



Health System Update

Clinical Research Update



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Penn Orthopaedics Human Subjects Research (HSR) has evolved considerably in recent years. Dr. Samir Mehta assumed the role of Medical Director of Clinical Research in November 2016 and Fabian Marechal, Senior Director of Operations has also rolled Clinical Research under his many duties. Our collaboration with Anesthesiology and Critical Care (ACC) remains intact, and our financial, regulatory, and operational position in FY18 exceeds expectations. Figure 1 demonstrates the complex relationship between clinical research income and effort. The number of FTEs has risen from 1 in 2005 to ≥ 17 in 2018, with the majority of these staff dedicated exclusively to Orthopaedic Surgery. Further, since Orthopaedic Surgery projects often extend through multiple years of follow up, the turnover of projects is infrequent and the activity has tended to accumulate. As shown in the figure, the number of active funded clinical research projects from 2011 to the first Quarter of 2018 (Q1-2018) has increased 20 fold.

The overall proportion of studies for each Division that are prospective and funded has shifted favorably in recent years and the current breakdown is shown in Table 1. Each Division

has its own funding mix which may include sponsorship from grants, gifts, government and foundation grants, sub-awards through other academic institutions, and of course industry sponsorship. There are also several achievements of note relative to Table 1.

The Adult Reconstruction Division has, at this writing, 5 new sponsored studies pending activation in addition to those captured in Table 1. The Divisions of Foot & Ankle Surgery and Sports Medicine, both have at least 1 funded study per surgeon. Our Hand Division boasts 2 studies where Dr. Levin is the Global Principal Investigator (Axogen RECON, Dr. Bozentka is the local PI; and Polyganics PROTECT NEURO; Dr. Gray is the local PI). In Sports Medicine, the honor of being Global Principal Investigator has fallen to Dr. Kelly for the Trice Medical, mi-Eye study and will soon be bestowed upon Dr. Carey with the Vericel MACI trial in addition to his leadership of the now-funded, ROCK Registry. Dr. Mehta remains the Global PI for the Microbion MBN-101 (Dr. Donegan is the local PI) study and the Penn site is also the enrollment leader for this breakthrough work on the first new antibiotic in 50 years.

