells. **(A)** The knock down of DLX5 in phase contrast as well as fluorescent images. **(B)** Cell viability at passage #17 was analyzed using MTT cell viability assay kit. ns = not significant
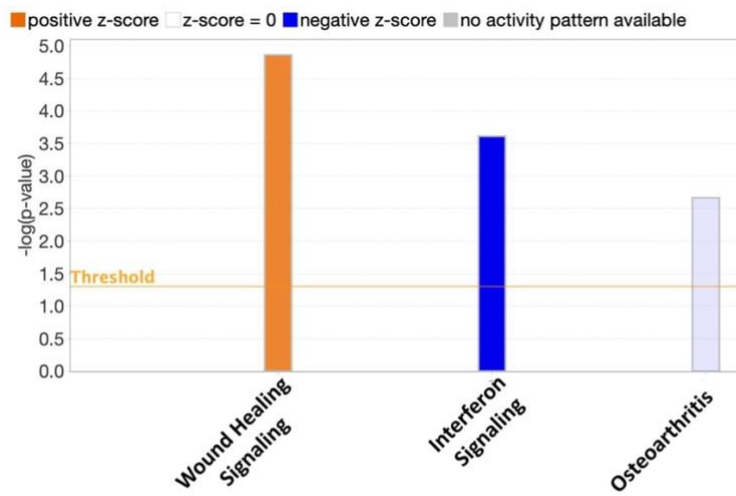

Fig - 2: DLX5 knockdown modulates cell signaling network in BM-MSCs. The wound healing pathway (Orange) is upregulated, and the Osteoarthritis pathway (Blue) is inhibited
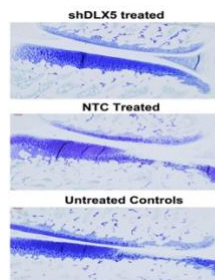

Fig - 3: DLX5 knockdown BM-MSCs injection results in better cartilage profile in rats. Representative images of knee cartilage histology stained with Toluidine Blue at 6 weeks post surgery of shDLX5-BM-MSC treated, non-targetting control (NTC)-BM-MSC treated and untreated animals is shown. Scale bar = 100 uM

Relationships between Schistosoma mansoni infection intensity and nutritional status and anemia among preschool–aged children in Uganda

2023 Lifespan Research Day Abstract Submission Contest

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Edridah Muheki AND Narcis Kabatereine, MD, Ministry of Health, Kampala, Uganda

Amaya L Bustinduy, MD, PhD, London School of Hygiene and Tropical Medicine

Jennifer F Friedman, MD, PhD, Professor, RI Hospital, Hasbro Children's Hospital, Brown University. Dept of Pediatrics

Abstract

Background: Schistosomiasis causes anemia and impaired linear growth among children. However, there is a paucity of evidence in pre–school age children (PSAC) because it was commonly held that they were not significantly infected, and studies addressing reversibility of morbidity with praziquantel (PZQ) are limited as PZQ has only recently been approved for children ages 1–4. As part of an ongoing NIH–funded phase II trial of optimal PZQ dosing for PSAC ages 12–48 months in Uganda, we present baseline findings assessing S. mansoni infection and nutritional morbidities.

Methods: Children with S. mansoni infection, detected by Kato Katz in duplicate stool samples, were enrolled from the Lake Albert region in Uganda. Anemia was defined as hemoglobin <11.0 g/dL. Undernutrition categories of underweight (weight–for–age z score<–2), stunting (length–for–age z score<–2), and wasting (weight–for–length z score<–2) were defined using WHO Anthro. Statistical analyses included multivariate linear and log binomial regression models adjusting for age, malaria co–infection, and father's education level.

Results: Of the 354 participants included, the median infection intensity was 72 EPG (IQR 24–258). Sixteen percent of children had malaria and 56.5% were anemic. Higher infection intensity was associated with lower hemoglobin concentrations (ß=–0.014, p=0.003), an increased risk for anemia (RR=1.05, CI 1.01–1.10). Infection intensity was not significantly associated with underweight (RR=0.71, CI 0.45–1.09), stunting (RR=0.89, CI 0.77–1.03), or wasting (RR=1.33, CI 0.68–2.63).

Conclusion: This trial offers a unique opportunity to assess S. mansoni–associated morbidity in PSAC who received PZQ treatment and will be followed for 12 months. At baseline, infection burden was associated with an increased risk for anemia, which may be explained in part by occult blood loss associated with schistosome egg–induced intestinal damage. Evidence of PSAC experiencing schistosomiasis–related nutritional morbidities further demonstrates the need for PZQ mass drug administration campaigns to include young children in endemic areas.

Clinical Implications:

Heart to Heart: Impacts of Social Support on Blood Pressure in Pregnancy
2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational

Primary Research Location: The Miriam Hospital

Funded By: NIH

Author(s):

Victoria N Scarfo, Staff, The Miriam Hospital. Dept of Psychiatry & Human Behavior

Amanda Desmarattes, Staff, The Miriam Hospital. Dept of Psychiatry & Human Behavior

Margaret H Bublitz, PhD, Associate Professor, The Miriam Hospital. Dept of Psychiatry & Human Behavior

Abstract

Background: Elevated blood pressure is a common occurrence in pregnancy that poses risk for adverse outcomes. One in ten women experience hypertensive disorders of pregnancy, yet no non–pharmacological interventions exist to prevent hypertension onset. Studies have indicated that social support plays a role in protecting individuals against various life stressors, and it has been identified as an indicator of cardiovascular well–being. Therefore, our objective is to investigate the relationship between self–reported and ecological momentary assessment (EMA)–reported social support and blood pressure levels in pregnant women.

Methods: Fifty–four pregnant participants in an ongoing clinical trial of prenatal mindfulness training for women at risk for hypertensive disorders of pregnancy (NCT04626245) were enrolled, and thirty–nine were included in this analysis. Participants completed the Prenatal Social Support Instrument (PSSI) and two weeks of ecological momentary assessments of positive and negative social support prior to randomization. Ambulatory blood pressure was monitored over 24–hours.

Results: Enrolled participants were 32 years old (SD=5) with an average gestational age of 17 weeks and 5 days. Twenty percent reported Hispanic ethnicity, 57% reported their race as White, 17% Black/African American; 37% of participants were nulliparous and 83% were partnered. Participants who reported higher partner support on the PSSI also reported lower EMA–based negative social support (r= −.749, p<0.001). Higher scores on both PSSI and EMA–based social support measures were associated with lower 24–hour blood pressure. Specifically, we found negative correlations between EMA–reported positive social support measures and daytime blood pressure (Systolic: r= −.451, p=0.046; Diastolic: r= −.553, p=0.011). We also found negative correlations between PSSI subscales of satisfaction with social support and healthcare–related social support and 24–hour diastolic blood pressure (r=−.415, p=.039 and r=−.333, p=.038, respectively).

Conclusion: We found that higher levels of perceived social support on both measures were associated with lower blood pressure during pregnancy. Incorporating strategies to enhance social support in expectant mothers may be valuable to perinatal care. Further research is encouraged to investigate the long–term effects of social support on maternal and fetal health outcomes.

Clinical Implications:

Development Of An Implantable Trapezium Replacement For Measuring In Vivo Loads At The Base Of The Thumb

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Trey Crisco, Professor, RI Hospital, Brown University. Dept of Orthopedics
Julia A Henke, Undergrad, Brown University. Dept of Orthopedics
Daniel McDermott, Undergrad, Brown University. Dept of Orthopedics
Rohit Badida, Staff, RI Hospital. Dept of Orthopedics
Amy M. Morton, Staff, RI Hospital. Dept of Orthopedics
Josephine M. Kalshoven, Graduate Student, Brown University. Dept of Orthopedics
Douglas C. Moore, Instructor, RI Hospital. Dept of Orthopedics

Abstract

Background: The thumb is a common site for trauma and repetitive workplace injury, often leading to the development of osteoarthritis, with altered joint loading a primary mechanism for these pathologies. However, the in vivo loads at the joints are not known. The goal for this project is to develop an instrumented replacement trapezium capable of measuring the loads in vivo.

Methods: A novel design utilizing a diaphragm as the load sensing element was incorporated into a trapezium bone replacement. Five strain gauges were bonded to the underside of the diaphragm. Calibration with a supervised neural network was performed by securing the diaphragm designs to a 6 DOF load cell, applying loads (F_x: 65.1N, F_y: 68.6N, F_z: 53.4N, M_x: 0.28Nm, M_y: 0.04Nm, and M_z: 0.26 Nm), and comparing the sensing element loads to the 6 DOF load cell loads. Loading along the longitudinal axis of the first metacarpal (F_y) was set as the most critical outcome measure. Accuracy was defined as the 95% CI of the range of the limits of agreement (LOA) using a Bland–Altman analysis.

Results: The 95% CI LOA in F_y was 1.9 N. Strain gauge removal had variable effects, depending on number and locations of the gauges removed. For example: Removing individual gauges increased the 95% CI LOA for F_y by 3.0 N, 3.9 N, and 5.0 N, respectively.

Conclusion: We present a novel design for a trapezium replacement instrumented with 5 strain gauges to measure loads across the thumb carpometacarpal joint. Many challenges remain before the device can be considered for FDA clearance and implantation in live humans. To minimize risk, the device will not be provided with a battery but will be inductively powered. Strain signals will be digitized and transmitted via a Bluetooth low energy chipset.

Clinical Implications: An instrumented trapezium capable of measuring loads at the base of the thumb will be immensely valuable to clinicians, researchers, and implant designers who need accurate load data to understand the role of joint loading in thumb pathophysiology, to refine musculoskeletal models, to standardize pre–clinical testing, and to develop more effective and cost–effective surgical treatments.

Development and Clinical Evaluation of a Device for Measuring Weight Bearing in Pediatric Standers

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Joseph Stevenson, Graduate Student, Brown University. Dept of Orthopedics

Joseph J. Crisco, Professor, RI Hospital, Brown University. Dept of Orthopedics

--- Abstract ---

Background: Assisted standing for children requiring wheelchairs for mobility has proven to be beneficial from both psychological and physiological perspectives. However, due to the current rigid design of standers, it has been demonstrated that children may not actually be fully weight bearing. The objective of this study is to develop a weight bearing device (WBD) to better understand foot loads while in standers in order to assist caregivers in improving positioning as well as a more precise metric in studies of the benefits of standing.

Methods: With IRB approval, fifteen individuals ranging between 8 to 18 years old who utilize a stander in a school setting will be recruited. To gather loading data, a custom WBD comprised of four full-bridge micro load cell sensors positioned across a 220 mm by 84 mm Aluminum plate was fabricated.

Results: In bench-top testing, the WBD was calibrated to acquire measurements of weight bearing on each foot, as well as distribution of body weight between left and right, toe vs. heal loading and well as medial and lateral loading. The output data is used to make real-time changes to the individual's standers straps to correct and improve their weight bearing capabilities. To date, data from four subjects have been collected over a 20-minute time period. The accuracy of the device for these tests ranged between 75–80%. Results were shared with the physical therapists at Meeting Street to refine the user interface and the specific data presentation.

Conclusion: The results to date have clearly demonstrated that the children are not fully weight bearing, but real time adjustment in stander positioning and strapping can improve weight bearing. This information can be used by the physical therapists to correct straps tightness or brace locations in order to achieve a higher weight bearing load.

Clinical Implications: Currently, physical therapists that utilize standers are unable to accurately tell how much the device's straps and braces are negatively affecting a patient's ability to optimally bear weight. The weight bearing device designed for this study supplies measurements that can be used for improving therapeutic techniques and ultimately an individual's health.

Biorepository and Molecular Microbiology Core Laboratory: Biorepository of Clinical Bacterial Isolates, Susceptibility Testing, and Bacterial Genome Sequencing

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational

Primary Research Location: 167 Point Street, Coro Building Suite 3229, Providence, RI

Funded By: NIH

Author(s):

Evgeny Yakirevich, MD, Professor, RI Hospital, Brown University. Dept of Pathology & Laboratory Medicine

Tao Hong, MD, Director of Clinical Microbiology, RI Hospital. Dept of Pathology & Laboratory Medicine

Swapna Charla, Staff, RI Hospital. Dept of Pathology & Laboratory Medicine

--- Abstract ---

Background: Resistance to currently available antimicrobials is a significant global public health problem. Biorepository and molecular microbiology (BMM) core for the Center for Antimicrobial Resistance and Therapeutic Discovery (CARTD) at Lifespan serves as a source of characterized clinical isolates for investigators aiming the use of microorganisms in their research projects.

Methods: Our main services include: (I) The BMM Core procure, store, track, and release clinical isolates. These clinical isolates are representative of regional patient population from the Rhode Island community in real time. (II) The bacterial organisms are confirmed by 16S ribosomal sequencing and yeasts by internal transcribed spacer sequencing. (III) The phenotypic resistance profile is determined by susceptibility testing as per Clinical laboratory standards Institute reference standards.

Results: BMM core holds a microbial collection of over 650 characterized clinical isolates from sterile body sites such as blood, tissue, and body fluids. The inventory includes clinical significance and epidemiological important isolates such as Staphylococcus Aureus, Vancomycin Resistant Enterococci (VRE), Pseudomonas Aeruginosa, E. Coli, Enterobacter cloacae complex, Streptococcus Pneumonia, Klebsiella Pneumonia, Klebsiella Oxytoca, Klebsiella Aerogenes, Citrobacter Youngae, Candida Albicans, and Candida Glabrata of various antimicrobial resistance profiles. The BMM Core provides genomic sequencing and bioinformatics analysis of clinical specimens/isolates. Targeted and whole genome Next Generation Sequencing (NGS) is performed on Illumina iSeq sequencer. Bioinformatics pipelines include all required steps from raw sequencing data to data output for applications including taxonomic identification/confirmation, phylogenetic relationships, and detection of antimicrobial resistance markers.

Conclusion: BMM Core is a regional biorepository for significant clinical isolates. Investigators from Lifespan, Brown University and beyond can have the access to BMM services. The microorganisms from the core facility can be requested by the researchers for their research project needs. Investigators from Brown and Lifespan actively use our services which are not just limited to clinical isolates but also microorganisms banking, antimicrobial susceptibility testing, microorganism sequencing and data analysis based on the needs of the user.

Clinical Implications: Our services would be of great benefit to investigators studying antimicrobial resistance, host pathogen interactions, therapeutic discovery, epidemiology, and diagnostic development. For further information, please contact Charla Swapna, MSc (401)–444–4371 scharla@lifespan.org

Longitudinally assessed maternal sleep position, measures of breathing during sleep, and fetal growth in high–risk pregnancies

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Juliana Katz, Medical Student, Brown University.

Laura Sanapo, MD, Assistant Professor, The Miriam Hospital, Brown University. Dept of Medicine

Margaret Bublitz, PhD, Assistant Professor, Associate Professor, The Miriam Hospital. Dept of Medicine, Psychiatry & Human Behavior

Melissa Guillen, The Miriam Hospital. Dept of Medicine

Ashanti Avalos, MPH, The Miriam Hospital. Dept of Medicine

Annaly Aldana, The Miriam Hospital. Dept of Medicine

Danielle Wilson, PhD, Institute for Breathing and Sleep, Austin Hospital. Dept of Research

Ghada Bourjeily, MD, Professor, The Miriam Hospital, Brown University. Dept of Medicine

Abstract

Background: Through a potential for hemodynamic compromise, supine position starting in mid–gestation may impact placental perfusion, potentially leading to fetal complications. Subjective recall of supine sleep position during pregnancy has been linked to increased risk of stillbirth, but objective, longitudinal data on supine sleep and fetal growth is lacking. We aim to examine how sleep position and breathing parameters change throughout pregnancy, then investigate the associations between maternal supine sleep, assessed objectively in early and late gestation, and fetal growth velocity in high–risk women.

Methods: This study is a secondary analysis of data from a study investigating maternal sleep, among women with singleton pregnancies and body mass index (BMI) =27 kg/m2. Participants underwent level–III sleep apnea testing. Maternal sleep position was assessed by accelerometry. FetalGPSR software was used to derive percentiles of estimated fetal weight (EFW) and birthweight. We calculated fetal growth velocity as a change in percentile/week between second–trimester anatomy scan and birthweight.

Results: In total, 446 women were included, with N=126 in the longitudinal sleep pattern analysis and N=83 in the fetal growth analysis. Sleep onset position and predominant sleep position were significantly correlated in both early (p=0.001) and late (p<0.01) pregnancy. However, supine going–to–bed position predicted predominant supine sleep in only 47% of women. There was a significant change in sleep position between early and late pregnancy (p=0.04) with a reduction in predominant supine sleepers (51.6% to 30.2%) and an increase in left lateral sleepers (24.6% to 37.3%). Percent of sleep spent supine and oxygen desaturation index, in third trimester, were significantly associated after BMI adjustment (B=0.018, p=0.04). Models did not suggest significant effects of supine sleep on growth velocity, in early or late pregnancy (p>0.05).

Conclusion: Going–to–bed position predicts predominant supine sleep position in less than half of women with overweight and obesity. Time spent supine throughout pregnancy correlates with measures of sleep–disordered breathing. Maternal sleep position patterns did not affect fetal growth velocity in this population.

Clinical Implications: Pregnant individuals can be reassured that despite an association with measures of sleep disordered breathing, supine sleeping during pregnancy is not associated with fetal growth abnormalities.

Anti–Mullerian hormone levels and respiratory parameters among pregnant women with overweight or obesity

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Ghada Bourjeily, MD, Professor, The Miriam Hospital, Brown University. Dept of Medicine
Lindsay Clark Donat, MD, Assistant Professor, The Miriam Hospital, Brown University. Dept of Obgyn

Abstract

Background: Obstructive sleep apnea (OSA) is a common disorder that is associated with adverse health outcomes. Through inflammation, oxidative stress, and endothelial dysfunction, oxygen desaturations, airflow limitations, and sleep fragmentation, key features of obstructive sleep apnea (OSA), can contribute to target organ dysfunction. Research linking OSA to ovarian function in females is scarce. We aimed to examine the association between OSA and ovarian reserve, a measure of ovarian function and fecundity.

Methods: This is a secondary analysis of baseline data of women with singleton pregnancies with overweight or obesity before 18 weeks of gestation. Consecutive participants with respiratory event index (REI) >5 events per hour were selected as the OSA group and consecutive participants with REI <1 event per hour as the control group. We collected medical and demographic information by questionnaires and chart review, and included in–home sleep apnea testing using Nox T3, level III device, which collected respiratory event index (REI), used as diagnostic criterion of OSA. AMH (anti–Mullerian hormone) levels were determined in serum using enzyme–linked immunosorbent assay. Linear regression analyses of the association of AMH with respiratory measures were performed.

Results: Ninety–one participants were included in these analyses, with a mean age of 32 years and a mean BMI of 36.9. Median AMH was lower in women with OSA (REI>5) compared to women with OSA (REI<1) (1.46 vs. 2.04 ng/mL), but this difference was not significant (p=.77). Linear regression analyses revealed that REI was significantly associated with AMH (ß =–.527, p=.017), after adjusting for covariates. There was a positive but non–significant association between nadir SpO2 and AMH. There were no other significant associations between respiratory parameters and AMH.

Conclusion: This study is the first to demonstrate an association between OSA and lower AMH levels in a general pregnant population. While the relationship between AMH and OSA is that of an association, it suggests a potentially modifiable cause of infertility in patients with OSA.

Clinical Implications: OSA constitutes a potential therapeutic target in infertility. Further research is needed to investigate the impact of OSA and OSA treatment on fertility outcomes.

