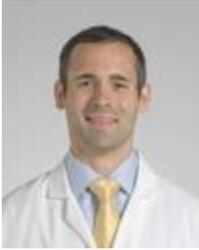


2013 Hatcher Fellowship Award Recipient
Summary
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The purpose of this letter is to provide an update regarding the progress made in my young oncology career because of the funds allotted to me by the MSTS Hatcher Fellowship opportunity. As you well recall, the “big picture” proposal that led to this opportunity was to open doors in collaboration between domestic and international institutions. I envisioned the September 2013 ISOLS meeting, with the purported theme of a “*Common Language for a New Century*,” as a stepping stone to beginning a relationship with an international institution in order to bring collaboration back to my institution. In time, I have hoped that efforts spent in cultivating relationships will then lead to not only questions being answered in a collaborative fashion, but also a future way of sharing data through secure registries in a manner meant to enhance power and dynamic application to oncology practice. With this collaborative approach, I set a personal goal to understand different approaches to database construction/collaboration, grant writing & funding opportunities, and multi-disciplinary prospective collection of data to help best determine the efficacy of treatments that become part of our practice. As a collateral benefit, I also found myself coming in contact with other institutions and orthopaedic oncologists that I had not intended to, allowing me to mold my plan as time went along, in order to enhance the future ramifications of this opportunity.

As an overall reflection, the goals that I set forth to achieve were accomplished in a manner that exceeded my expectations, with invaluable relationships founded and nurtured along the way. I can look back at my year of fellowship, beyond the technical training, to definitively voice that this year has proven foundational in terms of setting up mentors and colleagues in my life that will continue to mold how my practice and approach to academic oncology is focused.

ISOLS Meeting, September 2013 + AOA Traveling Fellows Visit to Nashville Spring 2014

I spent the week in Italy, with full expectations of coming away with a future appointed time to spend in Bologna following fellowship, but prior to starting clinical practice. As noted in my Hatcher proposal, I have been given the blessing by my home orthopaedic department to travel with the expectations of bringing ideas to a place in need of taking a “fresh” next step forward, concerning our approach to sarcoma care in Cleveland. After spending a week in Italy, speaking with multiple Rizzoli staff (including professor Ruggeri) I came to a realization regarding two points. First, this is a relationship that has been cultivated many times over around the world between multiple institutions and Rizzoli, making “freshness” a difficult thing to attain for my young practice. Second, the entire database is in Italian, which adds a degree of difficulty to attempted collaboration in the practice of a young oncologist. During a dinner in Italy, I had the opportunity to speak to one of the oncology fellows from Birmingham, England. This led to an introduction with Rob Grimer, who quickly became an individual that I felt I “must” get to know better. One of my passions that I have found during my fellowship year is the socioeconomic consequences of faulty care for sarcomas, especially soft tissue sarcomas (i.e. the ramifications of the incomplete excision). I have done work looking at medical malpractice and sarcoma, as well as a looking at separate questions pertaining to “why” we continue to have such a high incidence of incomplete excisions. My ultimate goal is to take the answers to questions we have raised as to why faulty practice patterns surrounding sarcoma care exist in the primary care and surgical communities, and apply this in an effort to reaching governing bodies for various medical

disciplines. Ginger [Holt] and I have already been asked to head up a symposium at the October 2014 ACS on soft tissue lumps and bumps, and we will be applying for the next round of meetings to perhaps do the same thing in a primary care meeting setting.

With that background, Rob Grimer and his group have worked on similar education attempts for soft tissue sarcoma, in a parallel fashion in the UK. With the power of a national database registry, collection of sarcoma care points of relevance is a mandatory part of the NHS mandate, making follow-up and entry into a database much more reliable. After setting up a visit to Birmingham in August/September 2013, I have aspirations of utilizing this database to help answer further questions regarding currently failing education attempts to reach the non-oncology community regarding sarcoma awareness. In addition to the research, I am also interested in observing a large, national tumor board and various techniques/implants that are utilized in the UK, but less popular currently in the USA (i.e. extracorporeal radiation-reimplantation, regular pelvic/sacrum navigation techniques for bone sarcoma resection, custom hemipelvic metallic reconstruction, silver implants, various growing implants, etc). I have also asked to spend time with the pathology team, in an effort to understand multi-disciplinary efforts in a large national sarcoma facility. After my discussions with Rob, I have set up a time to spend in the England, from August 18 to October 1, 2014 – and have since decided to forego my initial plan of visiting Rizzoli in the same extended fashion.

