EXPERIENCES IN CONTINUING INNOVATIVE BIOMEDICAL RESEARCH AMIDST THE COVID-19 PANDEMIC

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Abstract
The COVID-19 pandemic has brought unprecedented challenges for the world in every field. The academic sector has faced new challenges during this pandemic and the response of researchers, administrative workers and the student body has been remarkable, allowing education to remain an unstoppable journey and universities to continue as the birthplace of innovative science. At the University of Oklahoma, research and education have remained active by establishing strict, detailed protocols that aim to keep researchers and students safe while maintaining the academic momentum. In this paper, we present our experience at the Biomechanics and Biomaterials Design Laboratory (BBDL) under the ongoing COVID-19 pandemic. In our research group, productivity and student mentoring remained strong and eager despite university shutdowns and local regulations. By establishing in-lab protocols regulations to control the spread of the virus and by promoting contactless communications and scientific discussion, the BBDL has been able to continue to execute research projects in cardiovascular biomechanics, aneurysm therapeutic device design, and vascular tissue engineering. From literature reviews to virtual conference presentations, journal publications and biomedical device development, the BBDL has been able to produce research results and promote undergraduate professional development during these difficult times. In hopes of promoting a collaborative environment both locally and internationally, we present the lessons we have learned during the COVID-19 outbreak, outcomes of our experience and the current and future challenges for research and education.

Keywords*:*
Research experiences, virtual education,

Introduction

On January 30th, 2020, the World Health Organization (WHO) announced that the recently discovered SARS-CoV-2 virus had spread throughout China and other countries and declared a state of emergency, where international public health was deemed at risk due to the fast spreading of the virus (WHO, 2020). This declaration caused border closures worldwide, travel restrictions and the imposition of preventive health measures such as social distancing, constant handwashing, and the use of facemasks in all public spaces. A few days before the pandemic declaration, the first case of a patient in the United States being diagnosed with the infection of the virus was found in Washington State (Harcourt et al., 2020), with the first case of local transmission following shortly thereafter on February 26th, 2020 in California. Focusing more specifically on the state of Oklahoma, the first confirmed COVID-

19 positive case was reported on March 7th, 2020, in the city of Tulsa (Kemp, 2020), with several other counties reporting their first cases in the following days.

On March 15th, 2020, a letter from the president of the University of Oklahoma (OU) to the community confirmed the first COVID-19 case on OU's campus. This led to an initial 5-day lockdown for all OU community members and the creation of strict guidelines to transition into virtual teaching, telecommuting and telecounseling. Then, a second on-campus case of COVID-19 was reported then on March 20th, which made all temporal changes in university operations to continue indefinitely.

In the search of the safest way to maintain the productivity of the university, telecommuting became the best strategy for University employees, students, and researchers. However, certain activities were deemed as essential, where only a few employees were allowed into campus. Activities related to the overall maintenance of the university infrastructure and specific cases of research (i.e. care of living organisms, long-term studies, care of equipment, COVID-19-response research) were maintained during this period, and all other non-essential research tasks were ramped down and eventually stopped. Academically, the university allowed students to decide whether to have their classes approved using traditional numerical and letter grading or a pass/no-pass option to account for difficulties in learning during these difficult times.

These changes had a significant impact in the research environment at OU. Most research activities were considered non-essential, and the safety of research students and faculty was at risk, if precautions were not taken. Resiliency was a key factor for success during this period at research laboratories. Particularly, at the Biomechanics and Biomaterials Design Laboratory (BBDL), all experimental research was ramped down and, eventually, stopped. The BBDL is a laboratory at the Aerospace & Mechanical Engineering Department under the direction of Dr. Chung-Hao Lee, who is also affiliated faculty of the Institute for Biomedical Engineering Science and Technology. Our multidisciplinary laboratory focuses in several research topics, such as, heart biomechanics studies (Jett et al., 2018; Kramer et al., 2019; Laurence et al., 2019; Ross et al., 2019), biomaterial design for brain aneurysm therapeutics (Kunkel et al., 2018; J. Wang et al., 2019; Jingyu Wang et al., 2019) and cardiovascular tissue engineering. Our research is, by nature, experimentally based, where in-person operation of biomaterial testing devices, biomaterial synthesis and testing, and laboratory management activities is essential for our research productivity. In addition, the BBDL is also a laboratory that fosters undergraduate research and formation of independent researchers. This endeavor faced significant challenges during the university shutdown, and we believe that our learnings from this situation can be of great value to the academic community worldwide.