Safety Profile of Silver Carboxylate as an Antimicrobial Coating: Viability and Mechanism in Human Cells

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Valentin Antoci, MD, PhD, Associate Professor, The Miriam Hospital, Brown University. Dept of Orthopedics
Christopher Born, MD, Professor, Professor Emeritus, RI Hospital, Brown University. Dept of Orthopedics
Dioscaris Garcia, PhD, Assistant Professor, RI Hospital, Brown University. Dept of Orthopedics

Abstract

Background: The growing burden of antibiotic resistant pathogens warrants rapid attention to developing novel antimicrobial modalities. This is coupled with the heavy cost incurred upon hospitals and patients due to chronic surgical site infections, with 300k–500k cases occurring annually in the US and a monetary cost of upwards of $1.5B. The aim of this project is to analyze the cytotoxic effect of a novel antimicrobial, silver carboxylate, on human cells involved in surgical wounds. Silver carboxylate may provide an improvement to antibiotics in that silver induces bacterial death in a multimodal fashion, and the organic moiety improves entry of the silver ion into bacterial cells. We are specifically investigating the apoptotic versus necrotic mechanism with the goal of inhibiting apoptosis and improving human cell viability while promoting microbial death.

Methods: Human osteoblasts, endothelial cells, skeletal muscle cells, and keratinocytes were exposed to silver carboxylate in increasing multiples of the MIC for 24 hours. Silver carboxylate was delivered in a novel TiO_2–PDMS matrix to induce controlled release. Cell viability and apoptosis/necrosis were measured using specific fluorescent markers and fluorometry.

Results: The 1x MIC of silver carboxylate was shown to not impact cell viability, whereas the 10x–150x conditions did result in increased cell death. Preliminary mechanistic results suggest a 39% increase in apoptosis from the 1x MIC to the 10x MIC in skeletal muscle cells. The 1x MIC did not induce a statistically significant level of apoptosis.

Conclusion: Silver carboxylate does not impact human cell viability at the 1x MIC, and may induce an apoptotic–like mechanism of cell death in human cells above a 1x concentration. Further work is necessary to improve the power of the conclusion and further characterize results using flow cytometry.

Clinical Implications: Understanding the mechanism of cell death is critical because an apoptotic mechanism can be inhibited, resulting in improved cellular viability. Silver carboxylate in the TiO_2–PDMS matrix is being studied for application as a novel antimicrobial coating for surgically implanted materials, to mitigate the risk of chronic bacterial seeding post–operatively. This innovative biomaterial may also have beneficial synergistic effects when used conjunctively with current antibiotics.
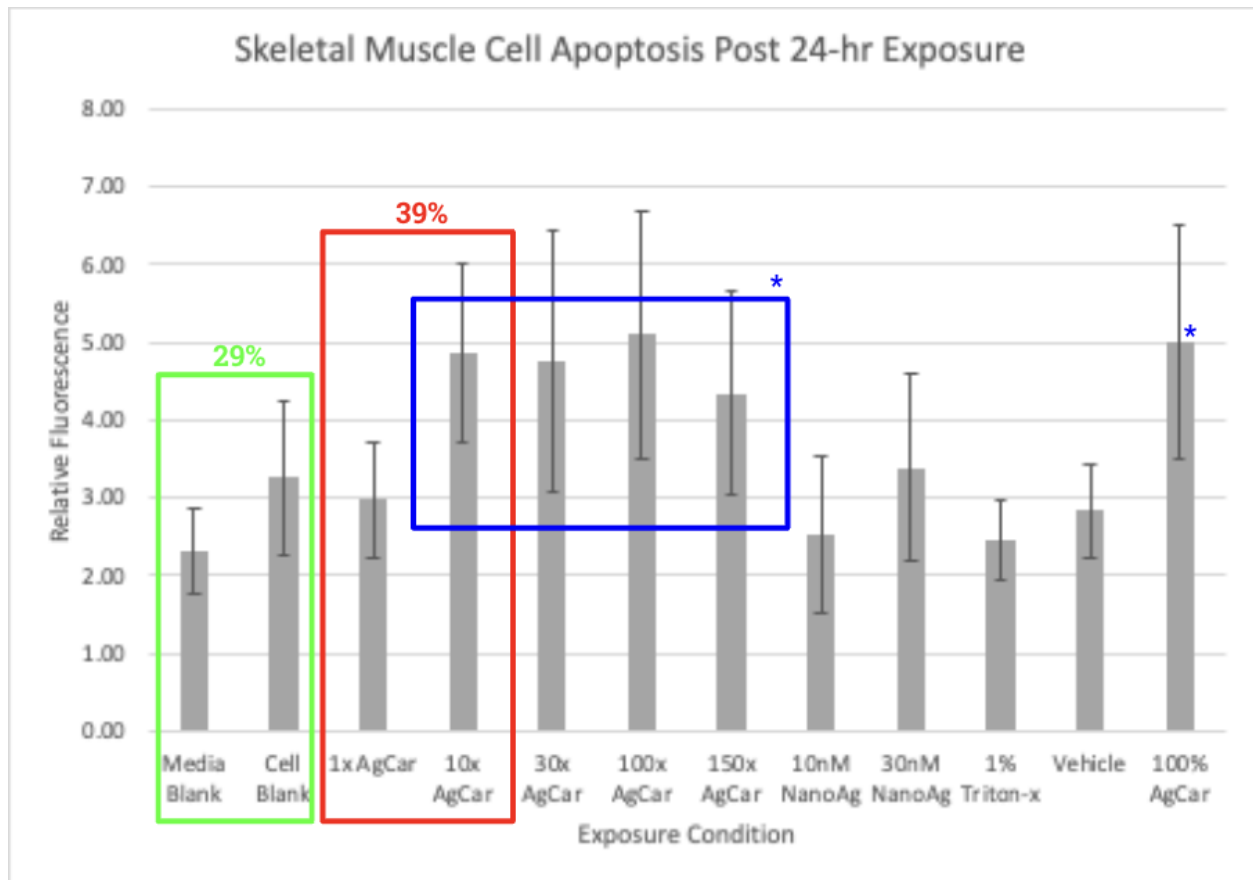
Figure 1. Levels of apoptosis in skeletal muscle cells after 24hr condition exposure. Statistically significant increase in apoptosis seen between the 1x and higher AgCar concentrations as well as the media and cell blanks. N=24

A Robot–Actuated In Vitro Testing Approach For Quantifying Passive Range of Motion in the Thumb CMC Joint

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Josephine M Kalshoven, Graduate Student, Brown University. Dept of Orthopedics
Rohit Badida, Senior Research Engineer, RI Hospital, Brown University. Dept of Orthopedics
Amy M Morton, Senior Research Engineer, RI Hospital, Brown University. Dept of Orthopedics
Douglas C Moore, Assistant Professor, RI Hospital, Brown University. Dept of Orthopedics
Joseph J Crisco, Professor, RI Hospital, Brown University. Dept of Orthopedics

--- Abstract ---

Background: Thumb carpometacarpal (CMC) joint range of motion (ROM) is reduced in osteoarthritis (OA), yet the underlying causes remain unclear. An in vitro ROM assessment could identify the influence of inherent stabilizing structures. This work's aim was to develop an approach to determine the multi–directional biomechanics of the CMC joint in vitro and demonstrate its implementation in six specimens.

Methods: Six human forearms (4M, 2F, 27–63 yrs.) were sectioned at the radius/ulna midshaft. Bones distal to the carpus were removed, except for the first metacarpal (MC1) and the proximal head of the second metacarpal (MC2). A TPM Sensor with 6 infrared markers was rigidly attached to the TPM via k–wires. The MC1 was mounted to the end effector of a 6–axis industrial robot (KUKA). Motion of MC1 with respect to TPM was computed based on bone coordinate systems (CS) generated from the principal directions of articular surface curvature of CT–segmented bone models. CS were directed volarly (+x), proximally (+y), and radially (+z). 32 tests were performed: maximum rotational ROM in flexion, extension, abduction, and adduction, and in 20 combined directions (15–degree increments from primary directions); maximum translation in volar, dorsal, radial, ulnar, and four combined directions. Rotations and translations proceeded at 1°/s or 1 mm/s until a resultant load of 1 Nm or 30 N, respectively. Polar plots were generated from max ROM in each direction.

Results: ROM varied widely, with an average standard deviation of 14° in rotations and 3mm in translations (Fig. 1). For 4/6 specimens, the greatest rotational ROM was in flexion and flexion–coupled regions.

Conclusion: Additional data and grouping by OA grade, age, or sex may yield clearer patterns, as the oldest specimen (with documented OA) demonstrated a larger extension and smaller flexion ROM than other specimens. Applying the presented method with specimens of varying ligament integrity and osteophyte volume could further indicate structural ROM influences.

Clinical Implications: These results demonstrate feasibility of determining in vitro CMC biomechanics across joint conditions. Such data would build a more–complete understanding of pathology and joint integrity, informing our understanding of disease progression and appropriate tactics for prevention, identification, and treatment.
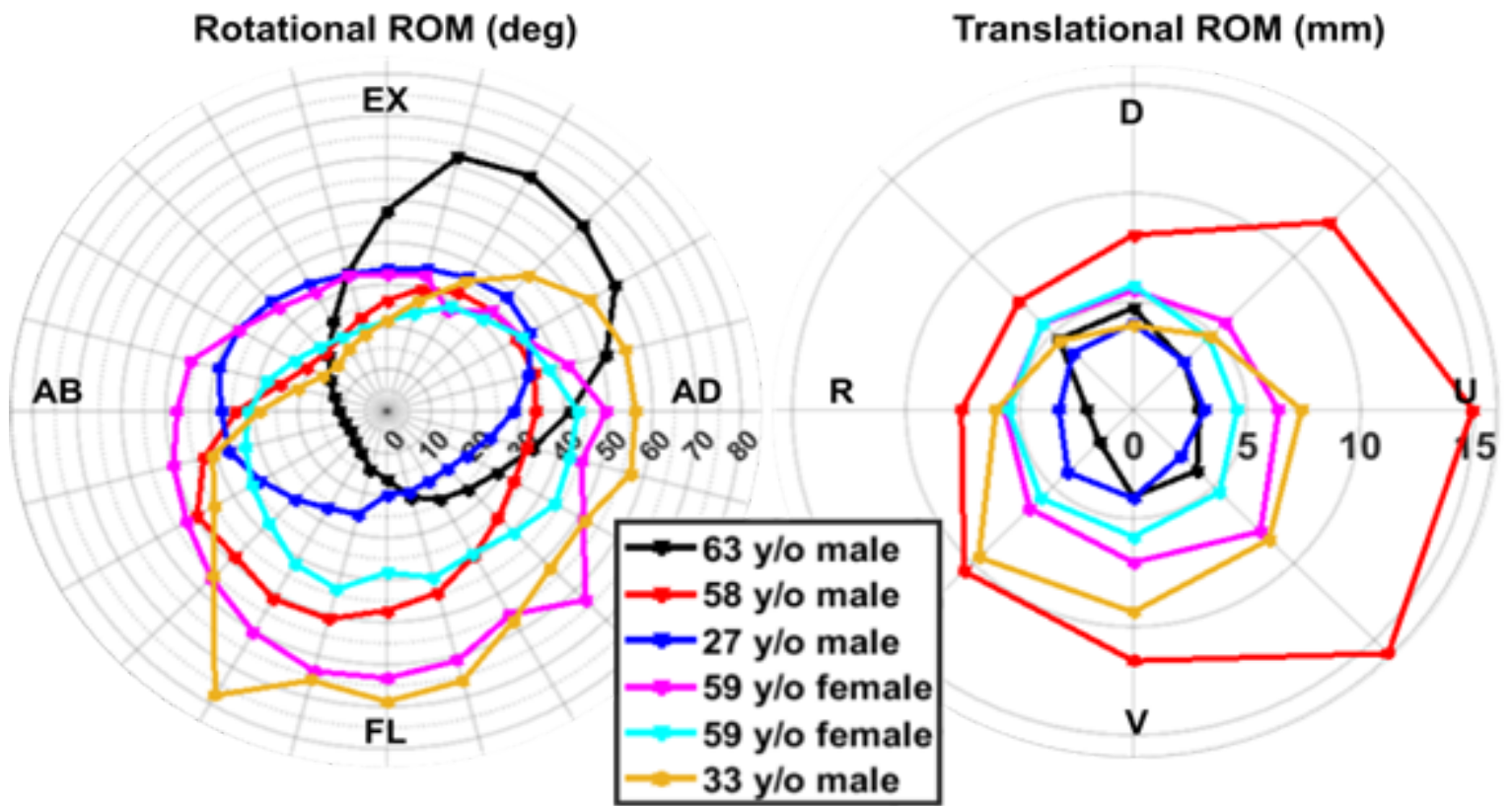
Figure 1. Rotational (left, degrees) and Translational (right, mm) ROM envelopes for 6 CMC specimens.
Flexion (FL), Extension (EX), Abduction (AB), Adduction (AD), Volar (V), Dorsal (D), Radial (R), Ulnar (U)

Accelerated FDA Approvals in Oncology
2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational

Primary Research Location: Rhode Island Hospital

Funded By: N/a

Author(s):

Samantha M Gage, MD, RI Hospital, The Miriam Hospital, Providence VA Medical Ctr, Brown University. Dept of Medicine

━━━━━ Abstract ━━━━━

Background: In 1992, the FDA began the Accelerated Approval (AA) Program, largely in response to the HIV/AIDS epidemic. The program became increasingly popular in the field of oncology starting in 2000, as 85% of drugs approved through the AA pathway between 2010 and 2020 were for oncologic indications. Surrogate end points are often used to predict clinical benefit prior to completion of full clinical trials, and sponsors are required to conduct confirmatory trials to obtain regular approval. We examined the outcomes of all FDA accelerated approvals in the oncology domain from 2000–2018, including changes in the label indication.

Methods: All oncologic therapies with initial FDA approval between 2000–2018 were identified and manually reviewed via analysis of HemOnc.org. From there, drugs that went through the AA pathway were selected for analysis. The exact wording of the accelerated FDA labels was then compared to that of the regular approval labels (if obtained).

Results: Of the 130 drugs reviewed, 46 (35%) of them became available for clinical use via an initial AA. 16 (35%) of these approved drugs had slight label changes for indication. Between 2000–2018, 68% of oncology therapies that first received AA went on to receive full approval. The remaining 32% of medications were either withdrawn due to lack of clinical evidence, or persist on the market without supportive evidence for full approval. The time from AA to full approval ranged from 0.5 to 18 years, with median 3 years.

Conclusion: As of 2023, the majority of medications approved through the AA pathway have been granted regular FDA approval. The most common fates observed are for regular approval to be granted with either no or minor changes in the label verbiage. Importantly, the label underwent changes in 35% of AA–cleared medications, suggesting that AA labels should be considered preliminary.

Clinical Implications: The AA pathway is vital for patients to receive earlier access to potentially clinically significant medications.

Using Outcomes Data to Drive Innovation in a Virtual Adolescent Partial Hospitalization Program

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Molly A Hedrick, PhD, Instructor, Bradley Hospital, Brown University. Dept of Psychiatry & Human Behavior
Emily May, PhD, Post–Doctoral, Bradley Hospital, Brown University. Dept of Psychiatry & Human Behavior
Gabrielle Beaudoin, Bradley Hospital. Dept of Psychiatry & Human Behavior
Marissa Marcus, Bradley Hospital. Dept of Psychiatry & Human Behavior

Abstract

Background: In a time of unprecedented mental health care demands, partial hospitalization programs (PHPs) are crucial to the overall continuum of care. PHPs are intensive programs that fill the gap between inpatient and outpatient services. They are more comprehensive than weekly outpatient care but allow for the development of coping skills within community environments rather than in a more restrictive environment (Vlavianos & McCarthy, 2022). Lifespan has been at the forefront of this model of care for several decades by providing partial levels of care to children, adolescents and adults (e.g., Musella et al., 2016; Musella & Hedrick, 2019; Zimmerman et al., 2023). During the COVID–19 pandemic, many of these programs were adapted for telehealth, leading to innovative models of care beyond the pandemic. This presentation aims to present research on the effectiveness of the Bradley REACH virtual PHP on adolescent psychosocial functioning compared to in–person programs.

Methods: Adolescents ages 12–18 participating in Bradley's in–person (N = 243) and virtual (N = 119) PHPs completed questionnaires at admission and discharge. Therapies were the same aside from treatment modality. The battery of outcome measures included the Difficulties in Emotion Regulation Scale, the Family Assessment Device, and the Youth Outcomes Questionnaire.

Results: Repeated measures ANOVAs demonstrated significant improvement in adolescent emotion regulation, family discord, intrapersonal distress, interpersonal difficulties, suicidal ideation, self–injurious behaviors, somatic problems, oppositional behaviors, and substance use in both the virtual and in–person PHPs from admission to discharge. Somatic symptoms improved more in the virtual PHP compared to the in–person PHP. All other treatment outcomes were the same across programs.

Conclusion: Data from Bradley Hospital's virtual and in–person adolescent PHPs suggests virtual treatment is feasible and effective for teens and their families. These results have propelled exciting opportunities to develop this evidence–driven care model to increase access to care in Rhode Island and beyond.

Clinical Implications: Virtual partial programming is an evidence–based and inventive approach to meeting the needs of the community and expanding access to mental health services for a variety of populations. This data provides evidence that supports the scaling process for Bradley REACH and other virtual mental health services.

Using the Science to Service Laboratory Implementation Strategy to examine SBIRT Implementation in Pediatric Trauma centers

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Geraldine Almonte, BS, RI Hospital. Dept of Emergency Medicine

Julie Bromberg, MPH, RI Hospital. Dept of Emergency Medicine

Sarah J Becker, Professor, PhD, Northwestern University. Dept of Psychiatry & Human Behavior

Janette Baird, Professor, PhD, RI Hospital, Brown University. Dept of Emergency Medicine

Mark R Zonfrillo, MD, Professor, RI Hospital, Brown University. Dept of Emergency Medicine, Pediatrics

Anthony Spirito Spirito, Professor, PhD, RI Hospital, Brown University. Dept of Psychiatry & Human Behavior

Michael J Mello, MD, Professor, RI Hospital, Brown University. Dept of Emergency Medicine

Abstract

Background: Screening, Brief Intervention, and Referral to Treatment (SBIRT) is an evidence–based approach that involves screening adolescents with a validated self–report or interview tool, delivering a brief intervention to teens who screen positive for substance use, and providing referral to treatment when indicated. The American College of Surgeons established a verification guideline requiring level 1 trauma centers to screen all admitted trauma patients and provide brief intervention for those screening positive; however, adherence to this guideline remains low. The Implementing Alcohol Misuse SBIRT (IAMSBIRT) study used the Science to Service Laboratory (SSL) implementation strategy which includes didactic workshop training, performance feedback, and monthly coaching to implement SBIRT across 10 pediatric trauma centers using a stepped wedge study design. This project presents findings from a qualitative sub–study aimed at identifying key themes regarding trauma center nursing, social work, and leadership preferences and experiences with the SSL during IAMSBIRT implementation.

Methods:

Results: Nurses, social workers, and study site leaders (N=36) from 10 pediatric trauma centers completed qualitative interviews at the end of the IAMSBIRT study. The interview questions were guided using the Consolidated Framework for Implementation Research model and assessed trauma center staff perceptions of the SBIRT implementation process, including strengths and areas for improvement. Qualitative interview data were transcribed and analyzed using a directed content analysis approach.

Conclusion: Study findings demonstrated a disconnect between intention to implement SBIRT among leadership and staff (nurses and social workers) not in leadership roles. Staff noted that receipt of SSL performance feedback and ongoing coaching were vital in improving SBIRT delivery. However, staff also reported that performance feedback and coaching were not routinely made available to non–leaders. Similarly, leaders generally reported adequate time spent preparing for IAMSBIRT implementation while some front–line clinicians noted additional communication and training needs.

