Project Report

A Novel Planning Paradigm for Augmentation of Osteoporotic Femora

Group 9
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Mentors: Dr. Mehran Armand, Dr. Ryan Murphy

Contents

Introduction

The one-year mortality rate after osteoporotic hip fracture in elderly is 23% [1]. Current preventive measures commonly do not have a short-term (less than one year) effect. Moreover, the risk of a second hip fracture increases 6-10 times in elderly with osteoporosis [2]. Osteoporotic hip augmentation (femoroplasty) is a possible preventive approach for patients at the highest risk of fracture and who cannot tolerate other treatment modalities. Recent computational work and cadaveric studies have shown that osteoporotic hip augmentation with Polymethylmethacrylate (PMMA) can significantly improve yield load and fracture energy [3]. However, higher volumes of PMMA injection may introduce the risk of thermal necrosis. In this project, we validate a modified planning approach to lower the injection volume as compared to the previous work [3]. This will likely reduce the risk of thermal necrosis caused by exothermic polymerization of PMMA.

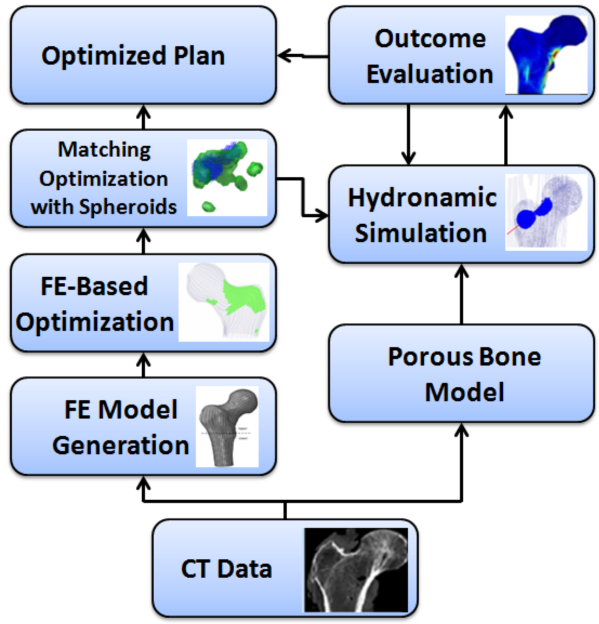


Figure 1 Preoperative Planning architecture

The modified planning paradigm involves three steps: 1) finite element (FE) optimization of the PMMA distribution, 2) geometric optimization for approximating the FE-optimized model geometry with spheroids, and 3) hydrodynamic simulation to predict the resulting PMMA distribution in the bone (Fig. 1). FE models of the femora were created using CT scans obtained from the specimens following the procedure described earlier in [4]. The boundary conditions simulated a fall to the side. For the first step of planning, three injection patterns were optimized utilizing the Bi-directional Evolutionary Optimization (BESO) method [5].

The surgical execution and tracking system has been described in detail in [3]. Briefly, we remove the soft tissue from the femora that has been selected for augmentation. We then attach a tracking rigid body with reflective markers (NDI, Waterloo, ON, Canada) to the femur. We then utilize an in-house navigation system [6] to register the bone to its CT volume. For this purpose, we first identify three landmarks on the femur utilizing a tracking digitizer and perform a rigid transformation from the camera coordinates to the CT. We then digitize several surface points and perform a point cloud-to surface registration utilizing the iterative closest point (ICP) method. In this setup, we use a hand drill (DeWalt Inc., Baltimore, MD) with a custom attachment for a tracking rigid body to drill the desired injection path (Fig.2).

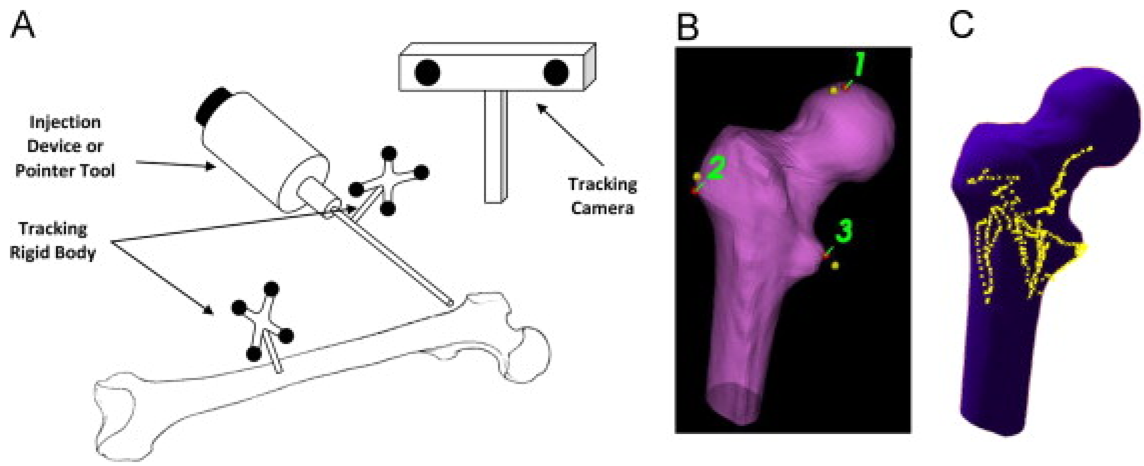


Figure 2 A) Injection setup B) Initial registration C) ICP Registration and surface points [3]

Project Goal

A modified planning paradigm has been created to reduce the injection volume for osteoporotic bone augmentation. The goal of this project is to validate this new planning approach through cadaveric experiments. In addition, we aim to create and validate a COMSOL Finite Element (FE) model to estimate the bone temperature after cement injection and compare the simulation temperature results with experimental data in three key locations. Finally, we intend to introduce a methodology "Conductive cooling experiment via a metallic K-wire attached to ice-water bath" to reduce the cement's curing temperature inside the bone.

Technical Approach

1) New Planning Paradigm for Osteoporotic Bone Augmentation

For the first part of our project, we obtained 4 pairs of osteoporotic femora from the Maryland State Anatomy Board. We then took computed tomography (CT) scan of each pair and keep them frozen at -20°C. We selected one femur from each pair randomly for augmentation and planned the injection per the architecture described above. One day prior to testing, we asked Bayview technician to take out femora out of the freezer and left at the room temperature (25 °C).

The injection experiment can be divided into four main steps: 3 points initial and ICP registration, drill pivot and rotation calibration, drill navigation and cement injection. For each experiment, after we registered the bone to its CT, we performed pivot and rotation calibration to guide the drill to the desired points of the injection with the aid of the camera and real time navigation. Then, we performed the cement injection using an automatic injection device from target point retracting all the way to the entry point.

After execution of the injection plans, we performed a mechanical testing simulating a fall to the side on the greater trochanter. The parameters we used for mechanical testing is 25 mm total displacement of the rate of 100 mm/s.