To add to this experience, the AOA Traveling Fellows spent 2 days in Nashville in the Spring 2014, and I had the opportunity to speak with 2 orthopaedic oncologists (Will Aston, Rob Ashford) from the London area. Will is a consultant surgeon in Stanmore (Eng), and is involved in the London Sarcoma Board, as well as entertaining a busy revision joints practice to supplement his oncology practice. After 2 days spent with him during his visit to Nashville, I have set up a 5 day visit to Stanmore in Mid-September, in order to spend time observing another high-volume sarcoma institution within the UK. We have chatted about similar collaborative aspirations that I have spoken to the Birmingham group about. I also am utilizing this visit to also spend time at the Stanmore implant headquarters, to familiarize myself with a recently FDA approved non-invasive growing implant option that seemingly has a pristine short to mid-term track record. Ultimately, the time spent in order to build familiarity with Mr. Aston (surgeons are referred to as “mister” in the United Kingdom) Will and his practice will lead to a lifelong relationship and open communication line that will only serve to benefit a young oncologist’s career.

Canada Trip June 2014

Mt Sinai (Toronto, ON) - I spent a couple days in Toronto, with a large portion of the time spent with the research staff. Anthony [Griffin] was an invaluable resource for me in understanding how a fluent research effort can be realized, slowly built over the course of many years. Beyond the actual endpoints that are collected in actual database, our conversation revolved around such concepts/questions of 1) What programs to use for data collection? 2) What avenues should I utilize to explore funding opportunities for research resources? 3) What concepts can I use to help motivate an orthopaedic department toward “buying in” to a supportive funding for staff and resources to allow for collaboration? 4) What is a realistic expectation for the utilized time of a dedicated part of full time research staff? and 5) How can I help tailor the job descriptions of the research personnel to keep my focus on clinical practice unadulterated by administrative paper trails, but also still keep those working with me motivated and happy with their efforts? I also specifically discussed how Cleveland can become a collaborative partner with Vanderbilt and Toronto for future follow-up questions. Toronto has become very keen toward collecting functional outcome data points with various validated forms (MSTS score, EQ-5D, TESS,

FACIT, etc). This was a new concept to me, and yet another topic of conversation for me to understand in terms of up-front future collection efforts in Cleveland, as part of our patient intake and follow-up data.

I did also spend time with Jay Wunder and Cara Cipriano (fellow) in the clinical aspect of the practice, getting yet another gauge for how a high-volume sarcoma practice center runs. Without a doubt, there are perceived differences and misconceptions that we can have in our minds of various centers prior to visiting an institution, and this portion of the visit helped enlighten my mind as to how the sarcoma care is approached in the nationalized Canadian system, and how resource utilization (and rationing) varies as compared to practice in the USA. I was able to sit in on the Mount Sinai tumor board, and see the mutli-disciplinary team at work in helping to formulate a plan for many difficult cases.

McMaster's University (Hamilton, ON) - I finished my Canadian trip in Hamilton, with Michelle Ghert, Mo Bhandari, and their wonderful research resident (Nathan Evaniew). This was perhaps the most impressive phase of my travels thus far, as I was blown away by the efforts that have been undertaken in order to get a randomized control trial in the orthopaedic oncology world off the ground. My main focus in visiting this institution was to familiarize myself with the question PARITY is asking (“What is the appropriate amount of time to prophylax a patient on antibiotics after a megaprosthesis reconstruction in the setting of an aggressive primary bone lesion?”), the process of how this question is being answered, and how can I make sure that my practice has the decision opportunity to be involved. The monumental undertaking that has been made to make PARITY a reality I am not sure is very well known. The sheer manpower cannot be understood without a behind the scenes look, and I even had the privilege of sitting down with the “think tank” team during their weekly coffee shop meeting to get progress updates on various participating sites, protocol updates, and various committee reports. I had some funding opportunity questions about research staff answered. I actually see Cleveland Clinic’s involvement in this study as a great opportunity to promote the “buy in” that I am seeking from my home department to aid the academic pursuit of sarcoma practice in Cleveland. To get a participating site “up and running,” many hours of paperwork and IRB/legal department discussion is needed, which cannot possibly be completed without the help of ancillary staff. IF an institution can believe in a vision and understand the work needed, startup funding and resource allocation can be made to help create the forward inertia needed. A highlight of the visit was meeting Mo Bhandari and sitting in his office. Realizing that PARITY is one of eight multi-national RCTs currently being run from the Methods Institute at McMaster’s is mind blowing. Understanding each of these trials in their basic conception, and whether or not an opportunity to have my colleagues converse with the people up here in Hamilton, was a focus of my conversation with Mo. Some people are gifted technicians, others gifted teachers, and yet others gifted scientists. Drs. Bhandari and Ghert are truly impossible to replicate, and were contagious in terms of their passion for science of forward thought in the orthopaedic profession.

