



## Clinical Research Update

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Pharma, Inc. (NCT03434275) and United Orthopedic Corp. (NCT02761499). Dr. Lee also collaborates with colleagues at the Rothman Institute on an unfunded project to investigate *The Utility of Next-generation Sequencing for the Diagnosis of Periprosthetic Joint Infection* (NCT03200470). Dr. Neil Sheth has started his first industry sponsored study with Medacta to evaluate their Masterlock® Hip device and has also secured funding from Medacta in parallel for an investigator initiated retrospective review of the transition from posterior approach primary Total Hip Arthroplasty (THA) to anterior approach THA. We are also introducing Dr. Christopher Travers as a new PI at Pennsylvania Hospital. Dr. Travers assumed the responsibility for two of Dr. Kamath's studies upon his departure. Easily the biggest news in Adult Reconstruction Clinical Research is the initiation of the Mymobility study. *A Prospective Multicenter Longitudinal*

Penn Orthopaedics Clinical Research continues to grow and evolve in response to the needs of our patient population, the availability of technology, and the innovative drive and reputation of our faculty. Each subspecialty has grown substantially and almost every Division has an assigned CRC. Some Division specific highlights for the year are noted. It has been a very exciting year and space does not permit full itemization. We hope that you appreciate the outstanding effort put forth by our faculty and staff highlighted in the following summaries.

The **Adult Reconstruction** faculty celebrates major accomplishments this year. Dr. Gwo-Chin Lee began work on an extramurally funded, investigator initiated, retrospective cohort study. The study, sponsored by Ferring Pharmaceuticals, investigates *Patient and Clinical Factors Related to Positive Response From Hyaluronic Acid Injections*. Dr. Lee also serves as Principal Investigator (PI) on four prospectively enrolling industry sponsored studies with Smith & Nephew (NCT03056534), KCI USA (NCT03274466), Recro

*Cohort Study of the Mymobility® Platform* (NCT03737149) seeks to enroll 600 patients at Penn Orthopaedics, and 10500 across all sites, to determine if mobile application-guided education and exercise, paired with accurate and sensitive activity monitoring captured from consumer wearables, can provide a viable (and potentially improved) alternative to current standard of care physical therapy for hip and knee arthroplasty. Dr. Craig Israelite is the PI for this study at Penn Orthopaedics, Drs. Charles Nelson and Eric Hume are sub-Investigators. Both Dr. Nelson and Hume have active Clinical Research portfolios of their own. Dr. Nelson is the PI on the PCORI co-sponsored PEPPER Study (NCT02810704). Dr. Hume is the PI for two DePuy sponsored post-marketing approval Ceramic-on-Ceramic Total Hip Replacement Studies (NCT02096211 and NCT01657435) and he also s Joint Replacement Registry (AJRR).

**FOP Clinical Research** has enjoyed multiple successes this year. The Clementia Pharmaceuticals sponsored research program to study Palovarotene, a RAR $\gamma$ -specific agonist, as the first therapeutic intervention against Fibrodysplasia Ossificans Progressiva continued with the addition of a Phase 3 study, NCT03312634. A second industry sponsor, Regeneron Pharmaceuticals, has joined the fight against FOP with the initiation of the LUMINA-1 Trial, NCT03188666. The LUMINA-1 Trial will test REGN2477 vs placebo over a 6 month dosing period followed by a 6 month follow up open-label treatment period. The study will assess the safety and tolerability of the investigational product in the target population and will attempt to measure the change from baseline in heterotopic ossification (HO) in patients as measured by 18-NaF uptake by PET and CT. Dr. Frederick Kaplan is the Global PI for the Clementia Program and the Global Study Advisor for the Regeneron Study. Dr. Mona Al Mukaddam is the Penn PI for all FOP Clinical Research. We are extremely hopeful that the combined efforts of these ongoing and planned studies will result in a therapy that will have minimal side effects and will restore these patients to a mobile lifestyle.



Dr. Al Mukaddam, CRC in training.



Dr. Kaplan, CRC in training.