Strengths and areas of improvement identified from these interviews may help to improve future utilization of the SSL implementation strategy to implement SBIRT in pediatric trauma center settings.

Clinical Implications: Results highlight the need for ongoing process evaluation and SSL strategy implementation modifications to ensure that strategy components widely reach their intended audience.

Perspectives of adolescents and young adult females with sickle cell disease on sexual and reproductive health education

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Maayan Leroy–Melamed, MD, Assistant Professor, Hasbro Children's Hospital. Dept of Pediatrics
Marcia Shew, MD, Professor. Dept of Pediatrics
Patrick McGann, MD, PhD, Associate Professor, RI Hospital, Hasbro Children's Hospital. Dept of Medicine, Pediatrics
Kerry M Hege, MD, Associate Professor. Dept of Pediatrics
Seethal Jacob, MD, Assistant Professor. Dept of Pediatrics

Abstract

Background: As individuals with sickle cell disease (SCD) live longer, sexual and reproductive health (SRH) topics are prioritized. Adolescent and young adults (AYA) with SCD seek SRH medical advice from their providers, most commonly their pediatric or adult hematologists. We aimed to quantify this potential medical and knowledge gap through patient experiences with SRH in an AYA SCD population.

Methods: We conducted a cross–sectional survey of AYA females with SCD. Participants were recruited from a pediatric SCD clinic at an academic medical center. Study data included self–reported demographics, SRH experiences and discussions with providers and guardians.

Results: A total of 12 participants were enrolled, aged 14–24 years of age (mean age 17.0 + 2.7 years). All self–identified as Black/ African–American and all self–identified their gender as female. All but one had reached menarche (mean age 13), and all denied a history of pregnancy. Most (N=9, 82%) endorsed menstrual complaints including dysmenorrhea (n=8), and sometimes associated menses with pain crisis (n=3). Of those who endorsed menstrual complaints, 2 had seen a provider, 1 was prescribed injectable contraception and 1 an implant. Three endorsed coitarche. Two participants had seen a provider for pregnancy prevention and were both prescribed the contraceptive implant. Most (N=8, 73%) had never seen a health provider for, or discussed, contraception.

Conclusion: This pilot study confirms our hypothesis that SRH concerns are common and not well addressed for AYA females with SCD. Menses contributes to the frequency and severity of painful VOE. These data support the routine incorporation of SRH within the comprehensive care structure for AYA with SCD.

Clinical Implications: SRH should be incorporated into comprehensive care for AYA in SCD.

A Multifactorial Analysis of Physical Therapists Ordering Radiographs
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Based on legislation passed in 2021, Rhode Island Physical Therapists (PTs) gained the temporary privilege to order radiographs, commonly referred to as x–ray imaging. Prior studies have shown that allowing PTs to order imaging results in lower healthcare costs, improved rehabilitation outcomes, and improves access to care, however there is limited research on factors associated with ordering practices by PTs in states with newly the acquired privilege to order radiographs. This study examined the effect that continuing education had on the knowledge and confidence of PTs with respect to ordering radiographs and measured the degree of appropriateness of PT radiograph orders.

Methods: Fifty–seven Rhode Island licensed PTs responded to a series of knowledge and confidence–based questions before, and again after completing a 5.5–hour continuing education course on musculoskeletal radiology, and reported on their subsequent radiograph ordering behavior. Each radiograph order was assigned an appropriateness score by a board–certified musculoskeletal radiologist, who was blinded to the identity of the ordering PT and patient, using the American College of Radiography (ACR) Appropriateness Rating Scale (lowest score 1, highest score 9).

Results: 1) Advanced PT practitioners had higher baseline knowledge than BS and MS trained non–specialists ($F = 3.92$, $p = .01$), 2) Advanced PT practitioners had higher baseline confidence than MS non–specialists ($F = 3.93$, $p = .01$), 3) Continuing education improved PT knowledge regardless of highest level of training ($p = .02$), 4) Continuing education improved confidence in MS and DPT non–specialists ($p = .02$), and 5) The mean ACR appropriateness score for PT radiograph orders was 8.41 ($n = 18$, $SD = 1.12$).

Conclusion: With respect to ordering radiographs, advanced PT practitioners tend to have higher baseline levels of knowledge and confidence than non–specialists. However, knowledge improves after continuing education regardless of highest level of training as a PT. Additionally, PT referrals for radiography, in states with newly acquired referral privileges, are appropriate.

Clinical Implications: The preliminary results of this study can be used to direct future radiologic continuing education for PTs, and support RI in its effort to pass permanent legislation for PT imaging referral privileges.

Comparative Risk of Epilepsy in Patients Using Antihypertensive Drugs: A Population–Based Study

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational
Primary Research Location: University of Rhode Island
Funded By: No Funding

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Abstract

Background: Hypertension, affecting more than 30% (greater than 1 billion) of adults worldwide, has been associated with a 2–fold increased risk of epilepsy, potentially mediated by the renin–angiotensin–aldosterone system (RAAS). Preclinical studies suggest that the use of angiotensin receptor blockers (ARBs) may reduce the incidence of epilepsy. This study aimed to compare the risk of epilepsy between ARB and other antihypertensive agents in adult patients with a diagnosis of hypertension.

Methods: Data were obtained from a national health administrative database on beneficiaries aged =18 years with primary hypertension (ICD–9 code 401 and ICD–10 code I10) who were dispensed at least one outpatient prescription of angiotensin receptor blockers (ARBs), angiotensin receptor enzyme inhibitors (ACEIs), ß–blockers (BBs), or calcium channel blockers (CCBs) from 2010 to 2017. Patients with a diagnosis of epilepsy, or dispensed antiepileptic drugs 12 months prior to or within 90 days after initiating the study drugs were excluded. Propensity scores were matched between patients who received either ACEIs, BBs or CCBs, and patients who received ARBs. Cox regression analyses were used to evaluate epilepsy incidence during follow–up in the ARB cohort compared to other antihypertensive classes. These analyses were repeated for the various sub–types of ARBs.

Results: A total of 656,522 patients were included in the ARB–ACEI and ARB–BB matched cohort whilst 638,968 patients were included in the ARB–CCB cohort. The mean age (SD) of the patients was 61.3 (13.0), 61.4 (13.0) and 61.6 (13.0) years in the ARB–ACEI, ARB–BB and ARB–CCB cohorts respectively. The use of ARB was associated with a decreased incidence of epilepsy compared to BB (hazard ratio (HR), 0.76; 95%CI, 0.63–0.93), CCB (HR, 0.80; 95%CI, 0.66–0.98), ACEI (HR, 0.85; 95%CI, 0.70–1.04) and all antihypertensive classes as a group (HR, 0.87; 95%CI, 0.71–1.07).

Conclusion: In patients diagnosed with hypertension, ARB therapy was found to be associated with a decreased incidence of epilepsy compared to other antihypertensive classes and this was significant in patients treated with losartan.

Clinical Implications: The results of the study suggest that ARBs particularly, losartan, may be useful in reducing the risk of epilepsy in patients diagnosed with hypertension.

Plasma Progerin in Patients With Hutchinson– Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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--- Abstract ---

Background:
Hutchinson–Gilford progeria syndrome (HGPS) is an ultra–rare, fatal, premature aging disease caused by the toxic protein, progerin. Circulating progerin has not been previously detected, precluding research using readily available biological samples. This study aimed to develop a plasma progerin assay to evaluate progerin's quantity, response to progerin–targeted therapy, and relationship to patient survival.

Methods:
Biological samples were collected by The Progeria Research Foundation Cell and Tissue Bank from a nonHGPS cohort cross–sectionally and a HGPS cohort longitudinally. HGPS donations occurred at baseline and intermittently while treated with farnesylation inhibitors lonafarnib ± pravastatin and zoledronate, within 3 sequential open label clinical trials at Boston Children's Hospital totaling up to 13 years of treatment. An ultrasensitive single molecule counting progerin immunoassay was developed. Intra–and inter–patient group statistics were descriptive. The relationship between progerin and survival was assessed using joint modeling with time–dependent slopes parameterization.

Results:
Study was originally published as 'Plasma Progerin in Patients With Hutchinson–Gilford Progeria Syndrome: Immunoassay Development and Clinical Evaluation'. Circulation. 2023;147(23), Gordon, et al. Mean plasma progerin in nonHGPS participants (N=69) was 351±251pg/mL, and in drug–naïve participants with HGPS (N=74) was 33,261±12,346 pg/mL, reflecting a 95–fold increase (p<0.0001). Lonafarnib treatment resulted in an average per–visit progerin decrease from baseline of between 35–62% (all p<0.005); effects were not augmented with pravastatin and zoledronate. Progerin levels fell within 4 months of therapy and remained lower for up to 10 years. The magnitude of progerin decrease positively associated with patient survival (p<0.0001). For any given decrease in progerin, life expectancy incrementally increased with longer treatment duration.

Conclusion:
A sensitive, quantitative immunoassay for progerin was developed and used to demonstrate high progerin levels in HGPS plasma that decreased with lonafarnib therapy. The extent of improved survival was associated with both the magnitude of progerin decrease and duration at lower levels. Thus, plasma progerin is a biomarker for HGPS and its reduction enables short and long–term assessment of progerin–targeted treatment efficacy.

Clinical Implications:
The quantitative relationship between plasma progerin and HGPS patient survival solidifies the clinical relevance of progerin measurement and its potential for use as a clinical treatment trial outcome measure.

Skin Motion Artifact of Radiopaque Bead Tracking Relative to Markerless Bone Tracking

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Quianna M Vaughan, Graduate Student, Brown University. Dept of Orthopedics
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Abstract

Background: Skin–based markers are often associated with soft tissue artifacts (STAs) when used to study skeletal kinematics. The magnitude of error is a function of many factors (e.g., joint, type and dynamics of task, marker location). This study quantified STAs of the wrist during 7 motion tasks, as measured by skin surface marker displacement in comparison to markerless bone tracking using biplanar videoradiography (BVR), the gold standard for measuring skeletal kinematics.

Methods: Six subjects (female, 51–68 yrs) with no history of wrist or hand pathology were instructed to complete seven wrist motion tasks, where motion was measured through five radiopaque beads placed on the dorsal surface of the hand. An average of 400 frames were recorded per task. The 3D coordinates of the beads were tracked for all motion using XMALab. Wrist motion was defined as the motion of the third metacarpal (MC3) relative to the radius and was computed using BVR bone tracking software (Autoscoper). STA was defined as the displacement of the average of the beads relative to a neutral pose and reported as a function of wrist motion within each task.

Results: Bead displacement was greatest in the pitcher pouring motion task (~12.5 mm) and least in radial ulnar deviation (~4.5 mm) (Figure 1a). Grasping motion tasks had a larger average of bead displacement (~11.2 mm) than open hand tasks (~5 mm), likely due to the stretch of skin in prehension. Circumduction had the greatest number of outliers. At maximum ulnar deviation, subjects experienced maximum flexion. Average bead displacement was the greatest (~5 mm) at peak ulnar deviation and flexion (Figure 1b).

Conclusion: Grasping tasks yielded a higher bead displacement compared to open hand motion tasks. The large ranges of data for bead displacement and degree of rotation measurements indicate that the motion task was not uniformly performed by all subjects.

Clinical Implications: Quantification of STA will help to contextualize and perhaps enable computational accounting for artifacts, allowing for more–precise assessment of human skeletal kinematics by simply using noninvasive skin–based markers, rather than implanted radiopaque beads.
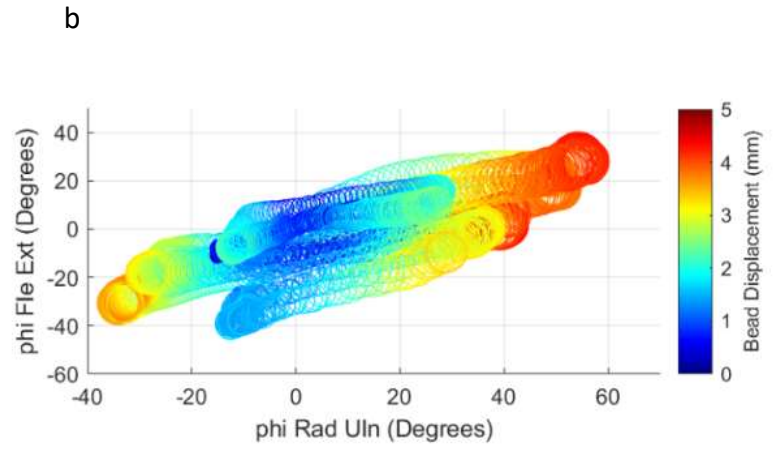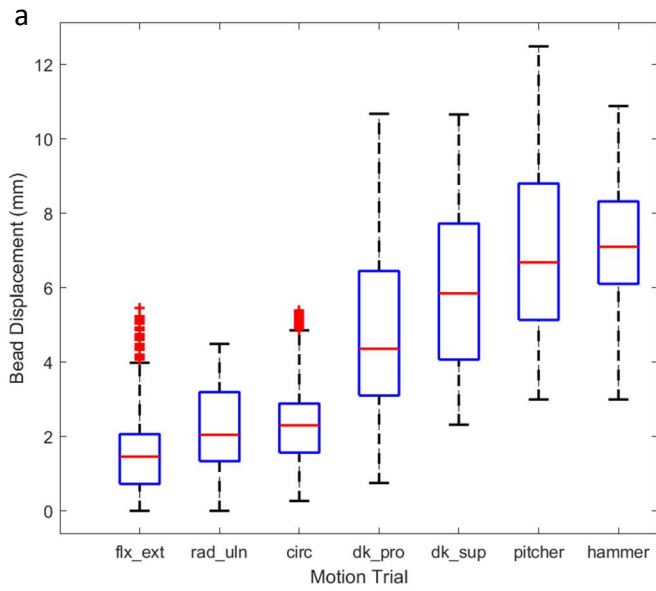
Figure 1. a) Box plot of the magnitude of average bead displacement for all subjects across seven motion tasks: flexion-extension, radial-ulnar deviation, circumduction, doorknob pronation and supination, pitcher pouring, and hammering.
b) Bead displacement at each degree of rotation (phi) for radial-ulnar deviation and flexion-extension wrist motion of all subjects (Radial-ulnar deviation motion trial)

Center of Biomedical Research Excellence (COBRE): Sleep and Circadian Methods Research Core

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: The goal of the COBRE Center on Sleep and circadian rhythms in child and adolescent mental health is to build a center that will help bridge the chasm between sleep and circadian science and child and adolescent mental health. The objective of the Sleep and Circadian Methods (SCM) Research Core is to support researchers in the appropriate use of sleep and circadian methods across the research process. Sleep and circadian data are complex and multimodal, requiring specialized expertise to select, acquire, score, analyze and interpret. The center helps by providing multidisciplinary resources focused on all aspects of the research process starting at study design moving through data acquisition and quality control to data processing and ending at analysis and interpretation. The Long–term goal of this core is to integrate pediatric sleep and circadian methods into Bradley Hospital infrastructure thus providing an enduring resource that will support research addressing the interplay between mental health, development, sleep, and circadian rhythms.

Methods: The aims of the SCM Research Core are 1) Support Center investigators in the selection, acquisition, scoring, analysis, and interpretation of sleep and circadian measures, 2) AIM 2: Facilitate access to in–lab facilities, instrumentation, software, and database resources, required for acquisition, storage, and scoring sleep and circadian data, and 3) Serve as resource for training in current best practices and for identifying novel methodological, measurement, and analytic approaches to sleep and circadian assessments suitable for pediatric mental health populations.

Results: We will report on the equipment that is available through the SCM Research Core, the number of consultations, trainings, and other support provided to Lifespan researchers, and the focus for the next year.

Conclusion: The SCM Research Core is an important resource to support research focused on sleep and mental health in pediatric populations.

Clinical Implications: Integrating sleep and mental health research will help improve mental health care for young people.

The Links between Parental Support and Criticism and Purpose in Life among Black, Latinx, and White Young Adults

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Among young adults, maternal support is associated with a high sense of purpose in life (PIL). However, less is known about the impact of fathers, especially among minoritized populations. Researchers have critiqued cross–cultural use of parenting measures, noting that there is a dearth of studies explicitly testing whether measures developed in predominantly White samples are measuring constructs similarly across minoritized groups. In this study, we tested measurement invariance (by race/ethnicity) of instruments assessing parental support and criticism and PIL among young adults. If measurement invariance was established, our goal was to examine the association between maternal and paternal criticism and support with PIL among White, Black, and Latinx young adults.

Methods: The sample consisted of 938 individuals (271 Black, 315 Latinx, 352 White; 51% female; mean age=22) recruited via an online research panel who provided self–reports of maternal and paternal support and criticism and PIL. Tests of psychometric equivalence across race/ethnicity evaluated configural invariance, metric invariance, and scalar invariance, followed by structural models of parenting constructs and PIL.

Results: All measures demonstrated configural invariance; full metric invariance (maternal support, paternal support, paternal criticism, PIL) or partial metric invariance (maternal criticism); and full scalar invariance or partial scalar invariance (maternal criticism). There were no effects of maternal or paternal criticism on PIL after accounting for the impact of support. Paternal support among Black (ß = .37, p < .00) and White (ß = .20, p = .01) young adults was associated with higher PIL (effects were null for the Latinx group). While the univariate effects of maternal support on PIL were positive and significant the multivariate effects were null.

Conclusion: Paternal support may be particularly important for young adults to develop a high sense of purpose in life. Importantly, this finding appears to be unique from the influence of mothers, especially in the case of Black young adults.

Clinical Implications: In the context of shifting societal norms around paternal involvement, greater scientific attention to paternal influences on youths' wellness is critical. Building structural backing to aid fathers in showing support may foster resilience among young people.

Effects of Brain–Derived Neurotrophic Factor (BDNF) Genotype on Transcranial Magnetic Stimulation Clinical Outcomes for Major Depressive Disorder

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Major depressive disorder (MDD) is a profoundly debilitating psychiatric condition. Transcranial magnetic stimulation (TMS) stands as an FDA approved treatment option for MDD, particularly for those with treatment resistant depression (TRD). Although TMS is a safe treatment with proven efficacy, response rates range from 45% to 60%, with remission rates reaching 30% to 40%. One possible explanation for the variability in treatment outcomes could be attributed to individual differences, such as genetic predisposition. Brain derived neurotrophic factor (BDNF) emerges as a plausible candidate underlying such differences, as the BDNF gene functional polymorphism Val66Met has been demonstrated to have a role in synaptic plasticity and antidepressant response. We examined the effects of BDNF polymorphism on treatment outcomes for patients undergoing a standard course of TMS Therapy for MDD.

Methods: 74 patients (20–70 years old; 65% female) who underwent TMS for MDD were recruited to participate from Butler Hospital's TMS Clinic. Depression severity was assessed via the Inventory for Depressive Symptomatology, Self–Report (IDS–SR) and the Patient Health Questionnaire (PHQ–9) scale throughout the course of treatment. Blood plasma samples were genotyped for the Val66Met BDNF polymorphism. Baseline and final treatment scores were assessed using independent and paired t–tests. Clinical response across treatment course was analyzed using repeated measures ANOVAs. Chi square tests were used to assess the relationship between polymorphism and TMS treatment outcomes (i.e., response, remission).

Results: No differences were found in baseline or final treatment on IDS–SR or PHQ–9 scores nor scores across the treatment course between the Val66Val and Val66Met groups. The distribution of responders, remitters, and non–responders was not significantly different between polymorphisms.

Conclusion: Our data suggest that BDNF polymorphism does not modulate the response to a standard course of TMS as measured by clinical rating scales and response rates. These findings are consistent with recent studies evaluating the effect of BDNF polymorphism on patients with TRD receiving ECT treatment.