Here, we want to present our experience facing the challenges that the COVID-19 pandemic brought to the BBDL, our strategies to cope with this unique situation and the future perspectives for our work and mentoring processes.

Research strategies during the Pandemic

When COVID-19 positive cases were detected at the University of Oklahoma, all in-person academic and research activities were suspended. The transition to remote research strategies began with a 5-day lockdown of all university campuses, which forced the BBDL to suspend experimental activities temporarily and shift towards telecommuting. However, the detection of more positive cases on campus in less than a week, forced a ramp-down of non-essential research activity indefinitely.

At the BBDL, this ramping down included the storage of biological tissues, shutting down non-essential equipment and preparation for remote access to our computational resources, as well as preparation of new methods for remote teaching in the field of biomechanics (Lee et al., 2020). The post-graduate students at our lab focused on data processing, analysis, and manuscript preparation during the first week of lock down. However, the indefinite shut down of campus activity and local regulations that mandated shelter-in-place forced us to start research activities that did not required the use of physical resources.

In the field of biomechanics, understanding the mechanical characteristics of biological tissues, such as heart valves, blood vessels and associated tissues, starts by the collection of experimental data. Our extensive characterization of different heart valves allowed the use of this data for the development of finite element analysis (FEA) models. This modeling stage of the project utilizes computational resources only, once data is acquired, which allowed that students involved in this discipline to continue their research endeavors. For others, experimental data that had been collected in the previous months to the pandemic, allowed for the preparation of manuscripts, which includes data visualization and scientific writing.

This initial approach was valid during the first weeks of the OU campus shutdown. However, plans for further progress had to be designed to provide our post-graduate and undergraduate students the chance to maintain progress on their scientific projects, while developing their professional skills. With this in mind, we developed a multidisciplinary team of post-graduate and undergraduate students that expressed their interests on different new fields of research for the BBDL. Each team developed new strategies for literature review, a fundamental process in scientific production.

Literature review projects consist of a series of activities that aim at providing scientific background on a field to the researchers involved and creating new research questions. Our teams utilized different scientific search engines to find, collect and summarize scientific papers in the field of tricuspid valve biomechanics, clinical research for tricuspid valve regurgitation treatment and tissue engineering of heart valves. Approximately 400 research papers were summarized by our team and this led to the drafting of two review papers that are currently being developed by our team.

This project was only possible thanks to the use of online tools that allowed communication and organization of the research teams. At OU, Canvas (a product of Instructure) is used as an online educational tool that, traditionally, was intended to publish class material, assignments and manage grading. In our lab, Canvas was used to design a BBDL Literature Review page that allowed to: (i) distribute review teams, (ii) schedule deliverables, (iii) send announcements related to lab management and (iv) create spaces to share leisure activities during isolation, with the purpose of maintaining a socially active community of co-workers. In addition to this project, post-graduate students also developed research proposals for fellowship applications and were the team leaders of each literature review group.

Re-start of in-person research

After almost two months of telecommuting, the university launched a pilot program to plan a phased return to normal operations in May 2020. To this end, the Vice President of Research & Partnerships developed a Phase 1 framework that aimed to restart non-essential work and field-based creative activity on campus. This framework included biosafety measures that included contact tracing, social distancing and COVID-19 testing for all individuals returning to campus. The laboratories that voluntarily wanted to participate on this pilot were required to design a Conduct of Operations Plan (COP), a document where the locations, individuals and nature of research had to be described, in addition to the lab-specific measures that would be implemented to preserve the health of researchers and slow the spread of COVID-19. Our COP aimed at the restart of activities at both of our research spaces, as well as collaborative offices, while ensuring that the lowest number of researchers shared spaces at a given time. Four projects were given priority under our COP:

1. Development of a biaxial bioreactor to study heart valve biomechanics and tissue engineering.
2. Development of an electrospinning device for synthesis of biomaterials for tissue engineering.
3. Biomechanical characterizations of porcine heart valve tissues.
4. Construction of a system to visualize flow patterns of intracranial aneurysm phantoms.