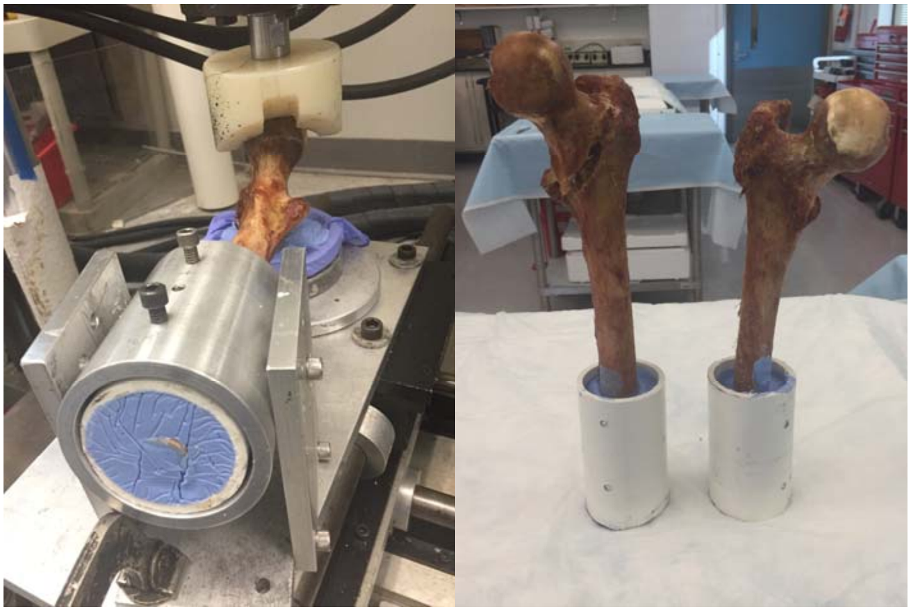


Figure 3 Mechanical Testing Setup Simulating a Fall to the side on the greater trochanter(left), The usual fracture Pattern (right)

Effectiveness of the augmentation was assessed by performing paired t-tests on the mean differences in the fracture load and fracture energy between control and augmentation sets.

2) Temperature Evaluation of the Bone Cement Injection

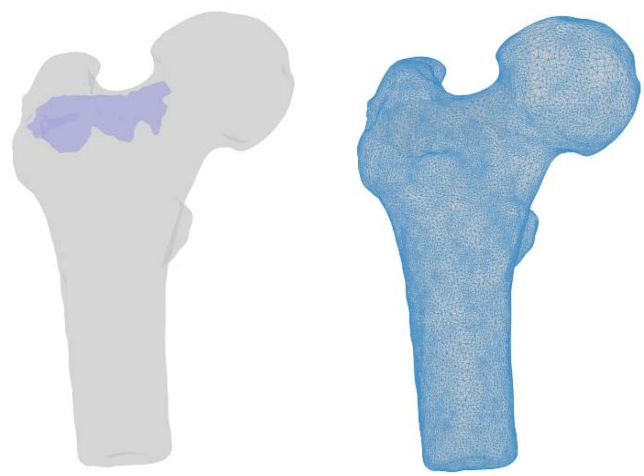


Figure 4 Finite element model of the bone-cement-interface

In the second part of this project, we created a COMSOL heat transfer model capable of bone temperature estimation prior to augmentation. We assumed a homogenous material property inside the bone and a uniform heat flow from the bone-cement-interface towards the bone surface (Fig 4) .We validated the model by direct temperature measurements of the bone surface during the cadaveric studies described above. For this purpose, K-type thermocouples were attached to the bone surface at three key locations (Trochanteric crest, Neck and Introchanteric Line) and compared to the temperature profiles of finite element model.

3) Bone Augmentation cooling system

In the third part of this project, we introduced and validated a methodology to reduce the PMMA's curing temperature after cement injection. For this purpose, we conducted controlled sawbone experiments with a k-wire via conductive heat transfer. The metallic k-wire was attached to an Ice-water bath and inserted through the injected cement to lower the curing temperature (Fig. 5).

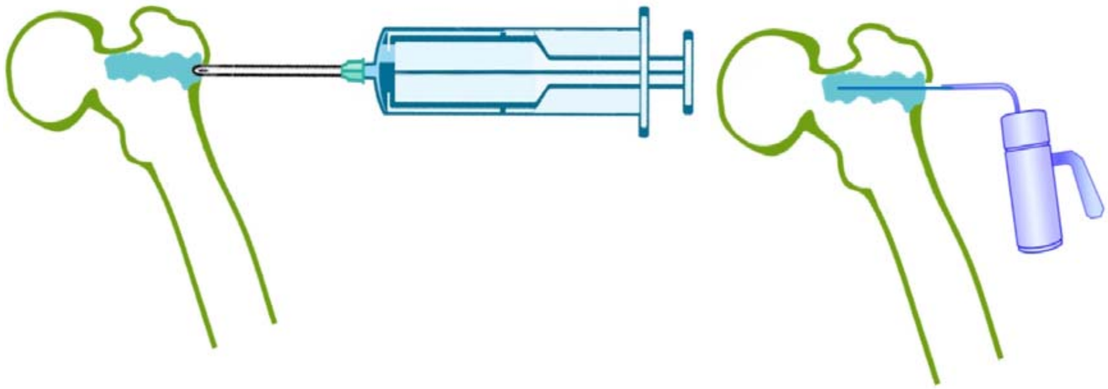


Figure 5 Initial design of the cooling system, the k-wire was inserted right after the injection

In a pilot experiment, 15 cm^3 was injected uniformly into a 130 mm x 45 mm x 40 mm block of an open cell block (7.5 PCF) resembling the human cancellous bone. Before injection, 30 cm^3 of canola oil was added to the block mimicking the bone marrow. In this setup, temperature profile of the bone-cement interface was measured via k-type thermocouple at 3 key locations. Experiment was repeated with the cooling system for comparison (Fig 6).