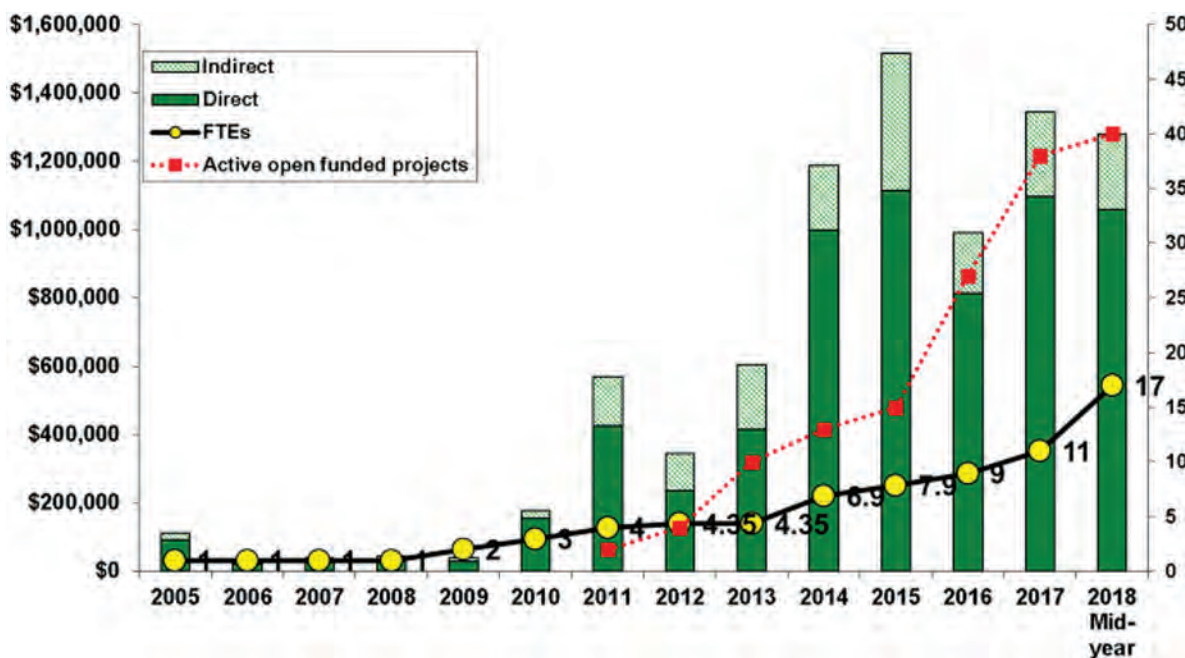


Figure 1. Orthopaedic Surgery Clinical Research Funding and Effort. Active open projects are captured from the time of study start up, and remain active as of FY18. (square symbols with dashed line). Funded studies closed in any year are not shown. Total funding for each year is reflected in the height of the column for that year. The proportion of indirect costs (patterned bars) vs direct costs (solid bars) is not uniform due to the differing indirect cost rates per funder in any given year. The total of FTEs (circles with solid lines) since 2014 includes those individuals paid by the Department of Anesthesiology & Critical Care, thus incorporating all the individuals on the team. Funding in FY11 reflects an accumulated back-payment from Smith & Nephew, in addition to a double processed payment for the portion of Said Ibrahim's NIH grant (ends 2015). The funding for FOP clinical research studies has been added back into this scheme and gift funding for Mehta project # 809094 has also been appropriately added. Not all income is available for salary support. FY18 funding is reflected only through December 2017. An additional 17 new funded Orthopaedic Surgery projects are at various stages of pre-study activity (site selection, CTA negotiation, budget approval, IRB approval, and site initiation as of 22 Jan 2018).

Table 1. Clinical Research Studies by Division.

Division	Total Studies	Funded Studies	Prospective	Retrospective or Mixed	Proportion Funded
Adult Reconstruction	42	17	26	16	40%
Foot & Ankle	9	4	5	4	44%
FOP	4	4	4	0	100%
Hand	11	5	7	4	45%
Shoulder & Elbow	13	3	6	7	23%
Spine	6	1	1	5	17%
Sports Medicine	30	6	18	12	20%
Trauma	33	12	18	15	36%
Total	148	52	85	63	35%



Figure 2. Clinical Research Staff. Pictured from L to R are our team of Clinical Research Coordinators serving Orthopaedic Surgery and Anesthesiology & Critical Care (ACC). **Front Row,** Samuel Oduwole (ACC), Aliaksei Basatski (Adult Recon), Thomas Rose (Ortho Trauma), Kamlesh Rai (FOP), Kim Lacy (ACC), Beth Howard (Sports Medicine) and Helena Moses (Adult Recon). **Back Row,** Renee Jurek (FOP), Vilair Feristin (ACC), Vance Doyle (formally FOP), Brandon Eilberg (Ortho Trauma), Matt Isenberg (formerly, Hand). *Not pictured* are Denise Knox (Project Manager), Melissa Redkar (Adult Recon), and new to the team, Bradly Fesi (Foot & Ankle), Rupa Chowdary (ACC), and temp Christine Branton-McMillon (Adult Recon), Robert Burgese (FOP), Evan Bannister (Shoulder & Elbow), Andrew Diederich (Hand), Shayla Awolusi (Spine) and Annamarie Horan, MPA, PhD (Director).

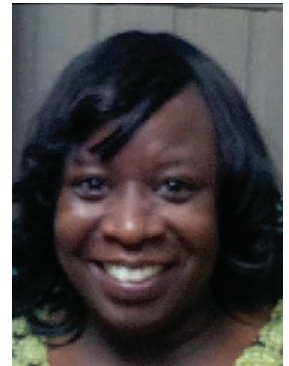
Drs. Kaplan and Al Mukaddam lead the FOP Division toward treatment interventions in FOP through the studies sponsored by Clementia Pharmaceuticals and in Q2-Q32018 will push forward the investigation of treatment options for this terrible disease by engaging with another sponsor, Regeneron Pharmaceuticals. As warranted, Dr. Kaplan will serve as the Global PI for the Regeneron study and with Dr. Al Mukaddam, should be commended for their unwavering commitment to not only new discovery, but to patient safety. The Regeneron study will also further strengthen our relationship with Anesthesiology & Critical Care by ensuring the highest possible on-site expertise at every patient treatment visit. Another special recognition goes out to Dr. Kuntz in Shoulder & Elbow for leading 3 new industry funded studies for his Division in the last year. Also breaking ground is Dr. Smith, who is leading the first industry study in Orthopaedic Spine Surgery (DePuy Vivigen) since at least 2008 with other studies in the wings.

The level of cooperation within Divisions and across service lines has been astounding and inspiring over the past 1 – 2 years and the rewards are evident as our successes continue to mount. We have multiple open studies that

involve institutional operational and scientific collaboration involving Penn Radiology, and Penn Anesthesiology, as well as other institutions such as The Childrens’ Hospital of Philadelphia, Medical University of South Carolina, Duke University, Vanderbilt University, McMaster University and Johns Hopkins University. These relationships may be study-specific or may be part of larger organizations such as the ROCK, MOON, or METRC consortia. The PCORI REGAIN study (PI: Mark Neuman, MD), an ongoing \$12M 40-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, Donegan, and Ahn) with faculty from Anesthesiology & Critical Care (Drs. Neuman, Elkassabany, and others) and is poised to meet its enrollment goal of 1600 evaluable subjects; 800 subjects have been enrolled at mid-study. In every Division, the rewards of the 4 Cs, collaboration, cooperation, congeniality, and compliance are evident from the Office of the Chair, to the faculty, our residents, and all the way through to our staff of CRCs, and most importantly to the patients we serve.