In Addition To...

Ohio State – Along my travels, I have had the opportunity to multiple times converse with Joel Mayerson at the James Cancer Center. As he is an alumnus from Cleveland, I first engaged him during his visit as an invited visiting lecturer in the Spring 2013. My interest in building a relationship with those institutions in close proximity to Cleveland starts with Case Western, Akron, and Ohio State. I became fascinated at the “rags to riches” story that Mayerson/Scharschmidt have employed in moving Ohio State to the high volume center that it is today. In their partnership with the OSU Veterinary School, they have a working mouse model in order to excised sarcoma tissue and test multiple new chemotherapy agents against various models. I see this as an opportunity to build relationships with a close proximity regional

institution, and become a collaborator in a promising basic science opportunity, through the role of sarcoma sharing and interval update manuscript collaboration. This is yet another way to help raise the academic standards in Cleveland for sarcoma care, but more importantly, a way to build groundwork for a form of a “Midwest Sarcoma Consortium.” It is a dream, but the opportunities if you take the time to converse, listen, and offer yourself are there. This visit was completed on August 11-12, and was very productive from a conversation standpoint. I found Joel and Tom to be very open to discussion, inviting, and full of advice. More so, despite our close proximity to one another, where there is always the possibility that potential “competition” can also ensnare one’s mind into believing that, I walked away feeling that I had a team of allies located 2 hours south of Cleveland, knowing that a partnership regarding research, second opinion visits, and constructive dialogue was a true reality with the OSU guys!

Current State of Affairs...

Royal Orthopaedic Hospital, Birmingham (England) – I am currently in week 3 of a 6 week time in England. The vast majority of the time is being spent in Birmingham, following the guys that have created one of the highest volume sarcoma practices in the world. Rob [Grimer], Lee [Jeys], Simon [Carter] and Roger [Tillman] have been fantastic to this point. I have spent a limited amount of time in the clinic with them, watching carefully the dialogue and diagnostic process that is had with each patient. Watching a multi-disciplinary effort has been realized with the Tuesday morning multi-disciplinary clinics, in which 30-40 cases are discussed in the course of 3-4 hours. I have been able to participate in the national Ewing’s Sarcoma MDT with practitioners from all of the UK, as well as chat with the multi-disciplinary partners here at ROHB. Observation in the OR has afforded me a new outlook on the endless possibilities for reconstruction techniques, as well as evidence-based discussions on treatment rationale and evolving practice patterns. Navigation in the pelvis has been shown to me in a new light with Lee Jeys, as I have already seen multiple patients in clinic turn up with tremendous results at long term follow-up. On the flip side, I have also see follow-up visits “when things go wrong,” and have walked away with new insight into “back up” planning ideas. The most important part for my participation out here has been the potential to continue on a collaborative relationship with the institutions back home. I have had many delightful discussions with Mr. Grimer regarding research efforts and mutual interests. We have settled on a few projects for which data collections and IRB approvals are underway, including studies to delineate outcomes for intercalary humerus reconstructions, understand the effect of delayed presentation in bone sarcoma patients (mirroring a similar paper that has been done by the Birmingham group in 2006 on Soft Tissue Sarcoma), and looking at the prognostic value of soft tissue carcinoma metastases. Mr. Grimer has been unbelievable in terms of his open attitude and encouragement, and has been helpful in making sure that there projects can make it off the ground, and come to fruition in the next year. I am working like mad to get the data cleaned up from the ROHB, with plans to then go back home and begin working on that data cleanup process, with eventual statistics and conclusions to follow. I hope that work with sarcoma education can become a paralleled front in the US and the UK, with the power of a great thinker like Rob Grimer being able to hone my mind to ask insightful questions – and answering these questions with a compilation of data that has been meticulously documented so as to provide truthful insight as to how our field must change in the future.

The McMinn Centre, Birmingham (England) – I did have the opportunity to stop for 2 days at Edgbaston Hospital with Derek McMinn, perhaps most well-known for his tireless energy in helping to revive the hip resurfacing procedure, and finally finding a heritage of success with the Birmingham Hip Replacement (BHR). I have sat down with the engineers, tribologists, lead administrators, and finally, the surgeon. The abundance of robust science behind the BHR is truly a testament to the scientific process and what can be accomplished with a good question, a

solid plan, and a dedicated team. Despite the lack of popularity in resurfacing since 2008, Mr. McMinn has held unwaveringly to his convictions of the BHR, with 17 year data showing rather impressive results in national registries. Spending time with him in the OR was a treat, a well, as I was able to chat with him about future directions and past mistakes while watching him operate. As a tumor surgeon, this trip still provided multiple merits for my own practice, highlighting to me the endless possibilities of the surgeon-scientist. Though this was a side-trip for my England stay, it was unforgettable in its own right!