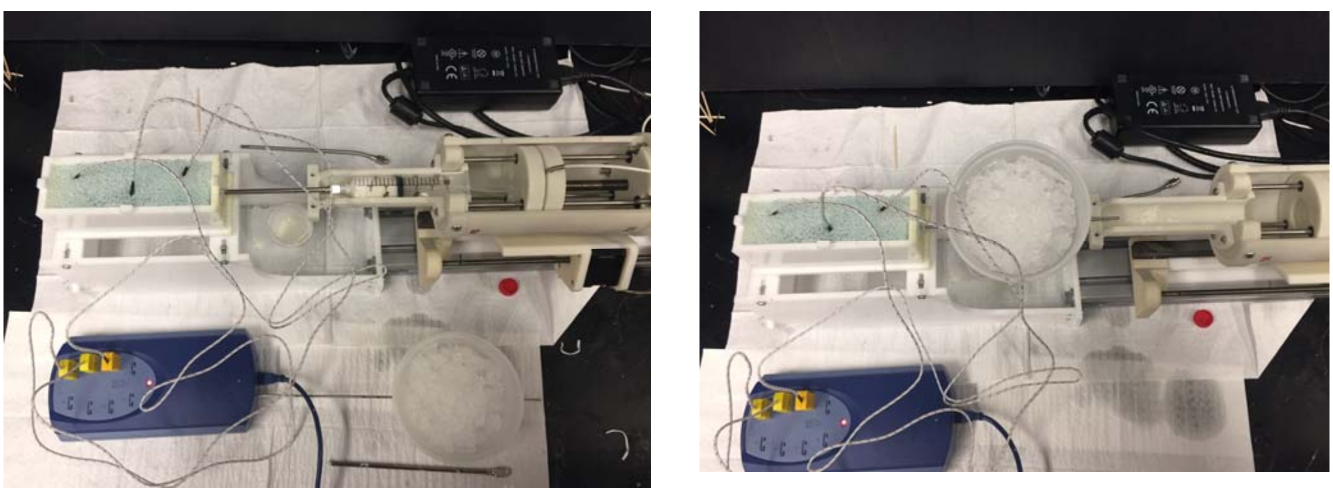


Figure 6 cooling experiment setup

In the first sawbone experiment, we were not able to take the k-wire out after curing temperature due to cement polymerization. In the second pilot experiment, we rotated the k-wire in a uniform motion with a drill while inserting it through the foam block (Fig 7). This time, we were able to successfully take out the k-wire; however, the optimized pattern of the cement profile has slightly changed due to the speed of the rotation which can be easily controlled in future experiments. Furthermore, this conductive cooling experiment via k-wire was tested in one cadaver experiment to validate its feasibility.

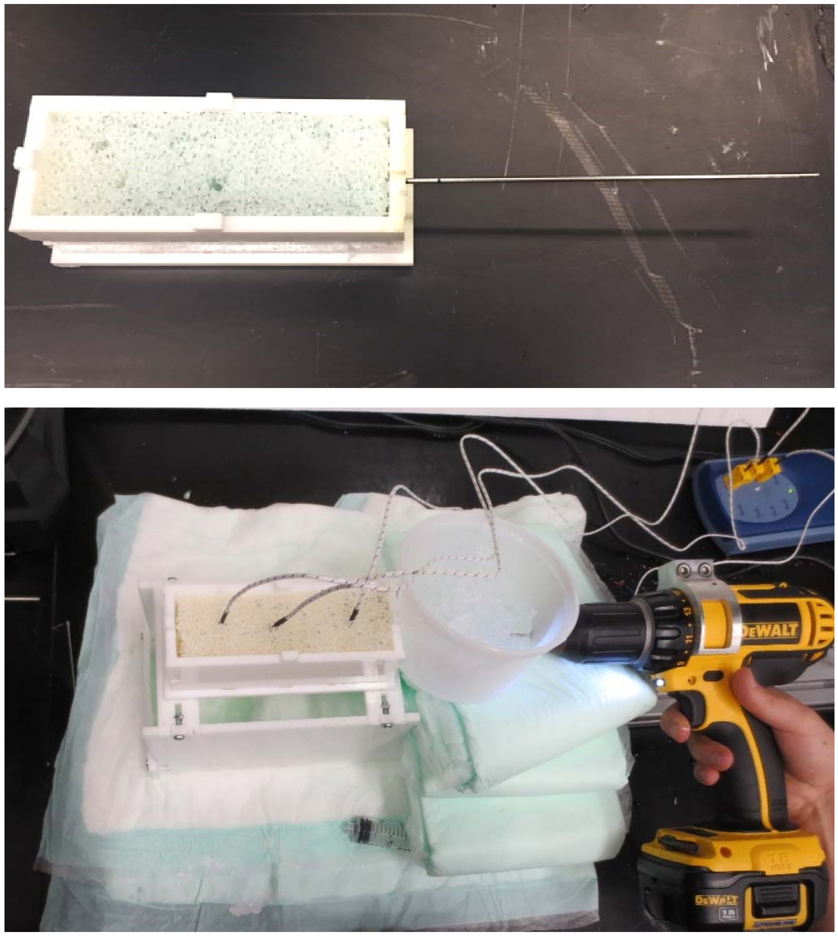


Figure 7 Cooling experiment with rotating the k-wire

Results

1) New Planning Paradigm for Osteoporotic Bone Augmentation

Table below shows the summery of the specimen demographics.

Specimen	Race	Gender	Age		Neck t-score	Group
1	White	Female	89	Left	-3.8	Augmented
				Right	-2.0	Control
2	White	Female	69	Left	-2.8	Augmented
				Right	-2.2	Control
3	White	Female	59	Left	-2.2	Control
				Right	-2.0	Augmented
4	White	Female	92	Left	-3.6	Control
				Right	-4.0	Augmented

FE analyses predicted an average yield load of 1713(±184) N for the control group, while that of the augmentation group before augmentation was 1738(±208) N and not significantly different from the control group (*P*=0.947). BESO simulations generally suggested augmentation of superior and inferior aspects of the neck as well as supero-posterior aspect of the greater trochanter to achieve the desired outcome with the least amount of cement which is similar to that of [3]. Figure below summarizes the results of augmentation experiments for the four cadaver experiments conducted.

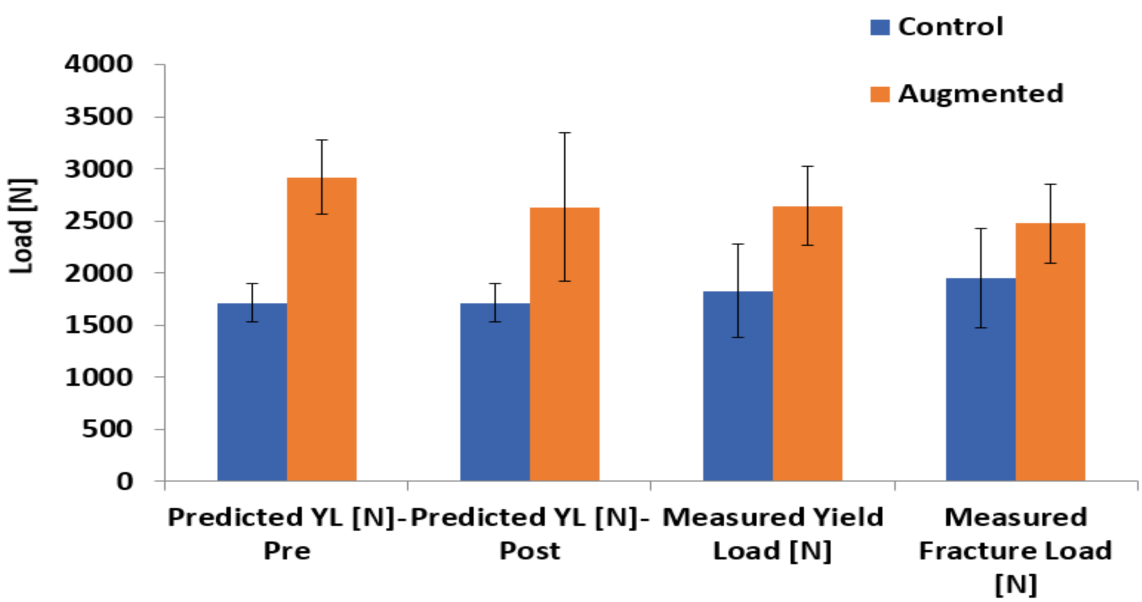


*Figure 8- **Biomechanical results of Bone Augmentation***

Results above indicate that the average of measured yield load for the control group is 1831(±475) while the average of measured yield load for the augmented group is 2648(±374) which is significantly different from the control group with an average increase of 27.1(%). In addition, the measured yield energy of the augmented group is significantly higher than those of the control with an average increase of 48.8%.