Clinical Implications: Our results suggest that BDNF polymorphism does not impact the response to clinical TMS therapy.

Characterization of the Antimicrobial Mechanisms of Silver Carboxylate (AgCar) Released via a Titanium Dioxide/Polydimethyl Siloxane Matrix in the Context of Serratia Marcescens and Methicillin–sensitive Staphylococcus aureus

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Anna Rezk, Medical Student, Brown University. Dept of Orthopedics
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Christopher Born, MD, Professor, Brown University. Dept of Orthopedics
Geronimo Garcia Jr., Medical Student. Dept of Orthopedics
Josue Marquez Garcia, Medical Student. Dept of Orthopedics
Blair Williams, Undergrad. Dept of Orthopedics
Patrick Barhouse, Medical Student. Dept of Orthopedics
Jorge Garavito, Medical Student. Dept of Orthopedics

Abstract

Background: Antibiotic resistance continues to be an increasingly difficult and impactful challenge to modern healthcare. The development of novel antibiotics is time–consuming, and current antibiotics are vulnerable to antibiotic resistance due to poor stewardship and overreliance on synthetic antibiotics sharing a similar chemical structure. For this reason, silver, which has been shown to possess multi–mechanistic antimicrobial properties, is a potential alternative or synergist to current 'last resort' antibiotics. However, cytotoxicity concerns due to the uncontrolled release of silver have lead to an 'smart release' formulation of silver, silver carboxylate (AgCar) within a matrix of titanium dioxide and polydimethylsiloxane (TiO_2/PDMS), which allows for controlled release of silver. While AgCar has been shown to be safe with predictable pharmacokinetics of release, the antimicrobial mechanism of action of AgCar has not been established. The aim of this project was to investigate the bactericidal mechanism of action of AgCar, including how it influences the release of reactive oxygen species (ROS) in Serratia marcescens and Methicillin–sensitive Staphylococcus aureus, two pathogens commonly encountered in orthopedic infections.

Methods:

Results: Bacteria were grown in 96 well plates and exposed to a gradient of AgCar ranging from 1x to 150x for 6 hours. 10nm and 30nm nanoparticle silver as well as 100% silver carboxylate with no TiO_2:PDMS served as positive controls. 1% triton X and titanium dioxide/PDMS vehicle–only served as negative controls. To detect the general release of ROS, bacteria were lysed and read via colorimetry for levels of hydroxylamine oxidation using the abcam Cellular ROS Assay Kit.

Conclusion: In Serratia marcescens, a 1x–30x concentration of AgCar produced a fold change of 1, or double the amount of ROS released when compared to the cell blank. AgCar 100x produced a 2 fold change and AgCar 150x produced a 3 fold change in ROS release, when compared to the cell blank. In Methicillin–sensitive Staphylococcus aureus, AgCar 1x–150x produced a fold change of 3, or a 300% increase in ROS production, when compared to the cell blank.

AgCar triggers the release of ROS in Serratia marcescens and Methicillin–sensitive Staphylococcus aureus in a more efficacious manner than nanoparticle silver, providing evidence for its bactericidal activity.
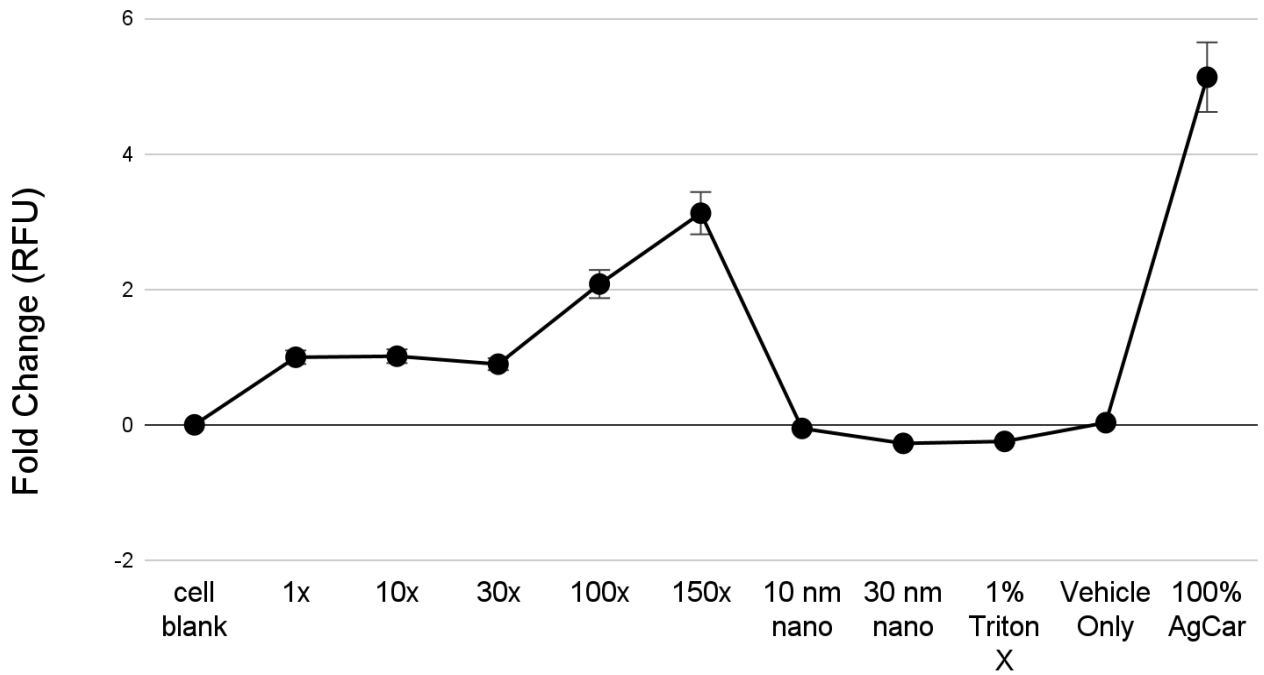
Clinical Implications:

Figure 1. *Serratia marcescens* release of reactive oxygen species (ROS) in response to AgCar gradients.

ACL Reconstructed Patients Land in a Higher Injury Risk Knee Position
2023 Lifespan Research Day Abstract Submission Contest

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Lauren R Parola, Staff, RI Hospital, Brown University. Dept of Orthopedics

Meggin Q Costa, Staff, RI Hospital, Brown University. Dept of Orthopedics

Janine Molino, PhD, Staff, RI Hospital. Dept of Biostatistics, Epidemiology, Research Design & Informatics Core

Braden C Fleming, PhD, Professor, RI Hospital, Brown University. Dept of Orthopedics

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Abstract

Background: Anterior cruciate ligament (ACL) injury is thought to occur when the knee is near full extension and the tibia translates anteriorly by ~22 mm at ground contact. Reasons why there is an increased risk of contralateral injury and premature joint degeneration after initial ACL tear remain ill–defined. While ACL reconstruction (ACLR) is the standard–of–care, it does not mitigate these risks; however, residual abnormal joint motion is thought to contribute in some way. The aim of this study was to investigate hop landing joint motion at a time when ACLR patients are expected to demonstrate early signs of joint degeneration.

Methods: Twenty–one participants were recruited: 10 ACLR patients 10–15 years after surgery and 11 control subjects. Dynamic knee position and range of motion were recorded bilaterally during a single leg hop activity using a sophisticated 3D video x–ray imaging technique that captures motion of the underlying bones with an accuracy of <1mm. The maximum anterior displacement of the tibia relative to the femur was extracted, and peak anterior tibial position as a function of flexion angle was also quantified. Generalized estimating equations were used to test for differences between ACLR patients and healthy control subjects in knee alignment and range of motion, and for differences between knees (i.e., symmetry) within groups.

Results: Healthy control subjects demonstrated symmetrical hop landing knee position and range of motion. Conversely, ACLR patients landed with their surgical tibia positioned 7.5–10.3mm more anteriorly for the same flexion angle of their contralateral knee. Compared to healthy control subjects, ACLR patients demonstrated decreased tibial range of motion in their surgical limb, which was constrained in a position of greater external rotation. The ACLR contralateral limbs also demonstrated greater anterior tibial translation as a function of flexion angle compared to that of control subjects.

Conclusion: ACLR patients may have either inherently different alignment that predisposes them to injury/re–injury, and/or the contralateral limb motion may change as the neuromuscular system attempts to regain movement symmetry.

Clinical Implications: The contralateral limb should not be considered equivalent to a healthy control in a research setting, and caution is warranted in using it as a functional rehabilitation target clinically.

Correlates of Bystander Intervention to Address Student Sexual Harassment among High School Teachers

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Lindsay M. Orchowski, PhD, Associate Professor, RI Hospital. Dept of Psychiatry & Human Behavior

Abstract

Background: Sexual harassment is associated with a variety of adverse outcomes (Bolduc et al., 2022). Among adolescents in the United States, sexual harassment is prevalent, impacting nearly half of seventh to twelfth graders each year (Hill & Kearl, 2011). Bystander intervention (BI) has emerged as an effective approach to prevent sexual harassment (Mujal et al., 2021), with teacher engagement in BI having the potential to be particularly impactful (Waterman et al., 2022). Results from prior research point to social norms and perceived barriers as correlates of teacher BI (Collier et al., 2015; Edwards et al., 2020; Meyer, 2008). However, research has focused primarily on teacher BI in relation to bullying. To address this gap in the literature, the present study examines correlates of teachers' self–reported likelihood to intervene in instances of peer–to–peer sexual harassment. It was hypothesized that: 1) teachers perceiving greater support for BI from educators and students would report greater BI likelihood; and 2) teachers with greater barriers to BI and greater perceived acceptance of violence among students would report lower BI likelihood.

Methods: Self–report surveys were administered to 936 teachers from 26 high schools in the Northeast United States. Surveys included measures of educator and student norms, barriers to BI, and self–reported likelihood to engage in BI in instances of peer–to–peer sexual harassment. Surveys were administered in the context of a larger evaluation of sexual assault prevention programming for high school students. Study procedures were approved by the local IRB, Department of Education, school principal, superintendent, and school board.

Results: Regression analyses indicated that teachers who perceived students as having more positive attitudes toward BI reported a greater likelihood of intervening in instances of sexual harassment among students. Educator bystander norms, perceived barriers to BI, and perceived student violence norms did not emerge as significant predictors of self–reported BI likelihood.

Conclusion: These results suggest that perceptions of student attitudes toward BI are an important correlate of teacher BI in instances of sexual harassment among students.

Clinical Implications: These findings can help to inform sexual harassment prevention efforts with high school teachers.

Effects of ACEs on Reaction to Pregnancy
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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LG Ward, PhD, Assistant Professor, The Miriam Hospital, Brown University. Dept of Psychiatry & Human Behavior, Center for Behavioral and Preventive Medicine

Natasha A. Sokol, Assistant Professor, The Miriam Hospital, Brown University. Dept of Psychiatry & Human Behavior, Center for Behavioral and Preventive Medicine

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Abstract

Background: Pregnant people's attitudes toward pregnancy are associated with pregnancy and birth outcomes. Adverse childhood experiences (ACEs) may influence feelings towards pregnancy, childbirth and parenthood. This study aims to evaluate how ACEs impact initial reactions of pregnant people to news of their pregnancy, and whether demographic factors modify these effects.

Methods: We analyzed N=474 pregnant people's open–ended responses when asked how they felt upon discovering they were pregnant. Responses were coded for emotional valence on two axes: anxious or not anxious; and positive, negative, neutral, mixed, changed over time, or uninterpretable. Logistic regressions estimated odds of reporting anxious, positive, or negative reactions. Adjusted models included race, household income, education, and marital status.

Results: Each additional ACE was associated with a ~8% reduction in the odds of reporting a positive reaction to pregnancy (unadjusted p=0.022; adjusted p=0.068), but ACEs were not associated with odds of anxious or negative reactions. Being married was associated with nearly 5 times the odds of reporting a positive reaction (p<0.001), ~75% the odds of reporting a negative reaction (p<0.001), and ~45% the odds of reporting an anxious reaction (unadjusted p=0.013; adjusted p=0.037). Low income was associated with an ~80% increase in the odds of reporting an anxious reaction (unadjusted p=0.008; adjusted p=0.025). In the adjusted model, non–white race was associated with ~30% the odds of reporting a positive reaction (p=0.095) and a ~66% increase in the odds of reporting a negative reaction (p=0.040).

Conclusion: Increased childhood adversity was associated with lower likelihood of reacting positively to news of pregnancy, and demographic factors did not modify this association. While formal testing is necessary, associations found with demographic factors have positive implications for the validity of the coding system.

Clinical Implications: Pregnant people with a history of ACEs may have more difficulty with accessing positive emotions when initially experiencing pregnancy, which may have implications for pregnancy and birth outcomes.

Table 2. Regression results

	Positive Reaction					
	Unadjusted			Fully Adjusted		
	OR	*95% CI*	*p-value*	*OR*	*95% CI*	*p-value*
ACES score	0.92	(0.86, 0.99)	0.022**	0.93	(0.87, 1.00)	0.068*
Non-white race	0.55	(0.38, 0.80)	0.002**	0.71	(0.47, 1.06)	0.095*
Low income	0.45	(0.31, 0.66)	<0.001**	0.74	(0.46, 1.18)	0.205
<HS education	0.60	(0.41, 0.86)	0.006**	1.30	(0.80, 2.10)	0.292
Married	4.93	(3.24, 7.50)	<0.001**	4.64	(2.76, 7.80)	<0.001**
Age (centered)	1.06	(1.03, 1.10)	0.001**	0.99	(0.95, 1.03)	0.668
Constant	---	---	---	0.65	---	---
	Negative Reaction					
ACES score	1.05	(0.97, 1.13)	0.217	1.04	(0.96, 1.13)	0.295
Non-white race	2.00	(1.26, 3.19)	0.003**	1.66	(1.02, 2.70)	0.040**
Low income	1.85	(1.19, 2.87)	0.006**	1.28	(0.76, 2.15)	0.353
<HS education	1.44	(0.93, 2.23)	0.103	0.84	(0.50, 1.40)	0.497
Married	0.23	(0.12, 0.44)	<0.001**	0.26	(0.13, 0.53)	<0.001**
Age (centered)	0.96	(0.91, 1.00)	0.048**	1.01	(0.96, 1.06)	0.648
Constant	---	---	---	0.23	---	---
	Anxious Reaction					
ACES score	1.04	(0.96, 1.11)	0.346	1.02	(0.94, 1.10)	0.689
Non-white race	0.82	(0.54, 1.25)	0.356	0.70	(0.45, 1.09)	0.111
Low income	1.76	(1.16, 2.67)	0.008**	1.78	(1.08, 2.96)	0.025**
<HS education	1.11	(0.73, 1.68)	0.628	0.71	(0.43, 1.16)	0.173
Married	0.54	(0.33, 0.88)	0.013**	0.53	(0.29, 0.96)	0.037**
Age (centered)	0.98	(0.94, 1.02)	0.383	1.01	(0.96, 1.06)	0.737
Constant	---	---	---	0.42	---	---

** Statistically significant at α=0.05

* Statistically significant at α=0.10 ("marginally" statistically significant)

Presentation of Inhibitory Control in Emerging Adult Cannabis Users
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Abigail Fleurima, Bachelor of Science, BS, Butler Hospital, Brown University. Dept of Psychiatry & Human Behavior

Olivia Stine, Bachelor of Science, BS, Butler Hospital, Brown University. Dept of Psychiatry & Human Behavior

Zachary Kunicki, Doctoral Degree, PhD, Butler Hospital. Dept of Research

Nicole CR McLaughlin, PhD, PsyD, Butler Hospital, Brown University. Dept of Psychiatry & Human Behavior

--------------------- Abstract ---------------------

Background: Cannabis is one of the most commonly used substances among young adults. Evaluation of young adults during acute THC intoxication has revealed that THC has a significant effect on inhibitory control; however there is insufficient evidence describing chronic THC's effect. This study assesses the effect of chronic cannabis use on inhibitory control and self–reported executive functioning skills using a Stop Signal Task (SST) and the Behavior Rating Inventory of Executive Function–Adult version (BRIEF–A).

Methods: As part of a neurostimulation research study, individuals 18–25 years were recruited from the community and local schools. Participants completed an online screener, a telephone screen, a three hour assessment, which included a semi–structured clinical interview and self–report surveys, and a 1 hour MRI. Baseline data was analyzed using Matlab and SPSS. An independent sample t–test assessed for any statistical differences between cannabis and non–cannabis users, for lifetime and current use. We hypothesized that lifetime and current cannabis users would exhibit decreased inhibitory control abilities compared to non–cannabis users.

Results: There were no significant differences between the performance of lifetime cannabis (n=30) and non–cannabis (n=14) users on the SST, or between and current cannabis (n=10) and non–cannabis (n=34) users. With regards to lifetime and current cannabis users, there were significant differences on the BRIEF–A Inhibit (p=0.013 and 0.003), Self–Monitor (p=0.012 and 0.009), Initiate (p=0.007 and 0.022), Working Memory (p=0.002 and 0.002), Plan/Organize (p=0.004 and 0.047), Organization of Materials (p=0.019 and 0.026), and Shift (p=0.031) subscales compared to non–cannabis users.

Conclusion: There were no significant between–groups differences on the SST; although we anticipated significant findings, there are mixed results in the literature regarding inhibitory control and cannabis use, which may explain these results.

Clinical Implications: Significant results on the BRIEF–A subscales are indicative of its validity to assess the behavior of emerging young adults in real–world settings in the context of how cannabis use affects their behavior or how their behavior exacerbates their cannabis use.

Reduction of the 30–Day Readmission Rate in a Skilled Nursing Facility with Older Adult Patients with Respiratory Conditions

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Mary L Benn, Doctor of Nursing Practice, RN, Assistant Professor, New England Tech. Dept of Nursing

Abstract

Background: Respiratory conditions are one of the most frequent causes of 30–day readmissions among older adults discharged to a skilled nursing facility (SNF). At the project site, 21% of the 30–day readmissions in the last fiscal quarter were for pulmonary conditions. The goal of the project was to decrease readmissions with a decline of at least 5%. This quantitative, quality improvement project aimed to implement an evidence–based respiratory exacerbation care algorithm that would impact 30–day hospital readmissions for older adult patients with respiratory conditions compared to current practice.

Methods: The project was conducted at an SNF over eight weeks with respiratory admissions (N = 17) collected using the Quality Measure (QM) report and analyzed using a Pearson chi–square test. The pre–implementation group had nine respiratory admissions (n =9) and the post–implementation group had eight (n = 8). The chi–square test showed no statistical significance between the pre–implementation (2, 22%) and post–implementation (1, 12.5%), due to a small sample. However, a 10% reduction in respiratory readmissions was accomplished through the use of the evidenced–based algorithm.

Results: These results validated the use of the algorithm for clinical significance. The algorithm prevented unplanned readmissions by the use of appropriate management of those requiring readmissions. Recommendations include sustaining and expanding the project to other settings with a larger sample.

Conclusion: This QI project used an evidenced–based algorithm that is applicable to practice. Although statistical significance in the respiratory readmission rates was not recognized over the short 30–day timeframe of this project, the project was clinically significant in that it was utilized by project site staff to prevent two unnecessary or unplanned readmissions

Clinical Implications: This project produced valuable information and is essential to clinical practice to reduce readmissions. The respiratory exacerbation care algorithm should be disseminated for use in simulations in nursing education programs or at annual competency skills training for all types of healthcare organizations. Further studies would be valuable to reduce overall readmissions and the use of algorithms.

Table 1

Frequencies for Admissions and Respiratory Admissions by Comparison Groups.