On other fronts, Dr. Kaplan's lifetime of selfless and relentless pursuit of a cure for FOP was recognized this year through the reception of the Grand Hamdan International Award - Musculoskeletal Disorders. This award is focused on those who are dedicated to the alleviation of the sufferings of humanity through research and exemplary service. For more information please visit <http://www.hmaward.org.ae/archive.php?termid=67>



With the initiation of the GE Healthcare sponsored VolumeRad observational study, NCT03856450, (Dr. David Steinberg, PI) **Hand Surgery** leads the Department in the metric that every faculty member in the Division is the PI on at least one extramurally funded study. Dr. David Bozentka is the local PI of *A Multicenter, Prospective, Randomized, Subject and Evaluator Blinded Comparative Study of Nerve Cuffs and Avance Nerve Graft Evaluating Recovery Outcomes for the Repair of Nerve Discontinuities (RECON)*, NCT01809002, which is sponsored by Axogen Corporation. Dr. Benjamin Gray is the local PI of the *Protect Neuro Trial Post Marketing Surveillance Prospective Cohort Evaluation of Neurocap® In The Treatment of Symptomatic Neuroma*, NCT02993276, sponsored by Polyganics BV. Dr. L. Scott Levin is the co-Global PI of the RECON study with Dr. Jonathan Isaacs, and Dr. Levin is the North American PI of the Polyganics study. Dr. Levin has himself secured an impressive amount of extramural research support in the past year. His dedication to Vascularized Composite Allotransplantation (VCA) surgery has resulted in the success of his partnering-PI relationship with the University of Delaware's Dr. David Tulsy and Dr. Scott Tintle of Walter Reed National Military Medical Center and Penn Orthopaedics. Together, Drs. Levin, Tintle, and Tulsy have been awarded a Department of the Army grant entitled, *Reconstructive Vascularized Composite Allotransplantation: Qualitative Approach to Enhance Patient Reported Outcome Metrics and the Candidate Screening Process*. This project will carefully and thoughtfully examine the entire process of VCA candidate selection, surgery, and post-operative outcomes to establish *de novo* multimodal candidate guidelines for this growing surgical subspecialty.

In other Divisions the activity from previous years is carrying forward with expansion on the horizon. **Shoulder & Elbow** has three active industry studies under Dr. Andrew Kuntz as PI. Two of these are sponsored by Integra Lifesciences and one is sponsored by Orthofix. Dr. Kuntz is fielding another study for the upcoming year as is Dr. Huffman. Both pending studies are from new sponsors. Dr. Harvey Smith has been transferring his skills and leadership in bench science to serve as the PI in the DePuy Vivigen study, NCT02814825. Dr. Smith is also courting other studies and sponsors for the **Spine Division**. Dr. Robert Wilson in **Orthopaedic Oncology** is

initiating human subjects research as well. We look forward to working with him and supporting his activity.

**Sports Medicine** clinical research now includes a NIAMS/PCORI co-sponsored trial through Vanderbilt University Medical Center, under the local leadership of Dr. John Kelly to study *Operative Versus Non-Operative Treatment for Atraumatic Rotator Cuff Tears (ARC)*, NCT03295994, with an overall target enrollment of 800 subjects and 12 month follow-up. Dr. James Carey is the Global and Local PI of the Vericel Corporation sponsored PEAK study, NCT03588975, entitled *A Study of MACI in Patients Aged 10 to <17 Years With Symptomatic Chondral or Osteochondral Defects of the Knee (PEAK)*. The objective of this study is to compare the efficacy and safety of MACI® vs arthroscopic microfracture in the treatment of patients aged 10 to <17 years with symptomatic articular chondral or osteochondral defects of the knee. Dr. Carey is also the local PI of the *Hyalofast Trial for Repair of Articular Cartilage in the Knee (FastTRACK)*, NCT02659215, sponsored by Anika Therapeutics, Inc., which evaluates the safety and efficacy of Hyalofast® scaffold with bone marrow aspirate concentrate (BMAC) compared to microfracture in the treatment of symptomatic cartilage defects of the knee. He also serves as the site PI of the ROCK Registry. Dr. Zgonis has recently initiated work on his investigator initiated study to examine *TIRho as a Surrogate for Cartilage Overload in Patellofemoral Malalignment* that was funded through the Penn Center for Precision Medicine.