2) Temperature Evaluation of the Bone Cement Injection

In the augmentation experiments discussed above, we measured surface temperature of each bone during augmentation at three different spots with k-type thermocouple. In figure below we have shown the temperature profile of these measurements and the corresponding location of each thermocouple on the bone for specimen 4.

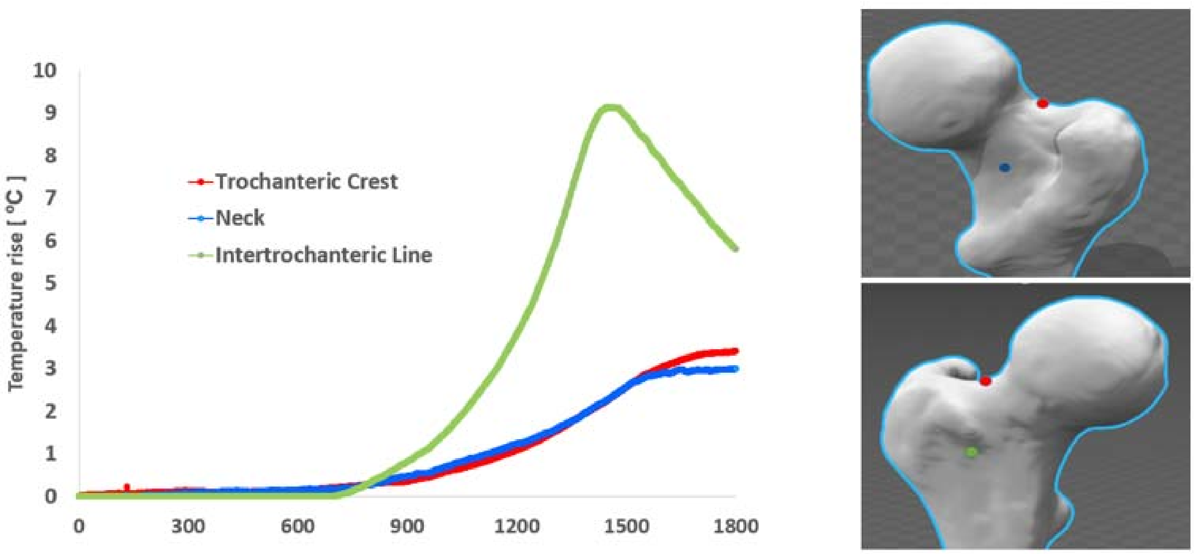


Figure 9- Direct Temperature measurements of the bone surface after Injection

Surface temperature-rise of the specimen 4 (augmented pair) at different time intervals (after injection) were calculated in the COMSOL simulations and are shown below. Simulation results demonstrates that the maximum temperature of the surface in the three key locations is 27.9 °C with increase of 9.3 °C.

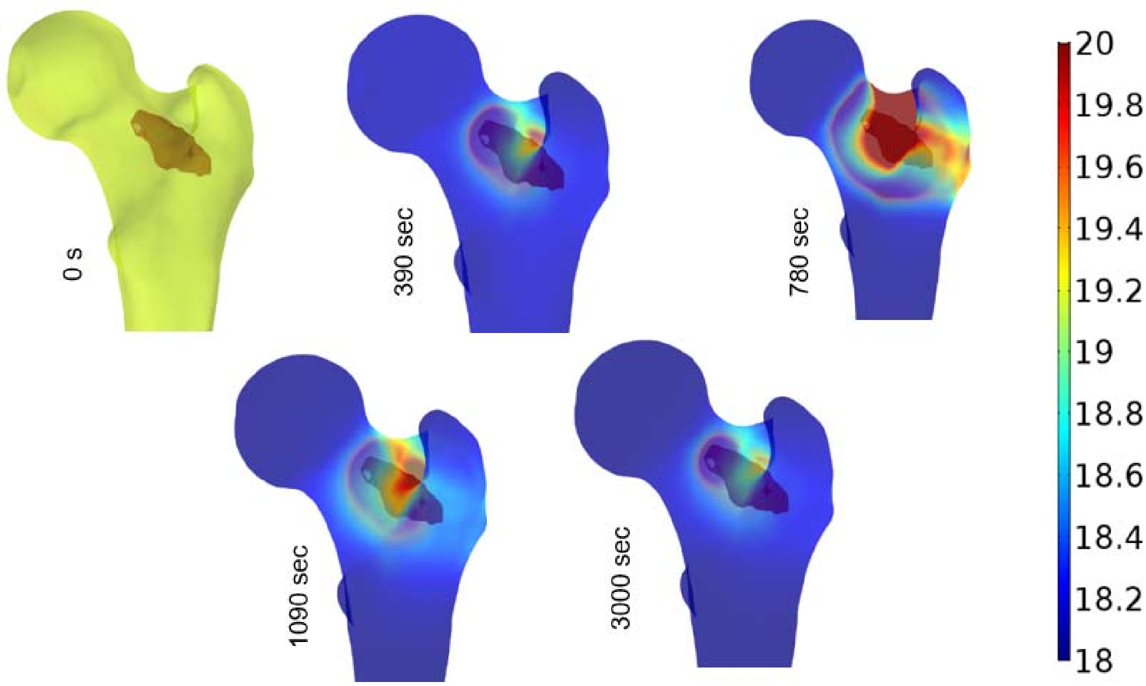


Figure 10- Comsol Simulation results for Bone Temperature after the time of Injection - Specimen 4

Figure below shows the Surface temperature of the specimen 1 (augmented pair) at different time intervals (after injection) from COMSOL simulations. Simulation results demonstrates that the maximum temperature of the surface in the three key locations is 27. 7°C with increase of 9.7 °C.