	Current Practice		Respiratory Algorithm		Total	
	n	%	*n*	%	N	%
Admissions	55	60%	36	40%	91	100%
Respiratory Admissions	9	16%	8	22%	17	18%

Note: Total Admissions (N = 91)

Table 2

Crosstabulation and Chi-square Test Between Current Practice & Respiratory Algorithm Groups

	Current Practice		Respiratory Algorithm		$\square^2$	*p*	*η*
	#	%	#	%			
Respiratory Admissions	9	53%	8	47%			
					.275	.600	.127
Respiratory Readmissions	2	22%	1	12.5%			

Note: $\square^{2-}$ *Pearson chi-square, *P < .05 -statistically significant, η – eta (effect size), Fishers exact test – p = .547.*

Cartilage-Derived Progenitor Cells Stimulate Meniscus Healing and Suppress NF-kB Pathway in Response to SDF-1

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Meniscus injuries that fail to heal can instigate catabolic changes in the knee, posing a high risk for the development of post-traumatic osteoarthritis(PTOA). We have established human articular cartilage-derived progenitor cell-lines(CPCLs) as a potential therapeutic tool for accelerating meniscus tissue healing. Characterization of these cell lines revealed that they are less catabolic and hypertrophic than marrow-derived stromal cells(BM-MSCs). The Stromal Cell-Derived Factor-1(SDF-1)/CXCR4 pathway is crucially important for stimulating the directional migration of CPCs to stimulate meniscal fibrocartilage repair. In this study, our goal was to understand how SDF-1/CXCR4 signaling might play an influential role in helping CPCs achieve their therapeutic efficacy.

Methods: Healthy(non-arthritic) human CPC cell lines were established by enzymatic tissue digestion followed by stabilization using SV40 transduction. For in vivo studies, a radial tear was created in the outer third of the medial meniscus of skeletally mature athymic rats. In the cell treatment groups, 3.2×10^6 cells were injected into the joint capsule following meniscus injury. 7-weeks post-surgery, knees were isolated and histological studies were performed using Saf-O/Fast green stains. In vitro expression of cell signaling markers was determined by western blot analysis.

Results: Injection of CPCL significantly reduces the area of meniscal tear defect in rats as compared to injection of a BM-MSC line or untreated control groups(Fig.1). Further, we were surprised by our novel finding that SDF-1/CXCR4 pathway is regulated differently, between CPCs and a BM-MSC line. Our immunoblot results indicate that the CPCL, unlike BM-MSCs, demonstrate significantly more inhibition of canonical NF-..B(Fig.2A) and Erk(Fig.2B) pathways, as compared to untreated controls in the presence of SDF-1. The MAPK pathway is downregulated in both CPCL and BM-MSCs upon SDF-1 stimulation(Fig.2B).

Conclusion: Our results demonstrate that Intra-articular injection of CPC following meniscus tearing stimulates fibrocartilage restoration and healing. Further, CPCs and BM-MSCs respond differently to the chemokine SDF-1. Collectively, our results show a precise fine-tuning of an intricate downstream network of the SDF-1/CXCR4 axis that may govern how CPCs mediate chondroprotective anti-catabolic effects on the joint when they are injected as biologic therapy.

Clinical Implications: This study focuses on refining our understanding of molecular signaling that regulates cell-mediated meniscus healing and the prevention of PTOA.
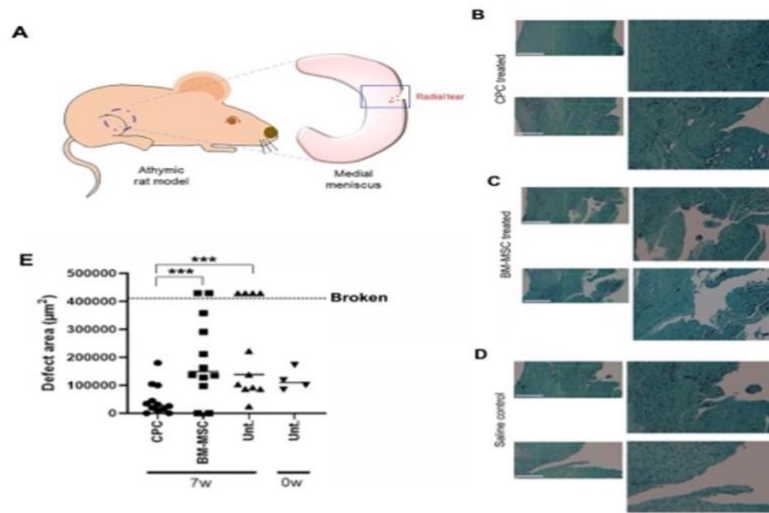
Fig – 1: Intra-articular injection of CPC line (CPCL3) following meniscus tearing stimulates fibrocartilage tear healing. *(A)* A radial tear was created in the outer third of the medial meniscus of skeletally mature athymic rats. Histology of meniscus tears 7 weeks following treatment with *(B)* CPCL3, *(C)* BM-MSCL, or *(D)* saline. *(E)* Open areas remaining within the meniscal tear channel were quantified by image analysis. Data points above the dotted line indicate menisci broken in two at the harvest time. Representative images in panels B, C, and D, were not obtained from these broken menisci samples. Scale bars represent 400 μm. N≥8 per group. ***, P≤0.005.
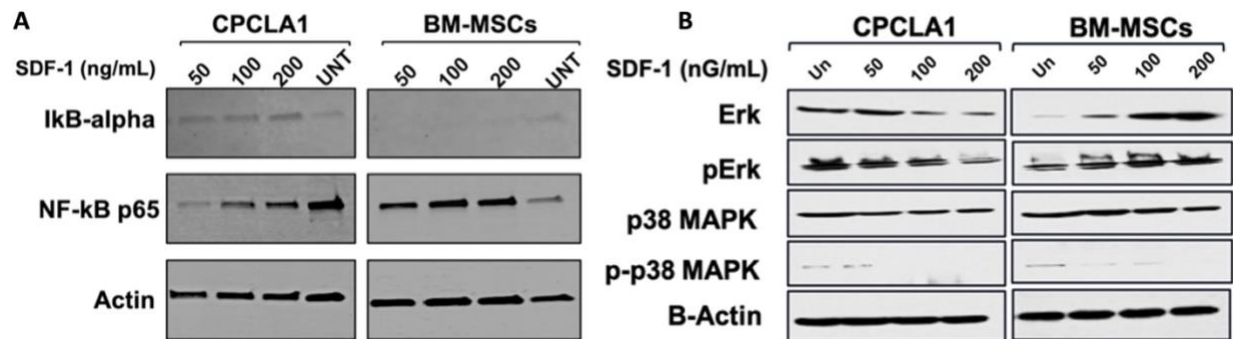

Fig – 2: *(A)* CPCs (left panel) and BM-MSCs (right panel) were treated with SDF-1. The activation of NF-kB pathway was determined by measuring the protein expression of downstream signaling molecules IkB-α and NF-kB p65, as well as their phosphorylation states. *(B)* CPCs (left panel) and BM-MSCs (Right panel) were treated with SDF-1. The activation of Erk and MAPK pathway was determined by measuring the expression of Erk and p38 along with their phosphorylation states (pErk) and (p-p38), respectively.

Predicting Survival of Lung Ablation Patients Using Deep Learning–Based Automatic Segmentation and Radiomics Analysis

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational

Primary Research Location: Providence

Funded By: n/a

Author(s):

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Zhicheng Jiao, PhD, RI Hospital, Brown University. Dept of Diagnostic Imaging

Aaron WP Maxwell, MD, RI Hospital, Brown University. Dept of Diagnostic Imaging

--- Abstract ---

Background: To identify radiomic features predictive of survival following image–guided thermal ablation (IGTA) of lung tumors segmented using a deep learning approach.

Methods: This HIPAA–compliant study was performed with a waiver for informed consent following institutional review board approval. Between January 1, 2004, and July 14, 2022, adult patients who underwent IGTA for primary and metastatic lung tumors were retrospectively identified. A pre–trained U–Net to segment lung fields was applied to the dataset of pre procedure scans. Following this, a U–shaped encoder–decoder transformer architecture (UNETR) was utilized to segment tumor zones. This model was then applied to both pre– and post–procedure scans to produce lung tumor segmentations. Radiomic features were then extracted from these segmentations. These features were then used to predict the risk scores of the patients using a Survival SVM model.

Results: 113 consecutive patients were evaluated (median age, 74.8 years; 47.8% Male). Of these patients, 87 experienced the mortality event, with a mean time to death of 4.3 years (minimum 0.7 years; maximum 14.2 years) following the initial IGTA procedure. Median tumor size was 1.8 cm (minimum 0.7 cm; maximum 4.3 cm), and 101 patients (89%) had primary lung cancer. The initial lung tumor segmentation using UNETR achieved a DICE score of .75, indicating a 75% overlap of the predicted segmentation and the ground–truth. The survivability prediction task on the post–procedure scans using radiomic features achieved a c–index of .70, showing a 70% chance the model will correctly predict which subject has a longer survival time out of a random pair. The most predictive features were 3D and 2D. The survivability prediction task on the pre–procedure scans achieved a c–index of .57, indicating that post–procedure scans are more predictive of the survival of patients.

Conclusion: Radiomic feature analysis of lung tumors following segmentation by transformer–based UNET may predict long–term survival following image–guided thermal ablation of pulmonary malignancies.

Clinical Implications: The incorporation of a survival prediction model based on radiomics features extracted from pre–procedure CT imaging by a deep learning algorithm may allow interventional radiologists to modify treatment approaches to optimize outcomes for patients.

Assessing the acceptability of a mindful eating mobile app for adolescents

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Mindful eating can decrease maladaptive eating, and may be a good adjuvant to weight management interventions. Mobile health (mHealth) interventions are viable for youth behavior change and there is scarce literature on their use. The Unified Theory of Acceptance and Use of Technology (UTAUT) integrates key predictive constructs for the behavioral intention to use technology. The study's aim was to assess adolescent perceptions of an mHealth mindful eating intervention, as part of a study to develop a mHealth mindful eating intervention for adolescents.

Methods: 25 youth with overweight/obesity were recruited at a weight management clinic. Mean age 14.6y ± 1.5y; BMI 36.4 ± 7.8 kg/m2; 60% male; 57% Hispanic, 20% AA. Participants viewed videos from a mindful eating phone app. They completed a semi–structured interview and a survey based on UTAUT constructs (Table 1). Survey data was analyzed to examine internal validity. Bayesian principal component analysis was used to inform interpretation. A Framework Analysis approach was used to analyze the interview data.

Results: 96% of participants answered 'agree'/'strongly agree' to the statement 'Using a mindful eating app will help me develop a healthier relationship with food,' and 80% answered 'agree'/ 'strongly agree' to the statement 'I will use a mindful eating app if I have access to it.' Most weights were large (.. > 0.5) except for facilitating conditions (.. = 0.01), which all teens endorsed (Table 1). The association with behavioral intention was positive (.. ^ = 0.15, 95% CI [0.07, 0.23]). Reliability was acceptable (0.70). Inductive codes included attitude, flexibility and overall perception. Deductive codes included easy to understand, educational, appealing, engaging. Results pointed to app features that adolescents consider important additions, including closed captions, a colorful interface, text reminders, and gamification. Interview responses supported the findings from the survey in that participants were overall receptive to a mindful eating app.

Conclusion: Survey data showed internal consistency reliability and concurrent validity. Qualitative data supported the findings from the UTAUT–based survey.

Clinical Implications: Use of a mindful eating app for adolescents is acceptable and feasible. Future directions include pilot testing the mindful eating app in adolescents with overweight/obesity.

Construct	Loading	Average (1-5)	Statements
Performance Expectancy	0.73 [0.34, 1.12]	4.20 [3.45, 4.70]	Using a mindful eating app will help me develop a healthier relationship with food
Performance Expectancy	0.23 [-0.19, 0.65]	4.29 [3.55, 4.75]	Using a mindful eating app will improve my chances of eating healthier
Performance Expectancy	0.69 [0.31, 1.14]	3.94 [3.16, 4.53]	Using a mindful eating app will help me be healthier overall
Effort Expectancy	0.24 [-0.19, 0.65]	3.47 [2.67, 4.18]	Learning how to use a mindful eating app will be easy for me
Effort Expectancy	0.43 [0.01, 0.83]	3.81 [3.02, 4.44]	I will find a mindful eating app easy to understand, use and navigate
Social Influence	0.76 [0.38, 1.17]	4.67 [4.06, 4.94]	My parents will think it is a good idea for me to use a mindful eating app
Social Influence	0.57 [0.15, 1]	3.94 [3.16, 4.53]	Other people who are important to me will think it is a good idea to me to use a mindful eating app
Facilitating Conditions	0.01 [-0.43, 0.42]	4.80 [4.26, 4.98]	I have what I need (smartphone, time, skills) to be able to use a mindful eating app
Attitudes Toward Technology	0.51 [0.14, 0.97]	4.58 [3.94, 4.91]	Using a mindful eating app is a good idea to help me eat healthy
Self Efficacy	0.66 [0.25, 1.14]	3.86 [3.06, 4.47]	I am confident that I will be able to use a mindful eating app
Anxiety	-0.69 [-1.16, -0.29]	2.27 [1.62, 3.07]	I think using a mindful eating app could make me worry or hurt my feelings
	Reliability	**Concurrent validity**	
Estimate	0.70 [0.50, 0.85]	0.15 [0.07, 0.23]	I will use a mindful eating app if I have access to it
		0.19 [0.11, 0.27]	I will participate if there is a study to use a mindful eating app for teens

Note: reported are the estimates and 98% CI. A more conservative 98% CI was selected because we had performed an interim analysis to be consistent with the alpha spending approach.

Influences on Physical Therapists' Decision–Making to Explore Pain Perceptions during the Evaluation

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational
Primary Research Location: Rhode Island
Funded By: none

Author(s):

Elke C Schaumberg, PhD, DPT, Assistant Professor, Johnson & Wales University. Dept of Physical Therapy

--- Abstract ---

Physical therapists (PTs) make numerous decisions when evaluating adults with chronic pain to determine both the need for and scope of the assessment of cognitive psychological factors. The aim of this qualitative study was to understand the factors and cues PTs attend to when deciding whether to explore patients' pain beliefs during the evaluation.

Background:

A total of 5 PTs (with 3 to 28 years of clinical experience) from single–discipline outpatient orthopedic physical therapy clinics in the Northeastern region of the United States were observed evaluating adults who were referred for chronic pain conditions. A multiple case study design informed by social constructionism was used. Semi–structured interviews of the PTs were conducted following the observation of the evaluation. An inductive cross–case pattern thematic analysis of the transcripts and observation notes was conducted.

Methods:

Analysis of the transcripts revealed that the decision–making process took place within the confines of a biomedically oriented and movement–focused language. Dominant conceptual frameworks shaped the manner in which the PTs viewed the psychological cognitive realm and ultimately influenced their decision–making processes. Decision–making was influenced by 'physical therapist factors' and factors external to the therapist. 'Physical therapist factors' included evaluation practices and the therapists' values, judgements and beliefs. The evaluation of psychological factors was viewed as an iterative process that often extended beyond the first visit. The questions posed by the PTs during the history–taking portion of the evaluation were predominately biomedically focused; the sequencing and content of the questions asked were remarkably similar among PTs. At the first visit, the development of a therapeutic alliance was prioritized over the evaluation of pain beliefs. The PTs' values, judgements, and beliefs that were shaped through personal and clinical experiences influenced their evaluation approach. External factors included 1) healthcare system issues such as documentation and reimbursement issues, and 2) patient cues to which therapists attended.

Results:

Conclusion:

Physical therapist–related factors and factors external to PTs influenced the decision–making processes used when the PTs decided whether and to what depth pain cognitions should be explored in adults with chronic pain at the first visit. The predominant use of biomedically–oriented language shaped PTs' history–taking sessions when exploring patients' pain beliefs.

Clinical Implications:

Educational interventions aimed at improving detection of maladaptive pain beliefs is needed to facilitate early identification of cognitive psychological contributions to patients' pain experiences. Ensuring PTs are equipped with the language needed to fully explore pain as not only a function limiting experience but also a psychological experience may improve their ability to ask about patients' lived experiences of pain.

Influences on Physical Therapists' Decision-Making to Explore Pain Perceptions during the Evaluation: A Qualitative Study

Elke Schaumberg PT, DPT, PhD[1]

Johnson and Wales University and Texas Woman's University

INTRODUCTION

Physical therapists make numerous decisions when evaluating adults with chronic pain to determine both the need for and scope of the assessment of cognitive psychological factors. There is little published research on the factors that influence decision-making and the cues physical therapists attend to when deciding how to assess pain cognitions at the first visit. Research has shown that maladaptive pain beliefs impact clinical outcomes and disability levels to a greater extent than pain intensity and emotional psychological factors in individuals with chronic pain.

PURPOSE

The aim of this qualitative study was to understand the factors and cues PTs attend to when deciding whether to explore patients' pain beliefs during the evaluation.
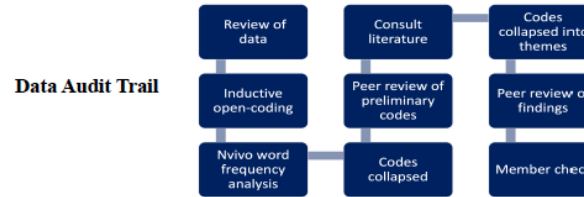
PARTICIPANTS

A total of 5 PTs (with a minimum of 3 years of experience) from single-discipline outpatient orthopedic physical therapy clinics in the Northeastern region of the United States.

PT	Gender	Years of Experience	Adv. Credentialing ABPTS	Entry-level Education	Residency	Course on BPS/PNE	PABS Score (F1, F2)
1	Male	7	Vestibular rehabilitation	Doctorate		no	(32, 31)
2	Female	20		Master's		no	(27, 39)
3	Male	3	Level 1 Dry needling/OCS	Doctorate	Orthopedics	yes	(41, 25)
4	Female	3	Manual therapy /OCS	Doctorate		yes	(33, 19)
5	Female	28		Master's		no	(32, 41)

METHODS

A multiple case study design informed by social constructionism was used. Semi-structured interviews of the PTs were conducted following the observation of the evaluation. An inductive cross-case pattern thematic analysis of the transcripts and observation notes was conducted.

Data Audit Trail

Review of data → Consult literature → Codes collapsed into themes

Inductive open-coding → Peer review of preliminary codes → Peer review of findings

Nvivo word frequency analysis → Codes collapsed → Member check

RESULTS

Analysis of the transcripts revealed that the decision-making process took place within the confines of a biomedically oriented and movement-focused language. Dominant conceptual frameworks shaped the way the PTs viewed the psychological cognitive realm and ultimately influenced their decision-making processes.

Language

- Biological
- Psychological
- Social

Story   Initial observations   How do you know?

PT-Related Factors

Evaluation Practices

Focus on biomedical/biomechanical
Therapeutic alliance prioritized
Assessment of psychological factors iterative

Attitudes, Judgements, and Beliefs

Professional experiences
Personal experience

External Cues/Factors

Patient Cues

Inconsistencies - presentation vs. objective findings
Hyper-focus on pain, past diagnostic testing
Body language or countenance

Healthcare Factors

Documentation requirements
Reimbursement

Decision-making was influenced by "physical therapist factors" and factors external to the therapist.

CONCLUSION

Physical therapist-related factors and factors external to PTs influenced the decision-making processes used when the PTs decided whether and to what depth pain cognitions should be explored in adults with chronic pain at the first visit. The predominant use of biomedically-oriented language shaped PTs' history-taking sessions when exploring patients' pain beliefs.