These projects were led by post-graduate students (both master's and doctoral students) who underwent COVID-19 testing prior to returning to campus. To ensure proper social tracking and biosafety, a Research Log and calendar was designed. Authorized researchers would only be able to perform research activities on campus after booking research hours to ensure that only one person visited each lab space at one time. After this, researchers were required to send a Research Log file to the principal investigator (PI), Dr. Chung-Hao Lee, reporting their body temperature (measured with IR thermometers), performed activities, social contacts and biosafety measures (i.e. use of personal protective equipment, cleaning surfaces, handwash, etc.). Non-compliance to these measures was cause of suspension of research activities for the individual.

Consequent Phases II and III included the return of more research laboratories and the use of offices and common spaces in the university. The use of face masks was mandated across campus and plans for the Fall semester were designed. In-person lectures were limited to a 40-person capacity and were scheduled with 30-minute gaps between lecture sessions. All other courses were moved online. In addition, undergraduate researchers were allowed to come back on campus, which created difficulties due to more frequent social contacts.

With the COVID-19 pandemic, the start of a new academic year implied a significant increase in population in Norman, due to its nature of a college town (Almond, 2020). The high influx of new students endangered all

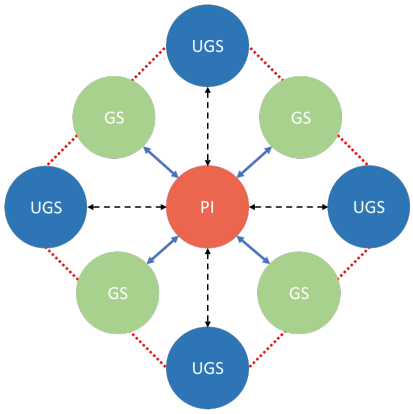
measures that had aimed at slowing the spread of the virus. As expected, the number of positive cases in Norman increased two weeks after move-in day, which called to action. Constant monitoring of undergraduate students, specially of those unexperienced, allowed to maintain the health of our research team and, ultimately, keep our goals in track for success.

Research Outcomes

Despite the difficulties, the BBDL was able to maintain research productivity. During this period of shutdown and consequent phased return to activities, the BBDL research team was active in scientific paper writing, publication, device design and construction, drafting of fellowship and grant proposals, among others. Table 1 summarizes some of our work during the COVID-19 pandemic.

Remote Formation of Undergraduate Researchers

The BBDL is compromised to the formation of researchers and development professional skills of its members. To do so, an organizational scheme has been designed to provide efficient mentoring to undergraduate students. During these difficult times, the mentoring of undergraduate researchers of all levels was limited to virtual meetings, creating the need for solutions to promote effective communication between mentor and mentees. To this end, the BBDL established roles for post-graduate students as "co-mentors" so they can assist the role of the principal mentor of the BBDL, Dr. Chung-Hao Lee. Each co-mentor, working in a separate field of the lab, assisted the development of technical, communicational and professional skills of undergraduate students. However, while our lab is a multidisciplinary team, our projects are of interest to all members, indicating that communication between co-mentors, co-mentees and PI was necessary. This model allowed us to provide feedback from different scientific and professional perspectives to the undergraduate student, ensuring optimal research and educational experiences. Scheme 1 shows a diagram that exemplifies the communication structure of our team. Periodic individual meetings between the PI and post-graduate students have allowed for the discussion of lab management issues, while meetings that include the co-mentees have allowed them to communicate their experiences and concerns.



Scheme 1. Communication diagram between principal investigator (PI), post-graduate students (GS) as co-mentors and undergraduate students as co-mentees (UGS). Dashed and dotted lines represent periodic communication and solid lines represent constant communication.

Table 1. Research outcomes at the BBDL during COVID-19 pandemic.

Research Outcome		Description
Type	**Item**	
Research Papers (Published)	Quantification of load-dependent changes in the collagen fiber architecture for strut chordae tendineae-leaflet insertion of porcine atrioventricular heart valves	Biomechanics studies
	A pilot in-silico modeling-based study of the pathological effects on the biomechanical function of tricuspid valves	