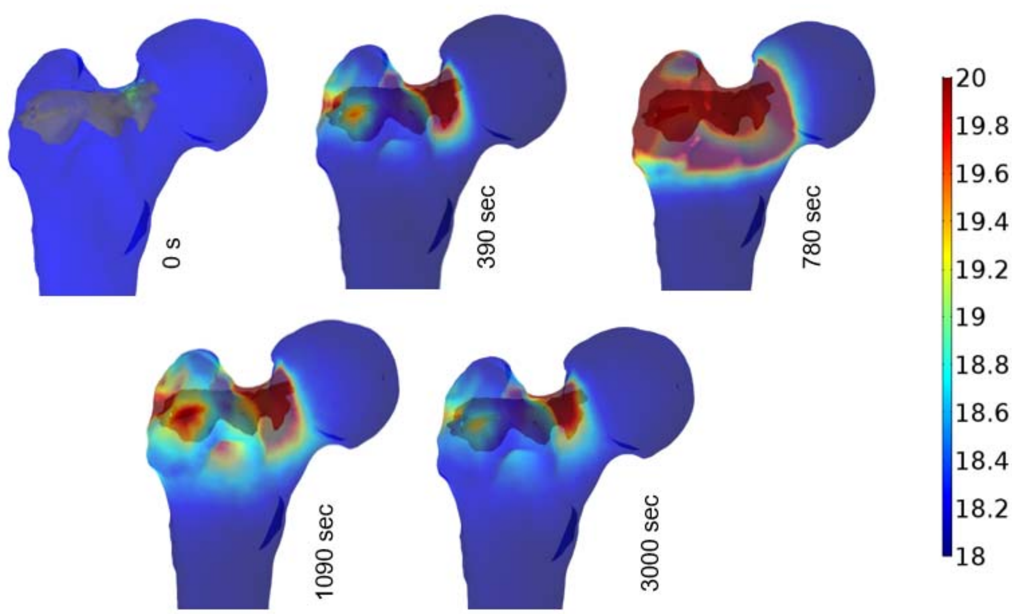


Figure 11- - Comsol Simulation results for Bone Temperature after the time of Injection - Specimen 1

Surface Temperature-rise of augmented bone were compared with the direct measurements at 3 locations mentioned above for specimen 1. Temperature-rise for trochanteric crest is shown below.

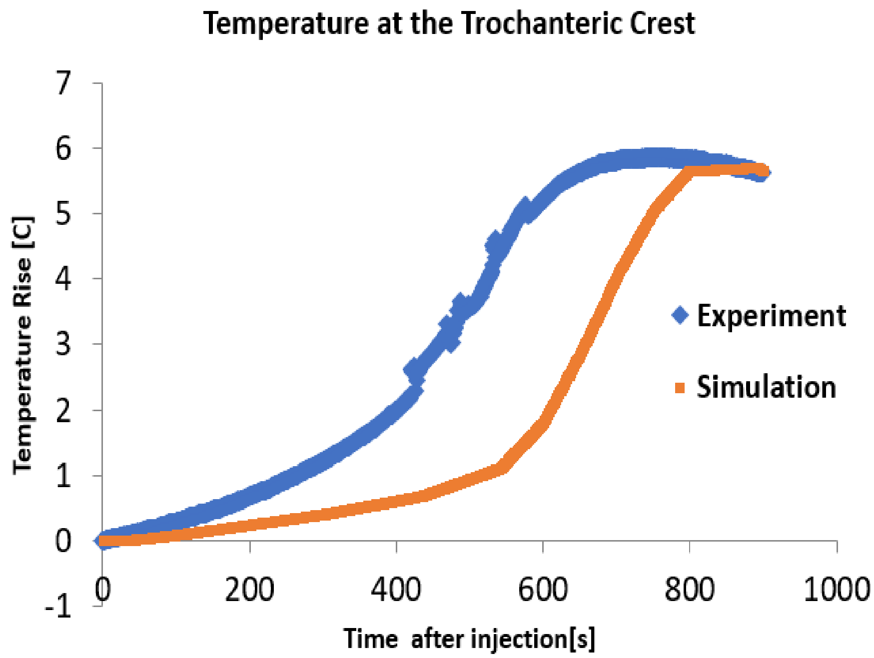


Figure 12- Temperature-rise at Trochanteric Crest- Experimental results vs. Simulations

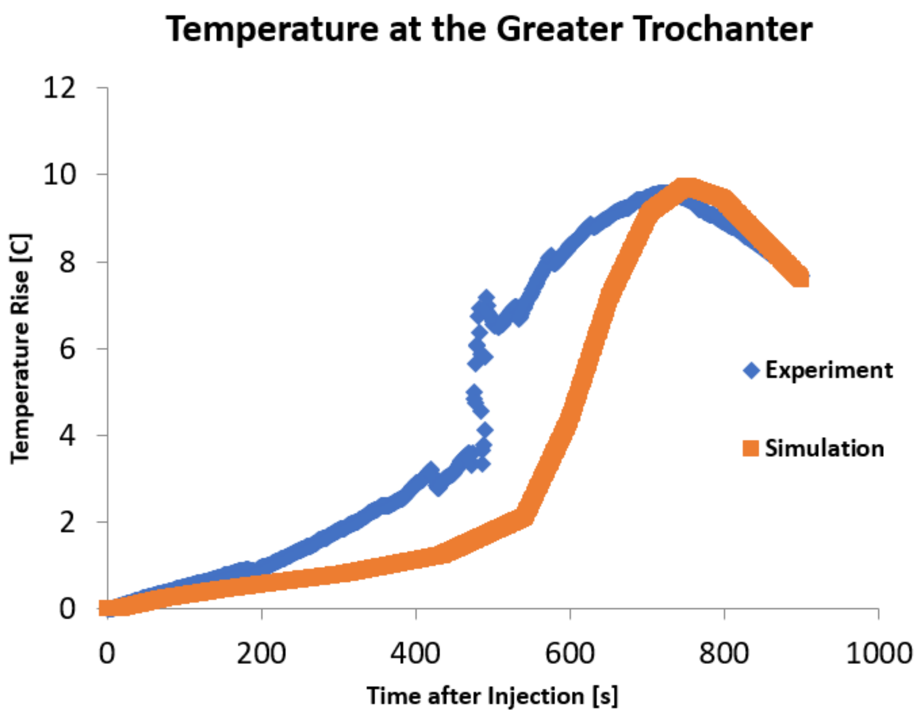


Figure 13- Tem**perature-rise at Greater Trochanter- Experimental results vs. Simulations**

3) Bone Augmentation Cooling System

Sawbone Experiments:

Figure below shows the temperature profile of the foam block at the foam-cement-interface. We have compared each thermocouple measurement of the injection with the cooling system with the corresponding measurments of the control (without cooling). In this experimet, the k-wire was stuck inside the cement after curing,