**Foot & Ankle** has undergone a few transitions this year as long time PI of the STAR Ankle study (NCT01284283) Dr. Keith Wapner passed the baton to Dr. Kathryn O'Connor. Dr. O'Connor also received and is executing her own study with Dr. Josh Baxter to *Correlate Tendon Diastasis with Functional Outcomes in Achilles Tendon Ruptures*, for which she won a McCabe Award. Dr. Dan Farber remains the PI of the *DJO CMF Bone Stimulation as Adjunct to Surgical Treatment of Ankle Fractures* (NCT02688855) and this study will be expanding to Presbyterian Medical Center to include the Ortho Trauma Faculty in order to boost recruitment.

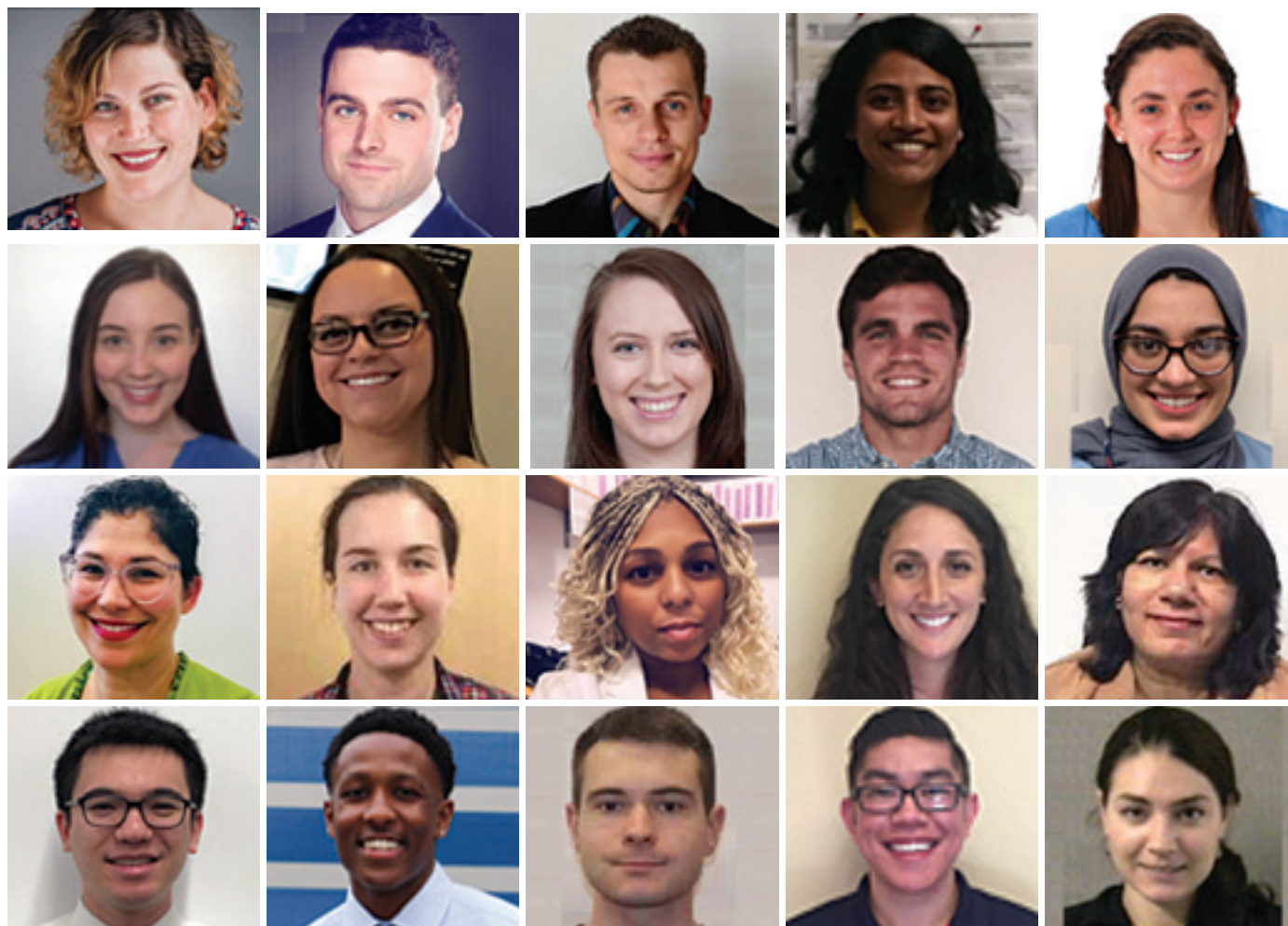
After a short period of maintenance and minor contraction, **Orthopaedic Trauma** is gearing up to launch several new funded studies. Last year, we told you about the PCORI sponsored REGAIN Trial (NCT02507505) (PI: Mark Neuman, MD), an ongoing \$12M 42-site multicenter trial to investigate the role of anesthesia delivery on functional outcomes after hip fracture surgery in the elderly. REGAIN incorporates a well-integrated team of Orthopaedic Surgery Faculty (Drs. Mehta co-I, Donegan, and Ahn) with faculty from Anesthesiology & Critical Care (Drs. Neuman, Elkassabany, and others) and is pressing hard to meet its enrollment goal of 1600 evaluable subjects; 1188 subject have been randomized to date (50 at Penn) and this study is already the largest to ever compare general vs spinal anesthesia in any indication. Next up for Ortho Trauma is another PCORI co-sponsored study with McMaster University that is directed through the University of Maryland entitled *Pre-operative Alcohol Skin Solutions in Fractured Extremities (PREPARE)* NCT03523962. The