At this time, it is important to recognize the individuals who tirelessly execute the daily operations of the clinical research program. Our team has grown, changed, and will continue to increase over the next few months. Shown in Figure 2 are most of the friendly and hard-working individuals on whom we depend to screen participants for studies, conduct research visits, capture data, and to ensure regulatory compliance and human subjects protections in our large and comprehensive program. Those unfamiliar with the execution of clinical research, express amazement at the quantity and quality of work that goes into even the “simplest” protocol. In the exceedingly busy clinics and ORs of our surgeons, these tireless staff members daily review the requirements of each active study against dozens of patients to ensure proper enrollment engage the prospective subjects and then follow them through to study completion. Every study is unique and brings its own challenges, that range from placing and ensuring the execution of study specific radiology and/or pharmacy orders to coordinating complex patient travel



Denise Knox, BS
Supervisor, Clinical Research.



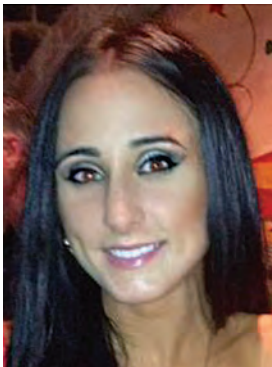
Dexin Li, BS, Database Administrator.



Team FOP, clockwise from L to R Lisa Gardo, BSN, Shannon Chester, BS, and Kamlesh Rai.



Kim Lacy, BSN and Rebekah Williams, BS and Marlon Schwarz, MD, Anesthesiology & Critical Care CRCs.



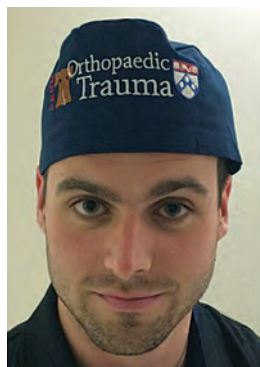
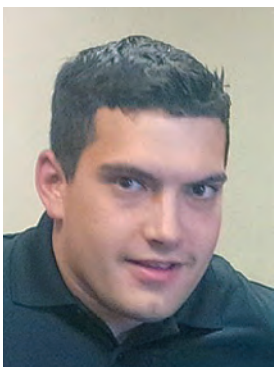
Kara Napolitano, BS Clinical Research Coordinator, Sports Medicine and Ava Marie Marcoon, CRC in training.



Kara Napolitano, BS serves Upper Extremity, Foot & Ankle, Oncology research.

schedules, resolving research billing issues, ensuring patient payments, diligently capturing and reporting adverse events, submitting all study activity for IRB and other committee review, and of course data capture. The work of our staff is routinely scrutinized by outside monitors and, to date, our team, with the cooperation of our faculty, continues to represent our Department(s) very well to outside parties, thus contributing to the likelihood of future site selections.

At this time, we heartily congratulate both Brandon Eilberg and Samuel Oduwole on their acceptance to Medical School (starting Fall of 2018).



Patrick Hesketh, BS and Evan Bannister, BS, aka OrthoTraumaTeamSix.

Additional congratulations go out to both Katherine Todor and Renee Jurek of the FOP team who have, at this writing passed the Clinical Research Coordinator Certification exam from the Association of Clinical Research Professionals and merit the designation of CCRC. This 3rd party certification validates the knowledge and commitment of these two individuals. Five others on our team are slated to sit for this exam in the spring of 2018. We also extend a loving welcome the newest member of the team, Murdock Hoagey-Howard (pictured but not visible in Fig. 2). We also wish to recognize other support staff throughout our institution without whom the proper conduct of clinical research would be nearly impossible. These individuals include but are not limited to the teams at the Institutional Review Board (IRB), the Office of Clinical Research (OCR), the Clinical Trials Contracting Unit (CTCU), the Center for Human Phenomic Science (CHPS), the Investigational Drug Service (IDS), the perioperative services teams, and countless Departmental clinical and other support staff.

Thank you to all the named staff above as well as the leadership of Penn Orthopaedics and Anesthesiology & Critical Care for their ongoing support of our team. Briefly, these include 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.



Annamarie Horan, PhD, Director of Clinical Research, Orthopaedic Surgery and Anesthesiology & Critical Care.

wish to recognize other



Samir Mehta, Chief, Division of Orthopaedic Trauma, Medical Director, Orthopaedic Clinical Research.