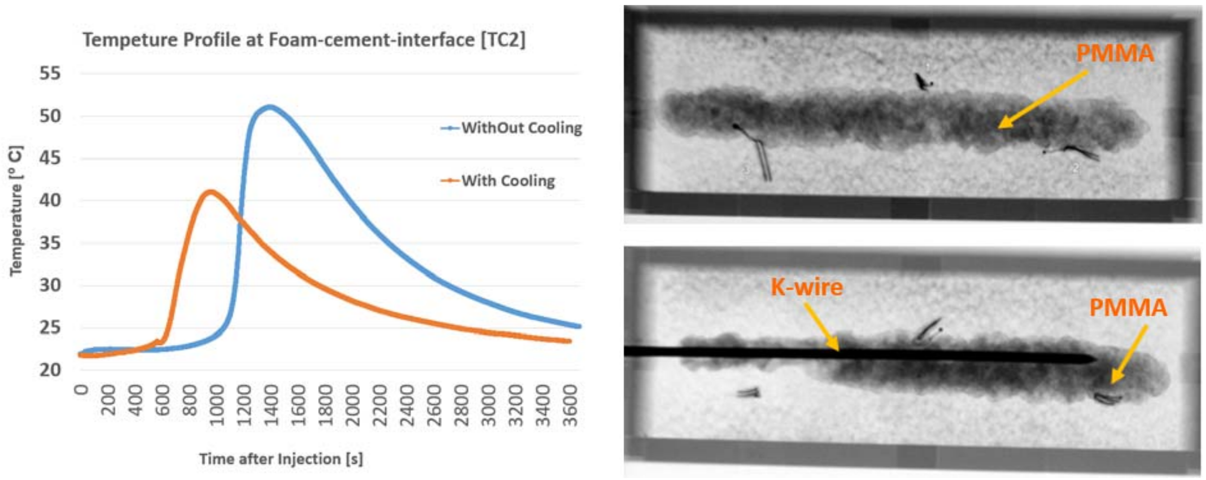


Figure 14- Temperature Profile at Sawbone-cement Interface

Sawbone expriment was repeated with rotating k-wire so that it can be removed. Results of the temperature at the sawbone-cement-interface are shown below:

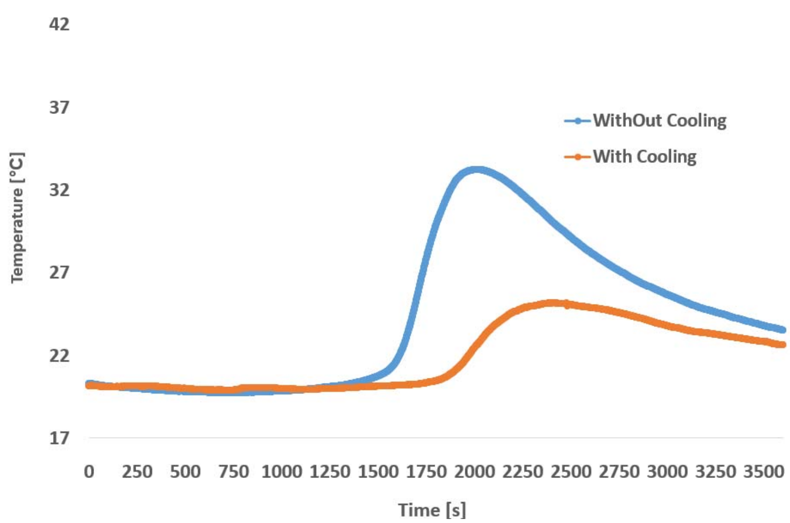


Figure 15- Temperature Profile at Sawbone-cement Interface

Cadaver Experiment:

The cooling system was evaluated in a cadaver experiment where we measured the surface temperature of the cadaver specimen 4 with similar injection pattern and cooling. Results below show the surface temperature at 3 locations similar to that the direct measurements:

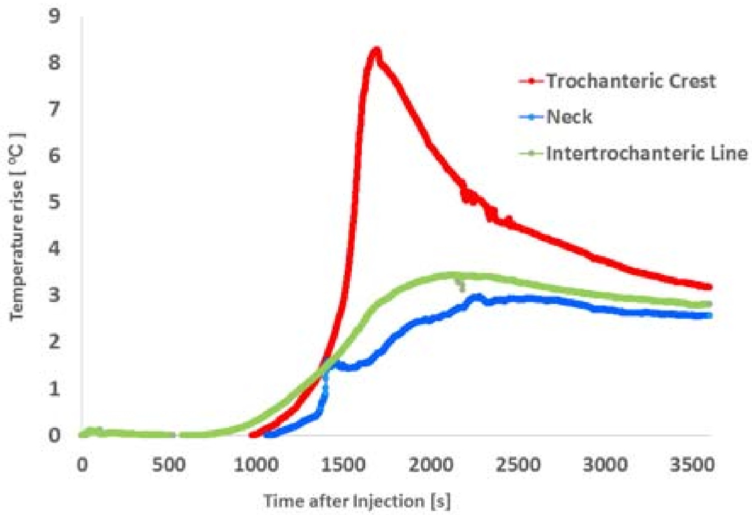


Figure 16- Direct Temperature measurements of the bone surface after Injection

This results show that the peak temperature measurement with the cooling system is 8.5 °C which is 17% lower than that of the augmentation without cooling.

Discussion

In the first part of the project, we performed 4 cadaver experiments. After mechanical testing and evaluation of the results, it was shown that the three osteoporotic specimens benefited from the augmentation, but the biomechanical strength of the osteopenic bone was reduced after augmentation. This can be due to biological variation between the augmented pair and control, but also the slippage of the bone during mechanical testing. The statistical power of these cadaver experiments can be increased via further experiments, but as of now, it has been shown that the new planning for osteoporotic bone augmentation can reduced the volume of injection, while improving the mechanical properties of the bone with a

Simulation results of COMSOL matched those of the experiments for specimen #1. This results would need to be evaluated with the second specimen which was simulated for validation. In this report, we have only shown the initial implementation of these simulations, but less details of how the simulation results are calculated in COMSOL. In the future, we would also indicate the heat transfer equations leading to these results and create mean to quantify the error between the simulation and experimental results. One of the concerns with this model is the assumption on homogeneity of the tissue. In the future, we hope to create a heterogenous heat transfer model which is capable of estimating bone surface temperature model accurately.

Although the cooling systems has shown promising results in the preliminary experiments, this system has a destructive effect on the cement profile which needs to be addressed. One of the concerns with the cooling system is the possibility of reducing the mechanical properties of the cement while helping to reduce the risk of thermal necrosis. In sawbone experiments, the peak temperature of sawbone-cement-interface and its corresponding time has been reduced when the k-wire is static. In the second experiment when the k-wire was rotating, the peak temperature was reduced but curing was delayed. In this experiment, pattern of injection was also effected by the cooling system.

Conclusion

In summary, we have shown a new planning approach for femoroplasty which reduces the volume of bone cement, while improving the biomechanical properties of the bone. This novel planning paradigm has been validated in four cadaver experiments. In addition, we have validated a COMSOL FE model capable of estimating the surface temperature of the bone after femoroplasty. This model was validated in a pilot cadaver experiment. Finally, we have introduced an approach to reduce the bone temperature after femoroplasty which has been validated in sawbone experiments and a pilot cadaver study.

Management Plan

We shared all the files related to the project in Dropbox to ensure that we both stay updated on the project and the changes made. As far as time management, we had weekly progress meetings with our mentors and discussed the schedule and progress of the project. We met at Bayview to conduct all the injections, mechanical testing and cooling experiments every other week. We used Microsoft Project for the schedule management section of the project. All the project deliverables were broken down to manageable tasks and work packages with assigned durations.