PREPARE study will compare the most common alcohol-based pre-operative antiseptic skin solutions used during extremity fracture surgery: DuraPrep vs ChloroPrep. Randomization will be cycled by time at each site and 8000 subjects will be followed for up to 12 months for primary and secondary endpoints. Other similarly sized studies in the Ortho Trauma queue include a grant from the AO Foundation to investigate the *Intersection of the Transcriptome and Microbiome*, this study will be starting to enroll imminently and will expand on previously published work.

At this time, it is important to recognize the **Staff**. We congratulate those who worked with us previously and who have moved on to other opportunities. At this writing, we

have recently said farewell to Rupa Chowdary and note that Alyssa Perez de Corcho will be departing our team. Both of these individuals worked well with us and have moved on professionally. John Flacco who served as a CRC for Adult Reconstruction has been accepted to Medical School and will be starting in the fall of 2019. Aliaksei Basatski, formerly of Penn Orthopaedics has transitioned into a Project Manager role in Penn Anesthesiology & Critical Care (ACC). We welcome Sarah Bart to FOP, Kelly Clark to Ortho Trauma, Dr. Mary Dooley to Hand, Zahida Halimi to ACC, and Aaron Tatad to Spine. We also congratulate those on our team who recently passed the ACRP exam to become Certified Clinical Research Coordinators (CCRCs): Alyssa Perez de Corcho and Beth Howard.

## FY 19 Clinical Research Team



**Figure 1** Top row, Sarah Bart (FOP), Evan Bannister (Shoulder & Elbow), Aliaksei Basatski (ACC), Rupa Chowdary (ACC), Rebecca Churchill (Temp), Kelly Clark (Ortho Trauma). Middle Row, Olivia Colarullo (PAH), Dr. Mary Dooley (Hand), John Flacco (Adult Recon), Zahida Halimi (ACC), Beth Howard (Sports Medicine), Renee Jurek (FOP), Helena Moses (Adult Recon). Bottom Row, Alyssa Perez de Corcho (PAH), Kamlesh Rai (FOP), Aron Schwartz (ACC), Shawn Simmons (Sports Medicine), Cody Sylvester (Temp), Aaron Tatad (Spine), Katherine Toder (FOP).

Thank you to all the named and unnamed staff and faculty on our team, the residents, fellows, and other clinical support staff, and especially the leadership of Penn Orthopaedics and Anesthesiology & Critical Care for their ongoing support of our highly active team. Specifically, we thank the Chairs, Drs. Levin

and Fleisher, the Vice-Chairs for Research, Drs. Soslowsky and Eckenhoff as well as the Chief Operating Officers, Neil Ravitz and Dennis Harris for your ongoing guidance and support in every way throughout the year.