	Load-dependent collagen fiber architecture data of representative bovine tendon and mitral valve anterior leaflet tissues as quantified by an integrated opto-mechanical system.	
	Mechanics and microstructure of the atrioventricular heart valve chordae tendineae: A review	Review paper
	Thermomechanical data of polyurethane shape memory polymer: Considering varying compositions	Shape memory polymer for brain therapeutics study
	Enhancement of stay-at-home learning for the biomechanics laboratory course during COVID-19 pandemic	Development of remote teaching strategies
Research Papers (Submitted)	A pilot study on biaxial mechanical, collagen microstructural, and morphological characterizations of a resected human intracranial aneurysm tissue.	Biomechanics case study
	Manifold learning-based data-driven modeling for soft biological tissues.	Computational biomechanics study
Device Development	Biaxial bioreactor to study heart biomechanics	Device that will be perform biomechanics studies with viable tissue to incorporate growth and remodeling of extracellular matrix.
	Electrospinning device for synthesis of biomaterials for vascular tissue engineering.	Device for nanofiber biomaterial synthesis for vascular tissue regeneration.
Ongoing projects	Vascular Tissue Engineering: design considerations and the role of smooth muscle phenotype modulation.	Review paper in tissue engineering.
	Polyurethane shape memory polymer with carbon nanotube embedding as a potential endovascular device for brain aneurysm therapeutics: design and characterization.	Shape memory polymer for brain therapeutics study.
	Computational investigations of shape memory polymer-based intracranial aneurysm treatment device.	Computational studies.
	Parameter evaluation and design of a steady and pulsatile flow in an *in vitro* aneurysm flow loop system.	Brain aneurysm studies.
Participation in Scientific Conferences	Summer Biomechanics, Bioengineering and Biotransport Conference (June 2020 – Virtual)	Poster (3) and Oral Presentations (1)
	Biomedical Engineering Society Annual Meeting (October 2020 – Virtual)	Posters (2) and Oral Presentations (2)
	International Mechanical Engineering Congress & Exposition (November 2020 – Virtual)	Peer-reviewed paper

Challenges and Future Perspectives

With the beginning of the Fall semester at OU, in-person activities have resumed, although restrictions are still in place. However, the effects of confinement, isolation and the stress of a world pandemic are impossible to ignore. The COVID-19 pandemic forced the worldwide community to self-isolate to prevent the spread of the virus. While necessary, a quarantine can take a significant toll on mental health, due to isolation and loneliness (Hwang et al., 2020). In addition, emotional distress caused by the social disorder and instability add to the sense of isolation, creating significant challenges for mental health management during the COVID-19 outbreak, as it is anticipated that anxiety and depression incidence will increase during this period (Cullen et al., 2020). Several studies around the world, demonstrated a significant increase in mental distress in the population that was subjected to isolation

(Czeisler et al., 2020; Mazza, 2020; Wang et al., 2020) and it is notable that student status (Wang et al., 2020) and healthcare workers (Babore et al., 2020) were strongly associated with psychological deterioration. While knowledge of the effect of confinement on post-graduate and undergraduate students that perform research is still limited, it is important that strategies are designed to promote healthy habits that aid in maintaining psychological stability of the student body, staff and faculty.

At the BBDL, strategies like shared spaces to discuss non-academic activities were designed. With the use of our Canvas BBDL page, we created discussion forums where students shared their leisure activities and new skills. Also, scientific meetings had breaks that allowed students to stay socially active and share their experiences during confinement.

In addition to mental health, further spreading of COVID-19 is a daunting issue that can cause further interruptions of academic processes. Projections for spreading of the virus predict cyclic flare-ups, where the period of peaking depends on the still-undetermined immunity post-infection and the existence of a vaccine in 2021 (Scudellari, 2020). Therefore, it is important that the use of personal protective equipment and social distancing is maintained until an effective vaccine is developed and deployed worldwide.

Conclusions

Here, we presented the development of the COVID-19 pandemic at the BBDL of the University of Oklahoma (Norman, Oklahoma, USA). Distinct measures were established both regionally and on-campus, which aided to maintain the overall safety of the student body, faculty, and staff. Also, the strategies that the BBDL established to maintain scientific and academic productivity were described, and research outcomes were listed. While we consider that these strategies allowed to keep or students on track towards accomplishing their academic goals, we also want to emphasize the importance of promoting habits to manage isolation-related stress and anxiety. Overall, we consider that our laboratory demonstrated the resilient capacity of students to excel even in the most difficult conditions. Our laboratory is compromised to maintain its goal of developing the scientific and professional skills of our students and we expect that sharing our learning experiences under these circumstances will help other creative and academic spaces with their goals.

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