Even though there were some delays with a couple of the tasks throughout the project but we still managed to finalize the main project deliverables of the project. As an example, the planning phase of 4 osteoporotic femora took longer than expected which delayed the injection and mechanical experiments of the last femur, furthermore there were few unexpected experimental challenges such as drill navigation which forced us to repeat few injections. Overall the minimum deliverable was accomplished with two weeks' delay based on original plan.; however, since neither the expected nor the maximum deliverable tasks were dependent of the outcome of minimum deliverable; we were able to start them on schedule. Moreover, COMSOL simulation finished with 10 days' delay based on the original schedule which again didn't cause a major delay on the maximum deliverable tasks.

Overall, even though we still need to repeat some of the cooling experiments to maintain the desired cement profile, due to the fact that we were able to reduce the curing temperature with K-wire and pulling out the K-wire after temperature rise, we can successfully conclude that the milestones of the project have been accomplished and the goal has been met.

The final timeline of the project is documented at the end of the proposal.

Assigned responsibilities:
Even though each team member were included in all the phases of the project, the chart below shows the responsibility distribution for each part of the project

-	Preparing the planning models of 2 femora	Mahsan
-	Preparing the planning models of 2 femora	Amir
-	COMSOL model simulation	Mahsan
-	Post-operative and statistical evaluation	Amir
-	Cadaveric, mechanical testing and thermal experiments	Mahsan & Amir

Final Deliverables status

The final minimum, expected and maximum deliverables of the project are listed as below:

Minimum

- Pre-operative planning models for 4 osteoporotic femora ✓
- Experimental post-operative results of osteoporotic femora ✓
- Efficacy and statistical analysis of the new planning approach for femoroplasty ✓ Next step: Improve the accuracy of the analysis.

Expected

- Temperature-rise measurements of the bone surface after the injection ✓
- Heat transfer FE COMSOL model to predict the curing temperature of PMMA inside the bone ✓ Next step: Expand the FE model
- Comparison of the experimental results with FE model ✓

Maximum

- A Methodology to reduce the curing temperature ✓
- Experimental results and validation of the cooling system ✓

Key Dates

Below are the key dates and milestone listed for minimum, expected and maximum deliverables of the project with planned and actual completion dates.

Minimum		Expected		Maximum	
Task	Planned/Actual	Task	Planned/Actual	Task	Planned/Actual
Conduct the Planning Approach for 2 Osteoporotic Femora	Feb 16/Feb 16	Measure and evaluate the temperature-rise of bone in cadaveric studies	Mar 23/Mar 23	Conduct few experiments for the cooling system proposed	Apr 28/Apr 28
Evaluate the post-operative results of 2 femora	Mar 8/Mar 8	Create COMSOL FE heat transfer Model	Apr 26/May 9	Evaluate the cooling system	May 5/May 11
Conduct the Planning Approach for 2 Osteoporotic Femora	Mar 17/Mar 17	Compare the simulation results with experimental data	Apr 28/May 12		
Evaluate the post-operative results of 2 femora	Mar 27/Apr 7				
Evaluate the new planning approach	Mar 31/Apr 14				

Lessons Learned

In addition to further investigating various steps of the planning paradigm of the femoroplasty, we learned how to deal with the challenges that comes along with the Cadaveric Studies. We also learned how to model and simulate the thermal finite element of the femur after the injection. This enables us to work with variety of the designing tool to segment and model the femur using the CT data. In the cooling experiments, the important objective was to apply our k-wire proposal and pull out the k-wire after the temperature rise by rotating it. And last but not least, we were able to enhance our project management skills throughout the project and implement several real world applications and procedures to our research project in order to ensure a more reliable progress and a high quality outcome. It goes without saying that every successful project is baselines on an accurate definition of project deliverables and work packages. By breaking down the project tasks, targets and goals we could track each aspect of the research project more confidently and decrease; if not completely eliminate; the unintended occurrences.

Future Work

Based on the scope of the project, the future work can be addressed as:

1. Planning and injecting more femora to increase the sample size of the specimens and evaluate the new planning paradigm of femoroplasty in more accurate and reliable analysis.
2. Expanding heat transfer finite element COMOSL model to include the distribution of the monomer leftover at the cancellous bone-cement interface during polymerization; thereby developing more accurate and valid femoroplasty simulation model
3. Repeating cooling experiment via K-wire with different speed and frequency of the rotation to better maintain the optimized planned cement profile.
4. Conducting cooling experiment using convective heat transfer rather than conduction with closed end needle tips and continuous water flow and comparing the results with conduction experiment via k-wire.
5. Boosting the result of the planning and cooling experiments with more comprehensive statistical analysis

Acknowledgement

We would like to thank our mentors, Prof. Mehran Armand, Prof. Russell Taylor and Dr. Ryan Murphy for their help with this project.

References:

[1] Cummings, Steven R., Susan M. Rubin, and Dennis Black. "The future of hip fractures in the United States: numbers, costs, and potential effects of postmenopausal estrogen." *Clinical orthopaedics and related research* 252 (1990): 163-166.

[2] Dinah, A. F. "Sequential hip fractures in elderly patients." *Injury* 33, no. 5 (2002): 393-394.

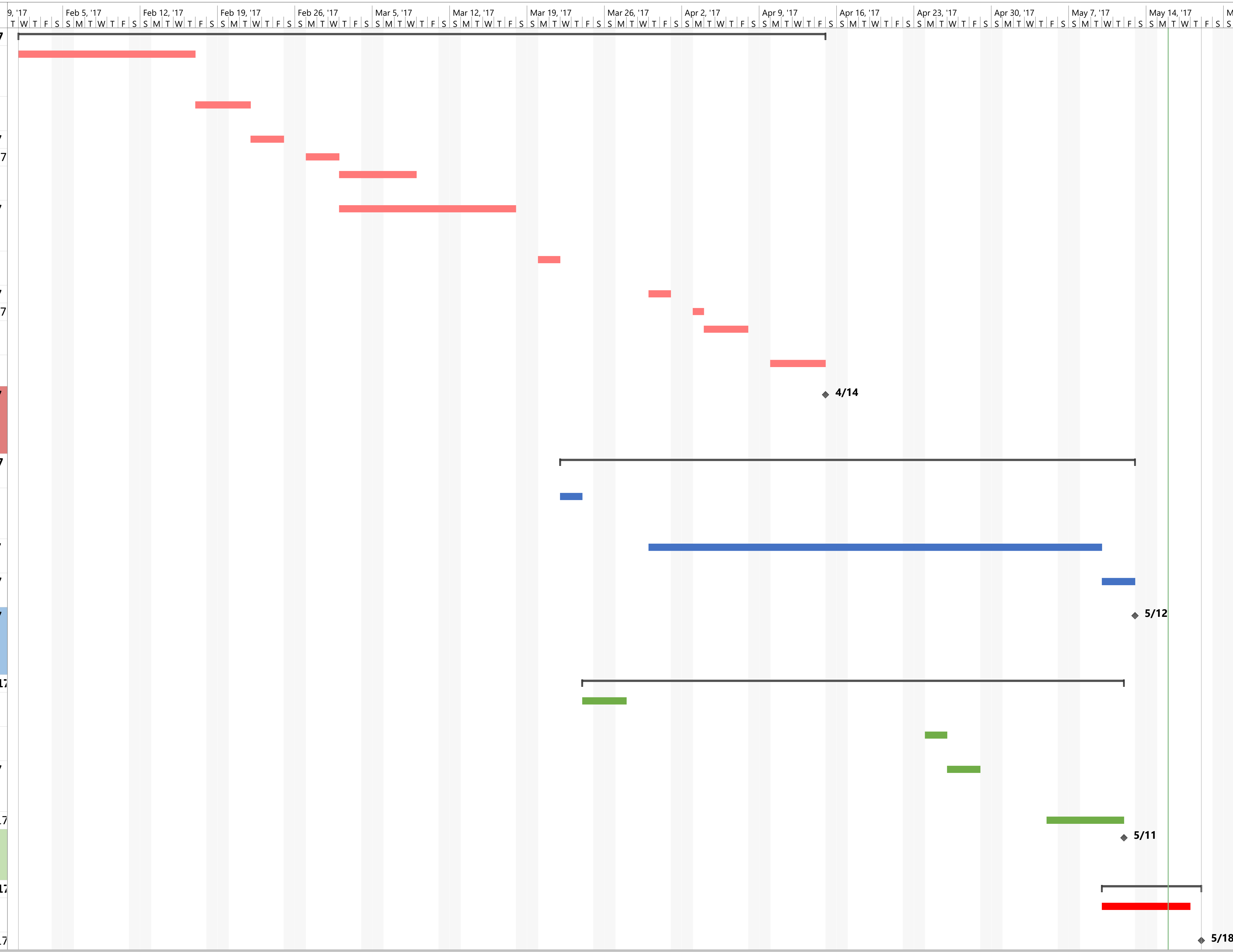
[3] Basafa, Ehsan, Ryan J. Murphy, Yoshito Otake, Michael D. Kutzer, Stephen M. Belkoff, Simon C. Mears, and Mehran Armand. "Subject-specific planning of femoroplasty: An experimental verification study." *Journal of biomechanics* 48, no. 1 (2015): 59-64.