CLINICAL RELEVANCE

Educational interventions aimed at improving detection of maladaptive pain beliefs is needed to facilitate early identification of cognitive psychological contributions to patients' pain experiences. Ensuring PTs are equipped with the language needed to fully explore pain as not only a function limiting experience but also a psychological experience may improve their ability to ask about patients' lived experiences of pain.

Predictors of Psychosocial History–Taking Practices of Physical Therapists who Evaluate Adults with Chronic Pain

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

Elke C Schaumberg, PhD, DPT, Assistant Professor, Johnson & Wales University. Dept of Physical Therapy

Abstract

Background: The biopsychosocial model is one of four constructs that inform physical therapy practice. Little is known about the psychosocial history–taking practices of physical therapists (PTs) when evaluating adults with chronic pain in the United States. The aims of the this study were to 1) determine whether gender, allowed evaluation time, completion of continuing education coursework in pain neuroscience education/biopsychosocial model, advanced physical therapist training (American Board of Physical Therapy Specialties certification; completion of residency, and/or fellowship), and years of clinical experience were significant predictors of the frequency that PTs asked questions about psychosocial factors, and 2) identify which predictor best explained the variance in PTs' psychosocial scores.

Methods: In this descriptive study, an online survey was used to measure the frequency that PTs asked adults with chronic pain about psychosocial (cognitive, emotional, behavioral and social) factors. The questions were scored on a 5–point Likert scale; a high score indicated a high number of questions were asked about psychosocial factors. Face and content validity of the survey were established through expert review. Psychometric testing demonstrated that the survey had strong test–retest reliability ($r = 0.87$, at $p < 0.005$) and good to excellent internal consistency (Cronbach's alpha$= 0.94$). Multiple regression analysis using forced entry method was used to investigate whether the above stated variables were significant predictors of PTs' psychosocial scores.

Results: Licensed PTs from 33 states (n=433) who at least occasionally treated adults with chronic pain participated in this study. The regression model was significant, at $F_{(5, 428)} = 18.23$, $p < 0.005$, $R^2 = .176$. Evaluation time allowed, years of clinical experience, and completion of continuing education coursework in pain neuroscience education/biopsychosocial model were significant predictors of the psychosocial score ($p < 0.005$). The best predictor was years of clinical experience (standardized beta$= 0.26$). A predictive equation was developed, the psychosocial score can be estimated using the equation: 89.87+ 0.53 (years of clinical experience) + 0.28 (evaluation time allowed) + 11.29 (PNE/BPS continuing education).

Conclusion: Evaluation time allowed, years of clinical experience, and the completion of continuing education in pain neuroscience education and/or the biopsychosocial model were positive predictors of PTs' psychosocial history–taking practices when evaluating adults with chronic pain.

Clinical Implications: In the face of reimbursement challenges and increased productivity pressures in the U.S., these findings underscore the importance of allowing PTs sufficient time at the first visit to fully explore the psychosocial factors that may contribute to adults' pain experiences and highlight the importance of educational interventions to improve PTs' psychosocial literacy.

Predictors of Psychosocial History-Taking Practices of Physical Therapists who Evaluate Adults with Chronic Pain

Elke Schaumberg PT, DPT, PhD

Johnson and Wales University; Texas Woman's University

INTRODUCTION

Little is known about the psychosocial history-taking practices of physical therapists (PTs) when evaluating adults with chronic pain in the United States when using the biopsychosocial model. Additionally, there is a paucity of published research that examines the affect provider characteristics such as gender, post-graduate clinical education, years of clinical experience, and allowed evaluation time have on those history-taking practices.

PURPOSE

The aims of the study were to

1) determine whether **gender**, **allowed evaluation time**, completion of **continuing education coursework in pain neuroscience education and/or the biopsychosocial model**, **advanced physical therapist training** (ABPTS specialist certification; completion of residency, and/or fellowship), and **years of clinical experience** were significant predictors of the frequency that PTs asked questions about psychosocial factors, and

2) identify which predictor best explained the variance in PTs' psychosocial scores

PARTICIPANTS

Licensed PTs from 33 states (n=433) who at least occasionally treated adults with chronic pain were eligible to participate in the study.
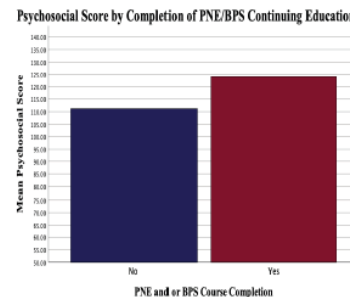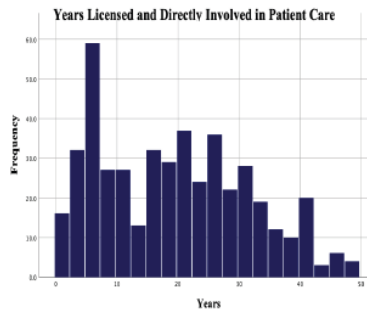
METHODS

An online survey developed by the author was used to measure the frequency that PTs asked adults with chronic pain about psychosocial (cognitive, emotional, behavioral and social) factors. The questions were scored on a 5-point Likert scale; a high score indicated a high number of questions were asked about psychosocial factors. Face and content validity of the survey were established through expert review. Psychometric testing demonstrated that the survey had strong test-retest reliability ($r = 0.87$; $p \leq 0.005$) and good to excellent internal consistency (Cronbach's alpha = 0.94).

The survey was sent via to physical therapists licensed in eight states. Snowball sampling was then used.

Data Analysis: Multiple regression analysis using forced entry method was used to investigate whether the above stated variables were significant predictors of PTs' psychosocial scores.

RESULTS

Descriptive statistics: n=433 PTs from 33 U.S. states completed the survey. Respondents had a mean of 19.4 years of clinical experience (SD=12 years) and 48.3 minutes (SD=16.6 minutes) of allowed evaluation time.

Years Licensed and Directly Involved in Patient Care

Psychosocial Score by Completion of PNE/BPS Continuing Education

Predictor Variable	Unstandardized Coefficient	Standardized Coefficient	p-value
(constant)	89.87		< 0.005
Years of experience	0.53	0.26**	< 0.005
Evaluation time	0.28	.18	< 0.005
Continuing Education	11.3	0.24	< 0.005
Gender	-3.88	-0.07	0.13
Advanced Credentialing	3.08	0.06	0.22
** Best predictor of psychosocial score			

The regression model was significant, at $F_{(5, 428)} = 18.23$, $p \leq 0.005$, $R^2 = 0.176$.
A predictive equation was developed, the psychosocial score can be estimated using the equation: 89.87+ 0.53 (years of clinical experience) + 0.28 (evaluation time allowed) + 11.29 (PNE/BPS continuing education).

CONCLUSION

Evaluation time allowed, years of clinical experience, and the completion of continuing education in pain neuroscience education and/or the biopsychosocial model were positive predictors of PTs' psychosocial history-taking practices when evaluating adults with chronic pain.

CLINICAL RELEVANCE

In the face of reimbursement challenges and increased productivity pressures in the U.S., these findings underscore the importance of allowing PTs sufficient time at the first visit to fully explore the psychosocial factors that may contribute to adults' pain experiences and highlight the importance of educational interventions to improve PTs' psychosocial literacy.

Optic Nerve Abnormalities in Lyme Meningitis: Preliminary Data of a Systematic Review

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Optic nerve abnormalities in Lyme meningitis can cause vision impairment. This systematic review aims to assess characteristic symptoms, treatment, and outcomes in patients with Lyme meningitis and associated optic nerve abnormalities.

Methods: Following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines, we conducted a comprehensive search of six databases in December 2021. We included peer-reviewed, English-language studies that reported on patients with Lyme meningitis and optic nerve abnormalities. Abstracts, conference proceedings, and non-English language publications were excluded. Additionally, studies were excluded if they lacked sufficient details on optic nerve abnormalities or if the patients did not meet the diagnostic criteria for Lyme meningitis or Lyme neuroborreliosis.

Results: The initial search yielded 5891 articles, of which 67 studies describing 96 patients met criteria. The most common ocular or neurological symptoms were vision loss (59.4%), headache (44.8%), and diplopia (25%), while the most prevalent systemic symptoms were fatigue (20.8%), myalgia (18.8%), and nausea (15.6%). Acute optic nerve abnormalities were observed in 84 patients (89.4%). Thirty-six patients had a lumbar puncture with reported opening pressure, 17 (47.2%) of which were elevated. The most common treatment option was intravenous antibiotic, typically ceftriaxone, followed by oral antibiotic, typically doxycycline. 56.3% of patients had full recovery, and 12.5% had partial recovery of vision.

Conclusion: The most common symptoms associated with optic nerve abnormalities in patients with Lyme meningitis include vision loss, headache, diplopia, fatigue, myalgia, and nausea. In most cases, the optic nerve abnormalities are acute-appearing, and treatment outcomes often result in full or partial recovery with the administration of intravenous or oral antibiotics.

Clinical Implications: Visual complaints in the context of Lyme meningitis should raise concerns about optic nerve involvement. Lumbar puncture is essential to assess for elevated intracranial pressure. Further investigation is needed to determine if treatment modality is related to clinical outcomes.

Measuring 'Real-World' Executive Functioning – The Relationship Between Clinic-Based Inhibitory Control and Self-Reported Executive Functioning Skills

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: There is limited understanding of the relationship between self-reported executive function (EF) and in-office evaluation of EF. One component of EF is inhibitory control. As clinic-based assessments often fail to show EF impairment in a 'real-world' environment due a well-controlled setting, self-reported EF provides insight that may more accurately reflect lived experience. Therefore, it is reasonable to conclude that understanding the relationship between self-reported EF and clinic-based assessments is necessary to create precise, valid definitions of cognitive-constructs.

Methods: We examined the relationship between the Behavior Rating Inventory of Executive Function – Adult (BRIEF-A) self-report and the stop-signal task (SST) through preliminary data from a study examining neurostimulation in young adults. The BRIEF-A and the SST were administered to 46 participants (33F:19, 69% white). In order to examine the relationship between the BRIEF-A and the SST, a Pearson's correlation was conducted between each measure's subscales. We hypothesized the Inhibit subscale would not correlate with SST outcomes, yet other EF subscales such as Working Memory would significantly correlate, in accordance with previous literature.

Results: Stop signal reaction time (SSRT), an estimation of the time it takes for an individual to stop a prepotent response, showed positive correlations with the Plan/Organize ($p=0.002$), Self Monitor ($p=0.010$), Working Memory ($p=0.013$), Task Monitor ($p=0.026$), Organization of Materials ($p=0.03$), and Inhibit ($p0.042$) subscales. Inhibition accuracy (i.e. whether they were able to stop when task instructions told them to) significantly inversely correlated with Inhibit ($p=0.042$). There were no significant correlations between 'go' reaction time or accuracy and BRIEF subscales.

Conclusion: This research examined the relationship between self-reported EF and clinic-based inhibitory control in young adults. Our findings suggest there is a significant relationship between 'real-world' EF and clinic-based measures of inhibitory control, which assists 'real-world' validation of cognitive constructs relevant in clinical and research-based settings.

Clinical Implications: This research utilizes the BRIEF-A, a self-report measure often used in clinical settings to obtain 'real-world' understanding of EF impairment. Understanding the relationship between this self-report and translational constructs may provide more accurate understandings of the tools used in clinical settings.

Investigating Mechanisms of HOXB8–Conditional Neutrophil Progenitor Engraftment in the Murine Host

2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Aim Neutropenia or neutrophil dysfunction are associated with increased susceptibility to severe bacterial and fungal infections. Recently, we characterized murine neutrophil progenitor cell lines (NPs) that are conditionally immortalized via HoxB8 expression and are uniquely capable of engrafting in the naïve murine host. We propose that NPs may serve as a therapeutic adjunct for reducing infection resulting from neutropenia or neutrophil dysfunction. To achieve this, it is first important to understand the mechanisms of NP engraftment in the hematopoietic niche. We have observed that NPs home and/or engraft via a VLA4–independent, beta1 integrin–dependent mechanism. We found that engrafted NPs proliferate and differentiate into mature neutrophils that are mobilized to the periphery via canonical CXCR2 signaling.

Methods: Here, we describe studies to determine the impact of cytoreductive conditioning of host niche space via antibody–mediated depletion of Ly6G–expressing cells or busulfan–mediated HSPC ablation on NP engraftment. To further evaluate the potential translational utility of NPs, we also probe candidate integrin alpha subunits and signaling receptors to determine their role in NP homing and engraftment.

Results: Mice depleted of neutrophils via anti–ly6G treatment prior to NP transplant did not result in increased engraftment capacity as measured by frequency or cell number compared to control mice. NP mutants which lack expression of integrin alpha 5 had reduced frequency and cell count in murine host bone marrow post competitive adoptive transfer compared to parental NPs.

Conclusion: Conditioning host bone marrow via anti–ly6G depletion of host neutrophils does not impact engraftment capacity of NPs suggesting that increased niche space created via cytoreduction specific to neutrophils do not increase engraftment capacity of NPs. Results demonstrate that integrin alpha 5 plays a role in NP engraftment capacity in the bone marrow and potentially plays a role in proliferation capacity once cells lodge in the bone marrow niche.

Clinical Implications: Engineered neutrophils, in theory, could be harnessed to treat cases of sepsis caused by traumatic injury to the lungs or peritoneal cavity and in cases of acute neutropenia, which results in high–risk vulnerability of infection induced by myeloablative conditioning for hematopoietic stem cell transfer (HSCT) efficacy.

Approach for Evaluating Cartilage Thickness Based on Patient Geometry
2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Anterior cruciate ligament reconstruction (ACLR) does not reduce the risk of developing post–traumatic osteoarthritis, a degenerative condition characterized by early articular cartilage swelling then progressive loss. The aim of this work was to develop an approach to systemically quantify tibiofemoral cartilage thickness and test the method's sensitivity. A secondary aim was to explore biological sex as a potential confounding variable.

Methods: All procedures were reviewed and approved by Lifespan IRB. 3D models of the tibiofemoral cartilage were constructed from magnetic resonance images from a total of 21 study participants: 10 ACLR patients (5M/5F) and 11 sex– and age–matched healthy controls (6M/5F). ACLR patients were between 10–15 years post–surgery when post–traumatic osteoarthritis is detectible. Cartilage thickness was mapped between the subchondral bone and cartilage surfaces. Models were subdivided into 90 sub–regions (average size $2.70\pm0.38mm2$) such that regions were evenly distributed across the tibiofemoral surfaces and scaled based on the overall knee size. The distribution of resulting sub–regions was evaluated qualitatively to assess the consistency in location across the 21 participants. To investigate the approach's sensitivity to variations in cartilage thickness, we focused on the 21 sub–regions spanning the medial femoral condyle (MFC) – a surface particularly susceptible to early degenerative cartilage changes following

Results: ACLR. A two–factor repeated measures ANOVA was used to test for between –group differences in the primary aim and –sex differences in control subject MFC data in the secondary aim.

The 90 regions were evenly distributed across the tibiofemoral surfaces based on visual inspection. ANOVA detected a main effect for sub–region location in MFC cartilage thickness ($p<0.001$) and a trend in the sub–region x group interaction ($p=0.052$). Healthy females had significantly thinner cartilage compared to healthy males ($p=0.034$).

Conclusion: Results suggest that the regional approach for analyzing cartilage thickness will be sensitive to variations in cartilage thickness – swelling and loss – due to ACLR, and that sex should be included as a co–variate in future analyses.

Clinical Implications: Coupled with AI–based algorithms for automatic cartilage model generation, the approach can be expanded to monitor cartilage changes earlier in the disease trajectory when interventions may be more effective.

The Efficacy of a Low Fiber Compared to a Clear Liquid Diet in Children's Colonoscopy Bowel Preparation.

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational
Primary Research Location: Hasbro Children's Hospital
Funded By: Department of Pediatrics at Hasbro Children's Hospital

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Abstract

Background: Colonoscopies are routinely performed in the pediatric population to aid in diagnosis of a variety of gastroenterological conditions. To attain the highest yield, an adequate bowel preparation is essential. Presently, a bowel preparation involves consuming laxatives with adherence to a clear liquid diet the day prior to the procedure. This poses difficulties to patients and their families including hunger, discomfort, parental anxiety, and poor adherence. Studies in the adult population comparing the use of a clear liquid versus a low fiber diet have demonstrated that the low fiber diet is better tolerated, and bowel preparation efficacy was similar to that of a clear liquid diet. The objective of this study is to evaluate the efficacy of a low fiber diet in preparation for colonoscopy. We hypothesized that when compared to a clear liquid diet, the liberalized low fiber diet would be better tolerated and equally efficacious. Additionally, we evaluated whether a low fiber diet is associated with improved adherence, especially among the younger population.

Methods: This was a prospective, single blinded clinical study with two arms – clear liquid (standard) diet and low fiber diet. Patients were randomly assigned. All subjects were offered the same medications for bowel preparation in keeping with our institution's standard protocol. Patients within the low fiber group were allowed an age–appropriate diet with meal options designed by our nutrition team, for a maximum of seven grams of fiber daily. Those in the standard group were allowed a light breakfast and drank clear liquids for the remainder of the day. Adequacy of the clean out was evaluated with the Boston Bowel Preparation Scale (BBPS).

Results: Preliminary results reveal an average BBPS score of 7 (indicating good quality bowel preparation) in both arms of the study.
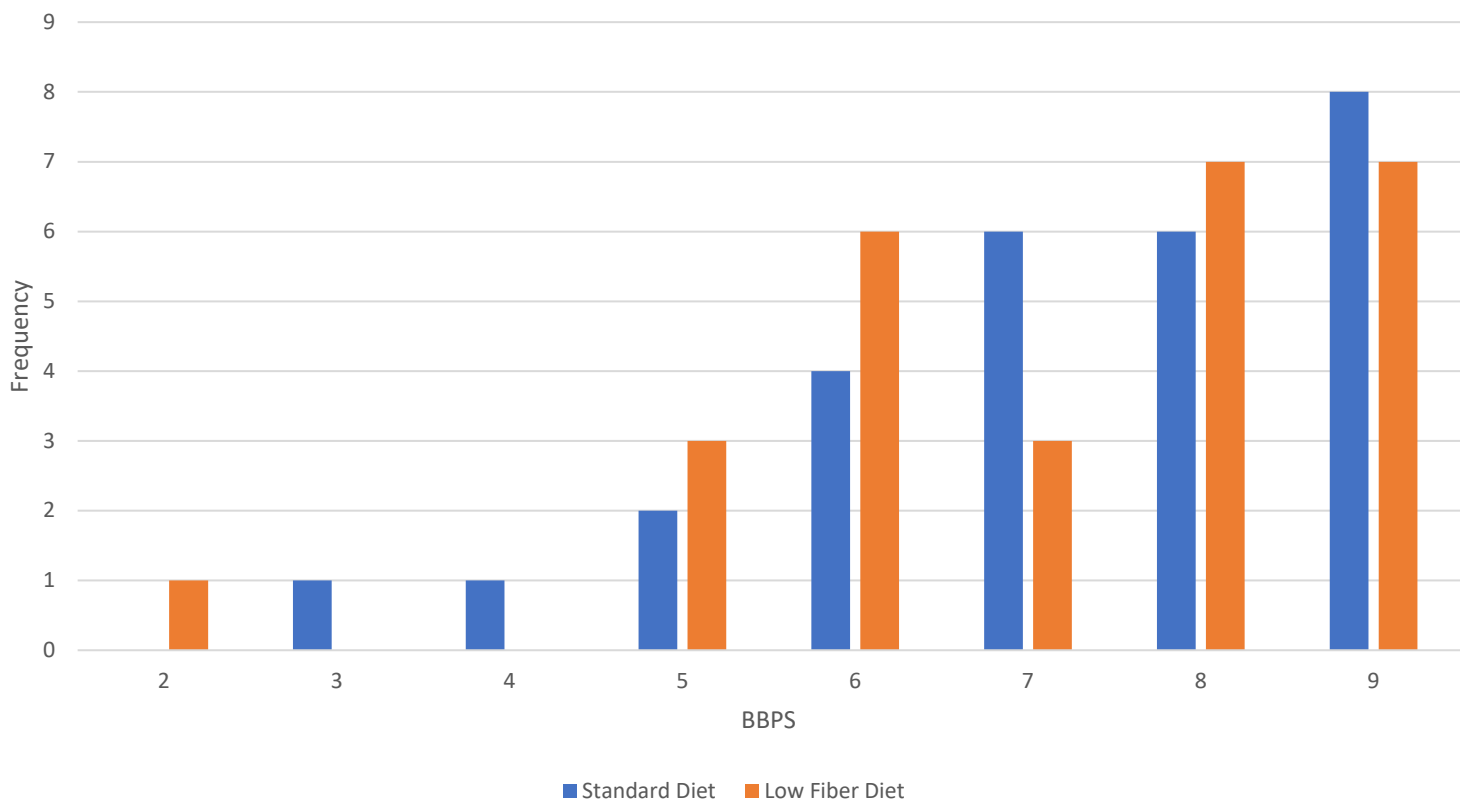
Conclusion: A low fiber diet is similarly efficacious as a clear liquid diet.