Stanmore (England) – I will be spending 1 week in the outskirts of London next week, seeing yet another of England's 5 centralized bone sarcoma centers. I look forward to seeing another working part in the National Health System (NHS), and building relationships with a second high profile international sarcoma institution.

Is Collaboration Possible?

In short, yes. But it takes work. And it takes a willingness to make yourself, both as an individual and an institution, vulnerable. Collaboration is not where it needs to be, with many series in the oncology literature being either from a single institution or harnessing minimal numbers (20, 30, or 50 patients). In a way, the United Kingdom sarcoma centers have some collaboration intuitive just by the nature of the socialized health system. But even these numbers, collected by the government, cannot tell the whole story. Studies that are completed within a single institution have, in theory, limited applicability. Can we really apply lessons learned from treatment in Canada, Australia, England, or India to change treatment in the United States? If so, can we apply it only in certain situations? Why do we care about silver implants, growing prostheses, or extracorporeal radiation in the United States, where the suffocating effect of the medical malpractice system and the FDA help make seemingly great technology advancement and/or resourcefulness occurring in other parts of the world insignificant to us at the moment? Or

The biggest obstacle to collaboration is ourselves. The Europeans are much better at it that we are in the US, at first glance. Currently, the VORTEX trial, (a RCT headed up by Rob Grimer looking into the downstream effects of reduced-dose XRT in the setting of a post-op sarcoma resection) is a great example of multiple institutions working together across the pond to determine if radiation dose can be safely decreased with regards to LR. While the approval process through the IRB and legal teams can be difficult at times in the US, it is a willingness in our own ranks to tackle such obstacles and come together. I do see our current collaborative attitude as being on the upswing. I have seen a growing message from the younger oncologists in the MSTS, with guys like Ben Miller and Lee Leddy, who have made a point of emphasis being collaborative research. MORI was formed for such a purpose. The problem is, however, that we are all young, recently having finished our practices in the past 5-7 years. We have limited numbers and no historical database. But we have questions – sometimes good, sometimes repetitive, and sometimes insignificant. But we are trying to stay stimulated, and improve upon the culture of single institution large database collection with large historical numbers stemming from a single institution's experience. Large collaborative projects do exist in our oncology community, but are uncommon. The medical oncology community is perhaps the pinnacle of the medical world with the amount of multi-center, international trials that are conducted with chemotherapy agents (EURAMOS, EICESS, etc) and trial regimens – each focused on answering an important question that will impact medicine in the years to come. The Sports medicine community (METEOR, MOON, etc) is similar with the study groups that have become commonplace in advancing the understanding of arthritis and injury, deciphering out effective treatments. Dr. Ghert and her team should be applauded for the work that they have done to move forward with PARITY, and I see this as an important opportunity to be part of a movement that can lead to something more. It's hard in a surgical field to come up with similar, and more

importantly, feasible ideas as some of our colleagues in the medical profession. And it all doesn't happen at once. How can I start now, in a small way, to slowly build a practice founded on answering questions to drive clinical practice. For me, personally, another obstacle is the internal pull that is within each of us to remain faithful to our families, while also putting in the extra time needed in a young career to build a springboard for the future. Time can be better managed with funding – both to fund a research team and to fund project participation. Funding, however, is not easy to come by. And I understand I must step out of my own comfort zone and participate in the writing grants, applying for scholarships, and networking with established individuals – both clinicians and philanthropists. A third obstacle is language, and one with which I do not have a great answer for how to address. The Rizzoli database is largely collected in Italian, and I am sure others are in the native language of their own country, such as Argentina, China, or Europe. Language clearly has not been a hindrance up until this point, as relationships between Moffitt and Rizzoli or China have recently produced manuscripts with good collaborative partnership.