[4] Basafa, Ehsan, Robert S. Armiger, Michael D. Kutzer, Stephen M. Belkoff, Simon C. Mears, and Mehran Armand. "Patient-specific finite element modeling for femoral bone augmentation." *Medical engineering & physics* 35, no. 6 (2013): 860-865.

[5] Basafa, Ehsan, and Mehran Armand. "Subject-specific planning of femoroplasty: A combined evolutionary optimization and particle diffusion model approach." *Journal of biomechanics* 47, no. 10 (2014): 2237-2243.

[6] Otake, Y., M. Armand, O. Sadowsky, M. Kutzer, R. Armiger, E. Basafa, P. Kazanzides, and R. Taylor. "Development of a navigation system for femoral augmentation using an intraoperative C-arm reconstruction." *Proc CAOS-International* (2009): 177-180.

ID	Task Name	Start	Finish
1	**Minimum Deliverable**	**Wed 2/1/17**	**Fri 4/14/17**
2	Conduct the Planning Approach for 2 Osteporotic Femora	Wed 2/1/17	Thu 2/16/17
3	Carryout the Cadaveric Experiment	Fri 2/17/17	Tue 2/21/17
4	Conduct Post-Operative CT	Wed 2/22/1	Fri 2/24/17
5	Perform Mechanical Testin	Mon 2/27/1	Wed 3/1/17
6	Evaluate Post-Operative Results	Thu 3/2/17	Wed 3/8/17
7	Conduct the Planning Approach for 2 Osteporotic Femora	Thu 3/2/17	Fri 3/17/17
8	Carryout the Cadaveric Experiment	Mon 3/20/17	Tue 3/21/17
9	Conduct Post-Operative CT	Thu 3/30/17	Fri 3/31/17
10	Perform Mechanical Testin	Mon 4/3/17	Mon 4/3/17
11	Evaluate Post-Operative Results	Tue 4/4/17	Fri 4/7/17
12	Evaluate New planning versus Old	Mon 4/10/17	Fri 4/14/17
13	Minimum Deliverable Met: Validation of the new planning approach for femoroplasty	Fri 4/14/17	Fri 4/14/17
14	**Expected Deliverable**	**Wed 3/22/17**	**Fri 5/12/17**
15	Measure and evaluate the temperature-rise of bone in cadaveric studies	Wed 3/22/17	Thu 3/23/17
16	Create COMSOL FE heat transfer model	Thu 3/30/17	Tue 5/9/17
17	Compare the simulation results with exprimental	Wed 5/10/17	Fri 5/12/17
18	Expected Deliverable Met:temperature rise evaluation and FEA simulation	Fri 5/12/17	Fri 5/12/17
19	**Maximum Deliverable**	**Fri 3/24/17**	**Thu 5/11/17**
20	Conduct the cooling expriment with Foam	Fri 3/24/17	Mon 3/27/17
21	Conduct the K-Wire Pullout Test	Mon 4/24/17	Tue 4/25/17
22	Conduct the cooling Experiment with a cadaveric femur	Wed 4/26/17	Fri 4/28/17
23	Evaluate the cooling systen	Fri 5/5/17	Thu 5/11/17
24	Maximum Deliverable Met: Method for reducing the temperature rise	Thu 5/11/17	Thu 5/11/17
25	**Closeout**	**Wed 5/10/1**	**Thu 5/18/17**
26	Prepare Cloesout Documents	Wed 5/10/17	Wed 5/17/17
27	Poster Session	Thu 5/18/17	Thu 5/18/17



Mentor: Dr. Armand

Questionnaire – Project # __09__

10/10 Overall project and progress

- Were you satisfied with the overall technical progress made in the course of the semester? yes
- Was the total accomplishment appropriate for the number and level (undergrad/graduate) of students on the project? yes
- Will the results be useful to you in the future? definitely
- Do you see a prospect for patents or publication to result? There will be publication prospects. With some additional work, I am expecting Amir and Mahsan publish these results.

9/10 Report (which the students should have shared with you)

- Does the project report accurately reflect the scope and accomplishment of the project? yes
- Were you given an adequate opportunity to review the report? yes
- Does the report and its appendices, together with the web site, provide sufficient information that subsequent groups can make effective use of the project results. Yes, but they could have used more references.
- In particular, are any project designs or code adequately documented. The experiments and simulations are adequately documented.

10/10 Web site

- Does the web site reflect the scope and accomplishment of the project? yes
- Do you wish the web site to remain password protected after May 30? If so, for how long? Yes. At least for one year or until they publish their results – whichever comes sooner.

10/10 Management

- Were the students fully engaged in the project? yes
- How often did they meet with you? Was this enough? On average once every two weeks or when substantial results were obtained. Yes, the meetings were sufficient.
- Were the "deliverables" and "dependencies" realistic? Yes, they did deliver more than what I was expecting.
- Was the plan realistic? Were unmet dependencies approached in an effective manner? Yes, the plan seems realistic.

Other comments or suggestions

- Do you have any other comments or suggestions, either about the specific project or about the overall structure of the course for next year?

  I felt the course structure was very good and helped the students to explore new directions for their research.