Clinical Implications: A low fiber diet can be considered an appropriate means of bowel preparation for colonoscopy in the pediatric population.

Comparison of BBPS Score Frequency between Standard Diet and Low Fiber Diet

Preclinical Evaluation of the Imipridone ONC212 in the KPCy Pancreatic Cancer Mouse Model

2023 Lifespan Research Day Abstract Submission Contest

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Alexander G Raufi, MD, RI Hospital, The Miriam Hospital, Brown University. Dept of Medicine, Pathology & Laboratory Medicine

Abstract

Background: ONC212 is a second-generation imipridone shown to have preclinical antitumor efficacy against human pancreatic cancer cell lines. The mechanism of action of ONC212 is incompletely understood but has been shown to bind to mitochondrial protease ClpP, expressed in pancreatic cancer cells, and suppress ClpX, the regulatory binding partner of ClpP. In doing so, it impairs oxidative phosphorylation by decreasing ATP production. While several studies have analyzed ONC212's capabilities in vitro, the sensitivity of KPCy mouse pancreatic cancer cells to ONC212 has yet to be evaluated in vivo. We hypothesized that like human pancreatic cancer cell lines, KPCy cells would demonstrate sensitivity to ONC212 in vivo. We aimed to test this hypothesis using several doses of ONC212 in KPCy-bearing C57BL/6 mice.

Methods: We tested five different doses/dosing frequencies of ONC212 (50 mg/kg; 25 mg/kg; 12.5 mg/kg dosed weekly or twice weekly) and compared them to vehicle-treated controls. Mice were injected subcutaneously with 3×10^5 KPCy cells in 100 L of PBS/matrigel solution into the flanks. Once their tumors were measured to be 50–75 mm3, ONC212 or vehicle was administered orally. Throughout the course of treatment, mouse weight and tumor size were measured every four days. Treatment was stopped once tumor volume reached 3,000 mm3 or if ulceration occurred. Tumor and blood samples were harvested for further analysis.

Results: ONC212 demonstrated efficacy at controlling KPCy tumor cell growth at multiple dose levels. Results did not appear to be dose-dependent as higher doses did not lead to significant differences in disease control. 50 mg/kg twice weekly led to reduced activity and significant weight loss, making lower doses preferable.
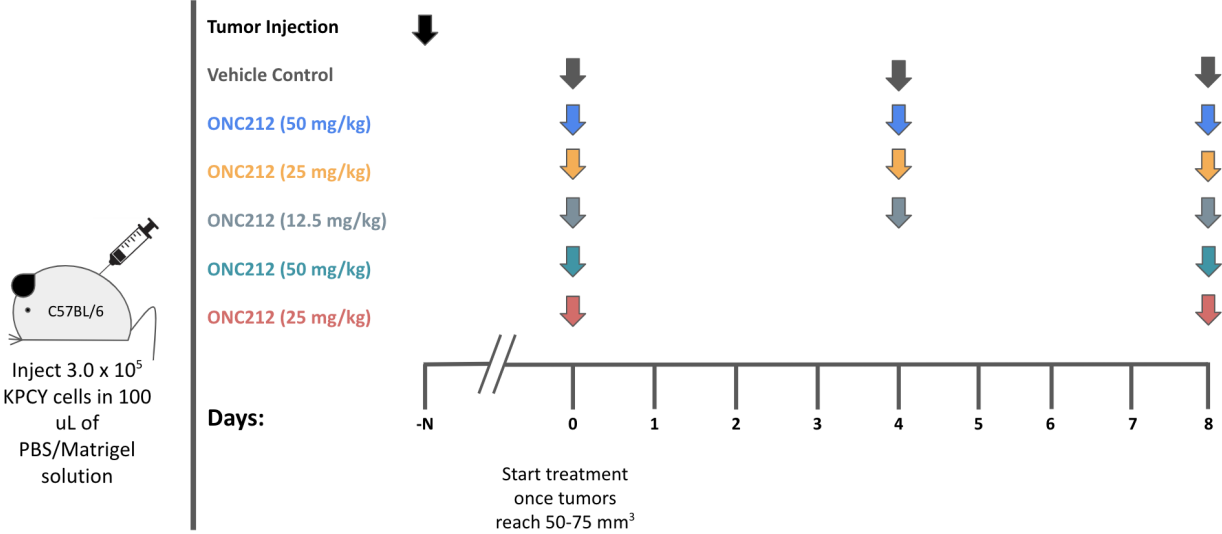
Conclusion: These experiments demonstrated that ONC212 can effectively control KPCy tumor cell growth in a heterotopic mouse pancreatic cancer model.

Clinical Implications: ONC212 is currently in preclinical phases of development and these experiments will inform future combination studies of immunotherapy and ONC212 to be performed in this immunocompetent rodent model.

Figure 1: Project Schema

	Tumor Injection
	Vehicle Control
	ONC212 (50 mg/kg)
	ONC212 (25 mg/kg)
	ONC212 (12.5 mg/kg)
	ONC212 (50 mg/kg)
	ONC212 (25 mg/kg)

Inject 3.0 x 10^5 KPCY cells in 100 uL of PBS/Matrigel solution

C57BL/6

Days: -N   0   1   2   3   4   5   6   7   8

Start treatment once tumors reach 50-75 mm^3

Determining Sensitivities of Two Bile Duct Cancer Cell Lines to ONC201 and ONC212

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Bile duct cancers will affect approximately 8,000 individuals in the United States each year. These are rare aggressive diseases with limited treatment options. ONC201 and ONC212 are members of the novel imipridone class of antineoplastic agents which have shown promise in pancreatic cancer cell lines. While ONC201 has been shown to induce both the integrated stress response and upregulate tumor necrosis factor (TNF)–related apoptosis–inducing ligand (TRAIL), resulting in apoptosis, the mechanism of ONC212 is thought to be mediated through binding to mitochondrial protease ClpP, leading to reduced oxidative phosphorylation from ClpX suppression. This project aims to determine the relative sensitivities of two bile duct cancer cell lines to ONC201 and ONC212, as well as traditional chemotherapy and other select agents.

Methods: Using viability assays, we established sensitivity of two bile duct cancer cell lines, RBE and HuCCT1, to ONC201, ONC212, trametinib, 5FU, palbociclib, oxaliplatin, olaparib, and gemcitabine. Cells were plated at 5000 cells per well and treated with each of these drugs after 24 hours. Results were analyzed after 72 hours of incubation using CellTiter–Glo Luminescent Cell Viability Assay.

Results: Both cell lines were susceptible to ONC201 and ONC212. The IC50 of these agents in these cell lines was 2.5uM, 2.0uM for ONC201; and 47nM, 39nM for ONC212 in RBE and HuCCT1, respectively. These IC50s compared favorably with those noted with gemcitabine and trametinib, 7.6nM, 9.8nM; and 7.0nM, 3.7nM, respectively, but were comparably lower than those noted with palbociclib (3.2uM, 4.2uM), olaparib (107uM, 31uM), and the other chemotherapeutic agents tested (5FU [1.3uM, 103uM] and oxaliplatin [5.0uM, 2.5uM]).

Conclusion: We demonstrate that ONC201 and ONC212 efficiently inhibit bile duct cancer cell growth in vitro. Comparing the IC50 values of ONC201 and ONC212 in each cell line to IC50 values with several commonly used chemotherapeutic agents revealed that imipridones may have a potential role in treating bile duct cancers.

Clinical Implications: These experiments represent the first in vitro studies of imipridones in bile duct cancers. Future combination studies of these agents with other potential synergistic partners will be conducted and may guide future clinical studies.

Does Sleep Regularity Link Child Maltreatment to Depressive Symptoms among Incoming First-Year College Students?

2023 Lifespan Research Day Abstract Submission Contest

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David Barker, Associate Professor, RI Hospital, Brown University. Dept of Psychiatry & Human Behavior

Eliza Van Reen, Co-Founder, Circadian Positioning Systems.

Katherine Sharkey, Associate Professor, Women & Infants Hospital, RI Hospital, Brown University. Dept of Medicine, Psychiatry & Human Behavior

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Abstract

Background: Sleep patterns may partially account for associations between early life adversity and poor health outcomes; however, few studies have empirically tested this hypothesis. We examined whether an index of sleep regularity mediated associations between child maltreatment (CM) and depression symptoms among emerging adults undergoing the major life transition of starting college.

Methods: First-year college students (N=731; 41% male; 48% Non-Hispanic White, 21% Non-Hispanic Asian, 15% Hispanic all races, 5% Non-Hispanic Black, and 11% Non-Hispanic other races) completed daily sleep diaries (DSDs) for 9 weeks and completed the Childhood Trauma Questionnaire (CTQ) and Center for Epidemiologic Studies Depression Scale (CES-D) following DSD completion. DSD data were used to compute participants' Sleep Regularity Index (SRI). We used a nonparametric SEM bootstrap approach to examine whether sleep regularity mediated associations between childhood trauma and depressive symptoms, controlling for sex, race/ethnicity, and US vs. international status. Separate models were run for CTQ total score and five CTQ subscale scores: emotional, physical, and sexual abuse, and physical and emotional neglect.

Results: The prevalence of moderate to severe CM was 20.7%, and 40% reported clinically significant depressive symptoms at the end of the assessment period. Significant indirect effects of CTQ total score (estimate=0.02, 95% CI=0.003, 0.036); emotional abuse (0.06 [0.004, 0.107]); physical abuse (0.08 [0.003, 0.164]); sexual abuse (0.06 [0.014, 0.114]); emotional neglect (0.04 [0.002, 0.075]) on greater depression symptoms through lower sleep regularity were observed; and we saw no significant indirect effect of physical neglect (0.04 [−0.015, 0.089]). The percentage of the total effect of CM (i.e., CTQ total score and subscale scores) on greater depressive symptoms accounted for by lower sleep regularity were CTQ total score: 6%; physical abuse: 24%; sexual abuse: 19%; emotional abuse: 7%; and emotional neglect: 5%.

Conclusion: Variable sleep patterns account, in part, for associations between CM and depressive symptoms among first-year college students, with the largest effects observed for physical and sexual abuse.

Clinical Implications: Sleep regularity should be included as a target in student health interventions on college campuses and may help buffer against poor mental health outcomes for students with CM.

Combining radiomics with miRNA–based liquid biopsy for noninvasive, less variable clinical outcome prediction of glioblastoma

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Glioblastoma (GBM), the most common primary malignant brain tumor of adulthood, is diagnosed by neuroimaging and tissue biopsy, usually obtained surgically. Both methods are limited in differentiating similarly–appearing neurological diseases and surgical risk respectively, hindering early GBM detection and prognostication. Liquid biopsy (LB) provides a less invasive alternative to tissue biopsy via fluid biomarker (eg, miRNA) analysis, and automatic tumor segmentation and radiomics feature extraction overcome limitations of human variability and human–determined thresholds for image interpretation. Both have individually demonstrated efficacy in GBM detection, yet no studies integrate them for optimizing performance. Here we integrate deep–learning (DL) multimodal magnetic resonance imaging (MRI) analysis with miRNA expression analysis to determine if this combination improves GBM clinical monitoring compared to separate applications.

Methods: This IRB–approved retrospective study at Rhode Island Hospital involved 65 GBM patients with both MRI and LB data available. MRI was performed every 2–3 months for 40 months, whenever possible per standard of care. miRNA was acquired at least once post–operation per patient, typically within 1 month post–operation and prior to disease recurrence. 315 pre–processed MRIs were studied, each including T1–non–contrast, T1–contrast–enhanced, T2, and FLAIR. miRNA expression data were quantified using Nanostring nCounter at Brown Genomics Core. Statistical models using JADBio software identified miRNA targets classifying samples via recurrence timeframe (eg, pre– versus post–recurrence samples). Separately, BraTS, a DL brain MRI–processing and tumor segmentation pipeline, and PyRadiomics, an automatic radiomics feature extraction package, identified radiomics features stratifying patients based on survival outcomes. Radiomic and miRNA features were then assessed for additive value in improving patient stratification according to recurrence time survival analysis.

Results: Four miRNA targets were observed individually predicting time–to–recurrence (p<0.01). Layering both miRNA and individually predictive radiomic features demonstrated improved patient stratification on survival analysis of recurrence–time (p<0.01), compared to single–timepoint miRNA features alone (Figure).

Conclusion: Both circulating miRNAs and MRI–derived features comprise potential biomarkers for accurate disease recurrence timeline prediction. Such stratification of GBM patients by recurrence–timeframe may improve with combining imaging and LB biomarkers.

Clinical Implications: Disease outcome prediction might be optimized by leveraging all available information, state–of–the–art LB and radiomic technologies, and DL models trained on clinical datasets.

hsa_miR_10b_5p

p = 0.00116

6	5	3	2	2	1	0	0
7	5	0	0	0	0	0	0
5	5	3	1	1	0	0	0
7	6	5	4	3	2	1	0
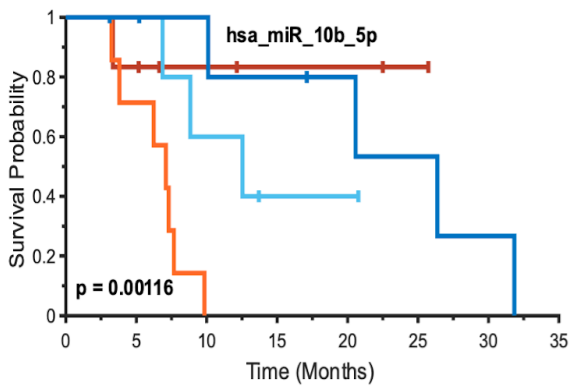
Legend:
- miRNA-High, Radiomics-High
- miRNA-High, Radiomics-Low
- miRNA-Low, Radiomics-High
- miRNA-Low, Radiomics-Low

hsa_miR_198

p = 0.00724
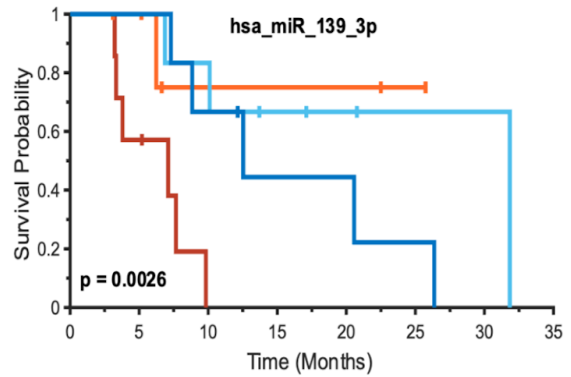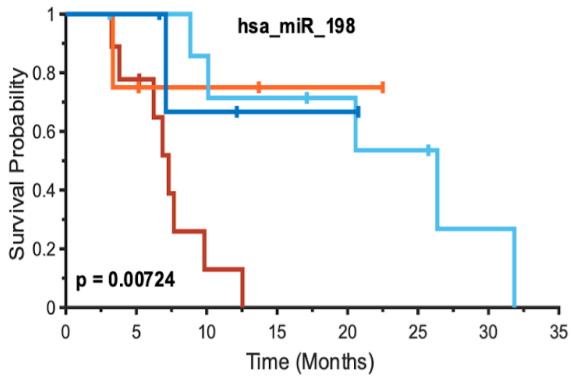
9	7	1	0	0	0	0	0
4	3	2	1	1	0	0	0
8	7	6	5	4	3	1	0
4	4	2	1	1	0	0	0

hsa_miR_139_3p

p = 0.0026

7	4	0	0	0	0	0	0
6	5	2	2	2	1	0	0
6	6	5	3	2	1	1	0
6	6	4	2	2	1	0	0

An exploration self–compassion, psychosis symptoms, and suicidal ideation among psychiatrically hospitalized adolescents

2023 Lifespan Research Day Abstract Submission Contest

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Robert Schattle, Undergrad, RI Hospital, Brown University. Dept of Psychiatry & Human Behavior

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Elizabeth C Thompson, Assistant Professor, RI Hospital, Bradley Hospital, Brown University. Dept of Psychiatry & Human Behavior

Abstract

Background: Self–compassion is an undervalued, yet teachable and powerful skill used to improve overall well–being. Among adults diagnosed with a psychotic disorder, higher levels of self–compassion have been associated with lower positive symptom (hallucinations, delusions) scores and lower levels of depression and anxiety. Similarly, an adult sample of patients experiencing persecutory delusions was found to have lower rates of self–compassion compared to controls, and suicidal ideation was highly correlated with low self–compassion in this sample. Research exploring the interrelations among these variables is limited and has yet to be explored in an adolescent sample.

Methods: The present study aimed to evaluate the relations between self–compassion, psychosis–spectrum symptoms, and suicidal ideation in a sample of 720 adolescents admitted to a psychiatric inpatient unit. Upon admission, adolescents completed self–report measures of self–compassion (via the State Self–Compassion Scale– Short Form), suicidal ideation (via the Suicidal Ideation Questionnaire– Junior), and psychosis–spectrum symptoms (via the PRIME Screen). A subsample of adolescents (n=327) also completed a semi–structured diagnostic interview; the psychosis module was used to assess current hallucinations and delusions.

Results: Correlations indicated that self–compassion was negatively associated with suicidal ideation ($r = -.51$), PRIME scores ($r = -.32$), auditory hallucinations ($r = -.20$), visual hallucinations ($r = -.18$), persecutory delusions ($r = -.18$) and mind–reading delusions ($r = -.20$). Regression results revealed a significant interaction between self–compassion and PRIME scores in the statistical prediction of suicidal ideation. PRIME symptoms were positively associated with suicidal ideation at all levels of self–compassion (low, mean, high), with the strongest effects at high self–compassion. In exploring self–compassion across groups of teens with (n=140) and without (n=177) psychosis–spectrum symptoms, those with symptoms had significantly lower self–compassion ratings. In particular, youth with psychosis–spectrum symptoms endorsed more negative/critical self–perceptions compared to other youth.

Conclusion: Contrary to our hypothesis, results indicated that there was a stronger association between psychosis–spectrum symptoms and suicidal ideation among those with high self–compassion. Discussion will include possible explanations and implications of these preliminary findings.

Clinical Implications: Further studies exploring the role of self–compassion on suicidal thoughts and behaviors among youth with psychosis–spectrum symptoms are needed to inform intervention initiatives for this population.