How can collaboration in my own practice become a reality – what conversations do I keep impressing upon myself? First, continue the communication lines that I have worked so hard to forge this year. Relationships take time. Trust is not built overnight. Partnerships rarely find a solid foundation in a fleeting moment. It takes work. But it's fruitful work. Staying committed to building a database, applying for funding to support a team to help maintain and collect into the database, and tweaking the database for future data collection to answer important questions down the road is important. Be persistent with your message, and approach multiple colleagues when you have an idea. Keeping it to yourself because of fear of having someone pirate it is not ideal, and hopefully with built trust over time comes a professional respect. Once an idea is set, start moving forward with setting the ground work. Data collection can occur in parallel with other institutions – and with the climate of HIPPA – it is mandated that data not cross over. But once data is collected and numerically coded for statistical purposes, it can be shared – and should be. But it takes a team where every member is dedicated to the idea, where work is appropriately shared, and timelines are held steadfast to in order to move the process forward. Database creation comes with its share obstacles. Setting aside the discussion on the sheer time needed to setup a vessel for collection, oftentimes I have found in my travels that even the most robust of databases have a large amount of missing data that must be identified and sought out. If routine collection occurs without a specific purpose, data can be neglected.. But prospective collection that is being motivated by a current clinical question can help improve upon this – as data all of a sudden become relevant to your current practice rather than a discrete method of “hoarding.” The problem with prospective studies currently, especially with regards to sarcoma, is that data can take years to collect in order to gain substantial numbers. If a question can be asked and multiple institutions involved, however, then prospective analysis can be done simply due to more efficient collection of numbers. Power is increased, and conclusions are more solidified. I will also note that I feel international collaboration is actually easier than collaboration within our own borders, as the IRB-equivalent process to gain approval for a study in many countries is not nearly as stringent. Lawyers aren't involved and endless paperwork is not required when another institution is involved. An explanation is made and the proper precautions are trumpeted. And then the research moves forward. Interestingly, information is still held sacred, and privacy upheld above all else. So why is the process so much different (and painful) in the US? I wish I knew.

A brief word about the database possibilities...Ease of database sharing can be done over the Internet, as there are multiple encrypted vessels that allow such. It's hard for me to imagine an easier venue for collaboration than such an idea. Some Internet-based collection vessels, such as REDCap have allowed tens of thousands of projects to be completed in a collaborative fashion. I started my Hatcher process discussing this opportunity, and still hold fast to my belief that

REDCap is a perfect opportunity in my own practice to help realize my goals. I have already begun moving forward to make Cleveland Clinic's orthopedic oncology program part of this well-recognized database registry. I have already made mention of Ben Miller's work in helping to start a young investigator's group, as well as secure funding for the same line of enthusiasm with database registry building. Over time, hopefully the voices that echo the same sentiments will become more influential, helping to instill a similar vision in all generations of our profession. The downsides can be real, many at the sacrifice of your personal time. It's hard even getting your partner's to understand that the added time committed to keeping up their portion of the practice in the database is well worth it. But again, perseverance can be contagious. If other institutions would begin collecting their data in the same manner, then collaboration becomes more efficient. Again – when the right question is asked, a project can be formulated and data combined with the click of a button. Online registries turn into spreadsheets. As a young surgeon, I must rely on colleagues to help me answer the questions that I hope to ascertain, while at the same time be enthusiastic to help partner to help others answer their own questions.

In Summary

The opportunity afforded to me by the Hatcher Fund is one that I likely would not have had without the funding awarded. I think it is important for the committee to know that this has been an invaluable year for sowing seeds, hoping that in years to come the harvest may start to yield crops. The tumor world is such a small world, and I am consistently puzzled by the small-ish series that we continue to base our practices off of. I spoke highly of the resource “REDCap” as a database collection tool in my proposal, as this is a powerful, Internet-based, secure collection device that has allowed >700 large-scale, multi-institutional studies around the world to be completed. The new MORI organization, started by Ben Miller, Lee Leddy, and other young oncologists is a promising attempt to get the young generations focused on collaboration. Ben and Lee have plans to utilize REDCap (thru my conversation with Lee at the recent AOA meeting) eventually for data collection, currently getting institutions collecting in a parallel fashion. Once institutions are able to “Cross-over” and being sharing data, collaborative questions that can be answered with proper technique and cooperation can offer a much more dramatic insight in how practice management should change based off past results. I have had a “snapshot” look into a few institutions. The knowledge and insight gained has been (and will be) invaluable.

At some future interval time, the discussion of setting up a collaborative “fellow share” program (between MSTs fellowship institutions) for a short period of time (3-4 institution visits) should be discussed. A fellow that can be given the opportunity to do what I have been fortunate enough to experience is one whom will be much more aware of the opportunities out there, and one that can build their personal and institutional practice based off successes and lessons learned from prior setbacks of others. In a world of funding shortages in USA healthcare, evidence-based practice is becoming more important toward building discussions surrounding needed change. In my microcosm practice, this trip has allowed me to supply the arguments to my department to institute such change, in small step-wise progressions, so that sarcoma care in Northeast Ohio can improve for the better.

Thank you very much for this opportunity.

Regards,

Nate Mesko