Silver Carboxylate Antibiotic–Independent Antimicrobial: Exploration of Potential Solutions for the Post–Antibiotic Era

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Antibiotic resistance has been steadily rising due to increased use of synthetic antibiotics, lack of novel antibiotics, and poor stewardship, leading to a perilous 'post–antibiotic era.' Prompt innovation is crucial to avoid millions of deaths from antibiotic–resistant infections by 2050. Organometallics offer a potential solution, and our group has developed a silver carboxylate (AgCar) compound with distinct bactericidal mechanisms. This study presents an overview of the release pharmacokinetics of AgCar in Titanium dioxide–polydimethylsiloxane (TiO2–PDMS) matrix, its safety concerning human–derived cell lines, antimicrobial efficacy, biofilm dysregulation, and impact on the viability of persister cells.

Methods: Antimicrobial efficacy was evaluated using Vancomycin–Resistant Enterococcus faecalis, Methicillin–sensitive Staphylococcus aureus, and Methicillin–resistant Staphylococcus aureus strains MW2 and VRS1 on 96–well plates and PEEK implants. Bacteria were exposed to varying concentrations of silver carboxylate, 'last resort' antibiotics, nanoparticle silver, colloidal silver, and controls, for 24 hours. The safety assessment of silver carboxylate on human–derived cell lines [osteoblasts, keratinocytes, and skeletal muscle cells (SKMs)] involved subjecting the cells to the same antimicrobial conditions, and cell viability was assessed using MTT assay. Each condition was replicated n=15, and biofilm imaging was performed using confocal microscopy.

Results: 10X minimal inhibitory concentration (MIC) demonstrated consistent, significantly greater elution than 1X at 96 hours, with sustained persister cell killing over 72 hours. Concentrations above 10X MIC improved biofilm eradication. 1X MIC showed comparable or lower cytotoxicity compared to crude silver and 'last resort' antibiotics, especially in SKMs. 10X exhibited increased cytotoxicity across all cell lines. Silver carboxylate outperformed most last resort antibiotics at 1X and 10X MIC against all tested pathogens. At 10X MIC, it effectively dispersed and neutralized biofilms.

Conclusion: Our study revealed that 1X silver carboxylate demonstrated comparable or lower cytotoxicity to crude silver formulations and tested antibiotics. 10X silver carboxylate showed higher antimicrobial efficacy in bacteria, persister cells and biofilms, however it also exhibited significant cytotoxicity across human lines.

Clinical Implications: Silver carboxylate in TiO2–PDMS matrix shows promise as a novel antimicrobial coating for surgical implants, potentially reducing the risk of post–operative bacterial infections. Our data suggests that this innovative biomaterial could be a viable alternative; however, further investigation into cytotoxicity is necessary.
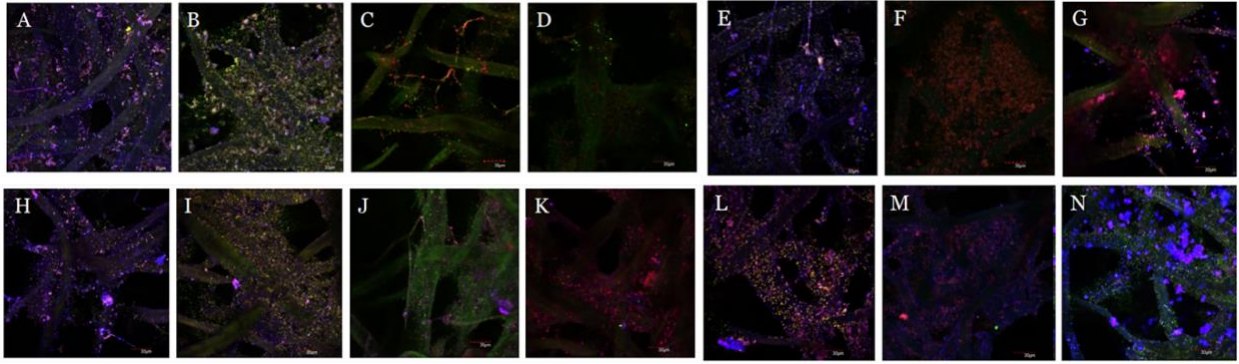
Figure 1: Biofilm Images of MRSA MW2 and VRS1 in response to silver carboxylate treatment: A, B, C, D, E, F, and G show confocal images of biofilms for MW2. Image A is an untreated biofilm, and Images B, C, D, and E were treated with 1x, 10x, 30x, and 300x AgCar, respectively. Image F was a positive control treated with 100% AgCar, Image G was treated with vehicle only. All biofilms were stained with SYPRO, TOTO-1, and Concanavalin A (594).

Escherichia coli Meningitis in an Immunosuppressed Elderly Patient
2023 Lifespan Research Day Abstract Submission Contest

Author(s):

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Abstract

Background: Bacterial meningitis is a devastating cause of infection–related death in the U.S., with a mortality rate of 6%–54% with antibiotics. Streptococcus pneumoniae causes 70% of bacterial meningitis cases in adults over 65.8 Community–acquired E. coli meningitis is responsible for just 1%, yet it is among the most deadly, with mortality rates from 50% to 90%. Common portals of E. coli entry include bacteremia and urinary tract infection. First–line therapy of bacterial meningitis is empirical intravenous antibiotic therapy and dexamethasone. However, only 30.36% of patients receive adjuvant dexamethasone, and corticosteroids are associated with unfavorable outcomes in up to 50% of cases of bacterial meningitis. The aim of this study is to summarize the literature concerning corticosteroid adjuvant therapy for bacterial meningitis and present a case in which the incidental use of corticosteroids immediately prior to infection may have prevented death.

Methods: Literature regarding prior cases of E. coli meningitis was reviewed. Patient records were analyzed.

Results: We present the case of a 72–year–old female with recent corticosteroid use who presented for a 1–day history of altered mental status. She was found to have nuchal rigidity with positive Brudzinski, headache, and fever. Blood and CSF cultures revealed E. coli meningitis bacteremia, and urine cultures revealed E. coli and Klebsiella UTI. A brain and cervical spine MRI ruled out an abscess as the source of infection. It was determined that her UTI was the likely focus of infection. The infectious disease team proposed that the patient's recent corticosteroid use suppressed inflammation sufficiently enough to prevent death in this elderly patient with multiple comorbidities.

Conclusion: E. coli is a rare but deadly cause of meningitis in the U.S. In immunosuppressed patients with UTI, the pathogen can spread to the meninges. While corticosteroids are associated with unfavorable outcomes for most etiologies of meningitis, they may adequately suppress inflammation to such an extent as to prevent death in severely ill patients.

Clinical Implications: The use of adjuvant corticosteroid therapy for bacterial meningitis requires a patient–centered discussion of risks and benefits.

New Potential to Restore Neuromuscular and Joint Function after ACL Injury: An Injury COBRE Project Proposal

2023 Lifespan Research Day Abstract Submission Contest

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Abstract

Background: Anterior cruciate ligament reconstruction (ACLR) using a tendon taken from elsewhere in the body is the current standard–of–care after ACL tear. ACLR typically restores knee function to within ~10% of values of uninjured counterparts; however, re–injury rates remain high and neuromuscular function and dynamic joint motion are distinctly different from those of matched uninjured controls. Conversely, bridge–enhanced ACL restoration (BEAR) is a new treatment that uses an extracellular matrix sponge as a temporary scaffold for the torn ligament ends to grow across, recapitulating the native ligament anatomy. Preliminary studies have shown that BEAR patients regain lower limb strength more fully and report significantly better quality of life and sport/recreation indices compared to ACLR. Based on these findings, our over–arching hypothesis is that BEAR surgery preserves neuromuscular activation patterns that, in turn, promotes normal hop landing joint motion and corresponding patient–reported outcomes compared to ACLR. This RIH Injury COBRE–sponsored project has 3 aims: 1) Apply our machine learning approach to classify neuromuscular activity patterns within ACLR, BEAR, and healthy Control groups; 2) Compare ACLR, BEAR, and Control subject anterior tibial position during a hop landing; and 3) Examine the agreement between functional measures (neuromuscular activity, tibial position) and patient–reported outcomes.

Methods:

Results: In a cross–sectional study design, we will recruit 26 subjects from the BEAR–MOON multicenter randomized clinical trial at their 2–year follow–up, and 13 proportionally matched healthy controls. Surface electromyography for neuromuscular function and xray videos for precise tibial position will be recorded. Patient reported outcomes relating to patient quality of life and return to sport will be collected using established questionnaires. Relationships will be tested using generalized linear models.

Our preliminary data suggest that BEAR promotes normal post–surgical neuromuscular function and joint motion (Figure).

Conclusion: We postulate that restoring the native ligament anatomy with BEAR promotes normal post–surgical neuromuscular function and joint motion, which in turn leads to better quality of life satisfaction and return to sport/recreational activities metrics, and a lower risk of reinjury.

Clinical Implications: At study completion we will be positioned to move our neuromuscular performance metrics into clinical practice to optimize rehabilitation and follow these same patients longitudinally.
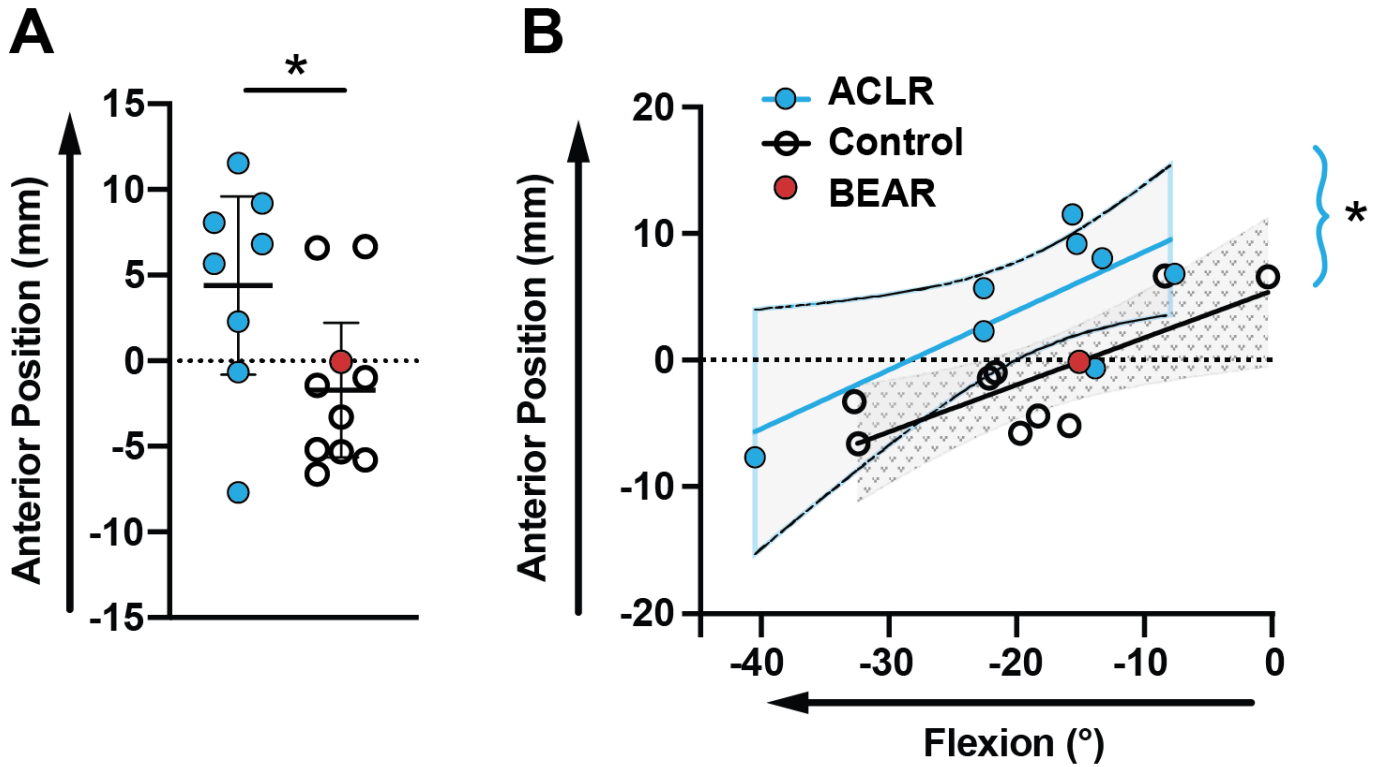
Figure. BEAR patient tibial position grouped with Controls **(A,B)** while ACLR tibiae were significantly more anterior compared to healthy Controls despite similar flexion angles **(B)**. "*" indicates significant difference between ACLR and Controls.

Characterizing the Antimicrobial Properties of Silver Carboxylate (AgCar)
in Multi–Drug Resistant Gram Negative Serratia marcescens
2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational
Primary Research Location: Diane N. Weiss Center for Orthopaedic Trauma Research Lab, Coro Building, RI Hospital
Funded By: Emerging Infectious Disease Scholarship

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Abstract

Background: The clinical management of Serratia marcescens infections are particularly challenging due to its intrinsic resistance to multiple classes of antibiotics. Antimicrobial resistance due to poor stewardship and management is a health crisis, which renders the exploration of alternative antimicrobials, such as organometallics a priority. Silver carboxylate (AgCar) released via a titanium dioxide/polydimethylsiloxane (TiO2–PDMS) matrix developed in our laboratory has emerged as a promising antimicrobial silver formulation. This study aims to further investigate and characterize the antimicrobial properties of AgCar by evaluating its capacity to inhibit catalase and trigger reactive oxygen species (ROS) release in Serratia marcescens.

Methods: Serratia marcescens was grown overnight to 1x10^6 CFU/mL at 37.... Bacteria was plated on a 96–well plate and exposed to a gradient of 1X–150X minimal inhibitory concentrations (MIC) AgCar for 2 hours. The levels of ROS and catalase were assessed via manufacturer's protocol from the respective kits. 10nm and 30nm nanosilver, and 100% silver carboxylate served as positive controls, and TiO2–PDMS vehicle–only and 1% Triton X served as negative controls.

Results: ROS assay revealed 0.997X, 1.01X, 0.896X, 2.08X, and 3.12X reactive fluorescence unit (RFU) fold changes for 1X, 10X, 30X, 100X, and 150X AgCar TiO2–PDMS matrices, respectively. 10nm and 30nm nanosilver had $-0.053X$ and $-0.274X$ RFU fold changes, respectively. $P < 0.05$ for all AgCar TiO2–PDMS vs. nanosilver comparisons. The catalase assay revealed 0.0779X, 0.0688X, 0.876X, 0.0812X, and 0.0723X RFU fold changes for 1X, 10X, 30X, 100X, and 150X AgCar TiO2–PDMS matrices, respectively. 10nm and 30nm nanosilver had 0.113X and 0.864X RFU fold changes, respectively. $P < 0.05$ for all AgCar TiO2–PDMS concentration vs. nanosilver comparisons.

Conclusion: AgCar TiO2–PDMS matrices induced statistically significantly more ROS than nanosilver. AgCar TiO2–PDMS matrices induced statistically significantly less catalase than nanosilver. Therefore, AgCar TiO2–PDMS induces ROS stress and inhibits antioxidant enzyme, catalase production. Further research into the antimicrobial mechanisms of AgCar is necessary.

Clinical Implications: Given the ROS generating and catalase inhibiting antimicrobial mechanism of action of AgCar TiO2–PDMS, AgCar TiO2–PDMS has the potential to be utilized as an antimicrobial, especially synergistically with other drugs.

Bridging Emergency Medicine and Public Health: Clinical Toxicology Laboratory Strategies to Characterize Local Drug Supplies and Drug Use Patterns

2023 Lifespan Research Day Abstract Submission Contest

Research Category: Clinical & Translational

Primary Research Location:

Funded By:

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Abstract

Background: The magnitude and complexity of the evolving overdose crisis – currently a poly–substance epidemic – is rendering classical approaches to drug testing and monitoring outdated and ineffective. The illicit drug supply is constantly and rapidly changing, with fentanyl analogs and other novel psychoactive substances increasing risk of adverse health outcomes and overdose among people who use drugs (PWUD). Research has shown that PWUD will adjust their use practices when provided with accurate information of what is in their drug supply. We sought to perform comprehensive drug testing on drug overdose patients and drug samples to determine 1) the feasibility of comprehensive drug testing in the emergency department (ED); and 2) the most common adulterants seen in the local Rhode Island drug supply to generate overview of drug use patterns and clinical needs.

Methods: We consented 76 overdose patients in the ED and, through close collaboration with community outreach partners, we obtained 125 drug samples in 2022. Participants had blood and urine samples tested, while drug samples included substances, baggies, and used equipment (pipes, cookers, cottons). All testing was performed in the RIH Toxicology Laboratory via the LC–QTOF–MS comprehensive drug screen. Results were rapidly disseminated back to participants and community partners through collaboration with the Rhode Island Department of Health. Participants completed surveys post–delivery of results.

Results: Fentanyl was found in 87% of consented overdose patients, typically alongside multiple other substances, including adulterants such as xylazine. In post survey respondents, 81%, reported 'yes, definitely' that they would use the service again. Immediately after overdose 46% reported that they were 'very concerned' about drug supply safety; after receiving testing results that number rose to 61%. Drug sample testing confirmed contamination of drug supply. Results are summarized in Figure 1.

Conclusion: Comprehensive drug testing in both overdose patients and drug samples reveals trends in substance use and the inherent poly–substance nature of the drug supply due to contamination and adulteration. Timely communication of results to PWUD enables harm reduction measures.

Clinical Implications: Incorporating comprehensive toxicology testing in clinical management can impact both individuals (patients) and public health by providing data that can inform local biosurveillance and harm reduction initiatives.

Table 1. Results of the first 125 samples

Sample characteristic	n (%)
Sample type	
Refuse	17 (13.6%)
Used paraphernalia	53 (42.4%)
Product	55 (44%)
Geographic location of sample[1]	
Urban	114 (91.2%)
Suburban	7 (5.6%)
Rural	4 (3.2%)
Substance category of sample	
Opioid	63 (50.4%)
Stimulant	39 (31.2%)
Benzodiazepines	8 (6.4%)
Unknown	8 (6.4%)
Hallucinogen	7 (5.6%)
Key substances and active cut in samples[2]	
Fentanyl and fentanyl analogs	84 (67.2%)
Xylazine	52 (40.8%)
Nitazene	1 (0.8%)
Cannabinoids	13 (10.4%)
Benzodiazepines	12 (9.6%)
Designer benzodiazepine	4 (3.2%)

[1]Land delineations used the following definitions: urban (i.e., $\geq$ 2,500 people per square mile and $\geq$ 50% of land are classified as developed), suburban (i.e., 500-2,499 people per square mile and $\geq$ 25% of land area classified as developed), and rural (i.e., <500 people per square mile or < 25% of land area classified as developed).

[2] Not mutually exclusive.

Snapshot: Adulteration of supply with fentanyl and xylazine

	Used Equipment			Product			Refuse		
	Samples	Xylazine	Fentanyl	Samples	Xylazine	Fentanyl	Samples	Xylazine	Fentanyl
Cocaine powder	1	—	—	4	—	1	2	—	1
Crack cocaine	9	1	3	6	—	1	1	—	1
Methamphetamine	2	—	2	4	2	3	—	—	—
Heroin	—	—	—	1	—	1	—	—	—
Fentanyl / Dope	27	20	27	16	8	16	9	5	9
Percocet	1	1	1	1	1	1	4	4	4
Unknown	8	4	6	—	—	—	—	—	—
MDMA or Ketamine	—	—	—	4	—	—	1	—	—
Xanax or Adderall	—	—	—	2	—	—	—	—	—
Total	48	26	39	38	11	23	17	9	15