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Subject-Specific Planning of Femoroplasty: A Combined Evolutionary Optimization and Particle Diffusion Model Approach

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Abstract

A potential effective treatment for prevention of osteoporotic hip fractures is augmentation of the mechanical properties of the femur by injecting it with agents such as (PMMA) bone cement – femoroplasty. The operation, however, is only in research stage and can benefit substantially from computer planning and optimization. We report the results of computational planning and optimization of the procedure for biomechanical evaluation. An evolutionary optimization method was used to optimally place the cement in finite element (FE) models of seven osteoporotic bone specimens. The optimization, with some inter-specimen variations, suggested that areas close to the cortex in the superior and inferior of the neck and supero-lateral aspect of the greater trochanter will benefit from augmentation. We then used a particle-based model for bone cement diffusion simulation to match the optimized pattern, taking into account the limitations of the actual surgery, including limited volume of injection to prevent thermal necrosis. Simulations showed that the yield load can be significantly increased by more than 30%, using only 9ml of bone cement. This increase is comparable to previous literature reports where gross filling of the bone was employed instead, using more than 40ml of cement. These findings, along with the differences in the optimized plans between specimens, emphasize the need for subject-specific models for effective planning of femoral augmentation.

Keywords

Femoroplasty; PMMA Cement; Finite Element; Optimization; Planning

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Conflict of Interest Statement

None declared.

1. Introduction

Hip fractures in the elderly with osteoporosis, mainly due to falls to their side on the greater trochanter, constitute a major health problem worldwide. In the United States, hip fractures are responsible for \$20 billion of annual hospitalization and treatment costs (Lane et al., 2000; Elffors, 1998). Current preventive treatments include hip protectors, special diets and drugs and bone strengthening exercises. But the cost, long delay in restoring bone strength, low patient compliance, and other issues associated with these treatments inhibit their use or efficacy (Delmas et al., 1997; Khovidhunkit and Shoback, 1999; Ettinger et al., 1998; Kannus et al., 2000). Femoroplasty – augmentation of bone mechanical properties by use of bone cement injection inside proximal femur – has been proposed as a candidate effective alternative measure (Heini et al., 2004; Beckmann et al., 2007, Sutter et al., 2010a). The procedure, however, involves risks and possible complications. Injection of a large amount of cement, which has an exothermic curing process, may lead to osteonecrosis i.e. death of bone tissue as a result of poor blood supply (Jefferiss et al., 1975). Also suboptimal injection can result in bone weakening due to stress concentration, mainly at the cement bone interface, and render the augmentation unsuccessful (Mann et al., 1997). Therefore the operation requires detailed planning and careful execution. Unlike its counterpart procedure for treating osteoporotic vertebral bodies, i.e. vertebroplasty (Sun, 2006; Sun and Liebschner, 2004; Heini et al., 2001; Liebschner et al., 2001; Teo et al., 2007), planning of femoroplasty has received little attention in the literature. Few experimental studies of femoral augmentation have shown significant increase in the fracture loads and energies (Heini et al., 2004; Beckmann et al., 2007, Sutter et al., 2010a). However, those studies used gross fillings of femoral neck and trochanter, resulting in a significant increase of bone surface temperature (Beckmann et al., 2007). Sutter et al. (2010b) attempted neck- or trochanter-only augmentations with 15ml of cement and observed no improvements in the bone mechanical properties. In the study of Beckmann et al. (2011), when a double drilling of the neck was used, mechanical properties deteriorated significantly, seemingly because of the weakening of the bone cortex. In a recent study, Fliri et al. (2012) employed a “V shape” augmentation approach by drilling two paths starting from the lateral cortex in the greater trochanter, one directed to the superior and one to the inferior aspect of the neck. They then injected the bone with 10.8ml of cement that increased the fracture energy of the specimens, but did not affect the yield or fracture loads. van der Steenhoven et al. (2011) used a slightly different technique where they pre-drilled a cavity inside the femoral neck, either using an inflatable balloon or an eccentric drill, and then filled the cavity with Elastomer material. The augmentation resulted in less fracture displacement, but neither technique affected the fracture load of the specimens.

Similar to vertebroplasty, femur augmentation can benefit from modeling and planning using computational techniques for biomechanical evaluation. In our previous studies we have developed a computational model for finite element (FE) analysis of femoral strength and the effect of femoroplasty on it (Basafa et al., 2013a), as well as a diffusion model for predicting the cement diffusion pattern inside porous trabecular bone using CT scan data (Basafa et al., 2013b). In this paper we propose a new paradigm for planning of femoroplasty using a combination of those previously validated numerical techniques. We

also show simulation results of the method applied on a series of osteoporotic femur bone models.

2. Methods

Seven pairs of fresh-frozen osteoporotic femur specimens (average neck T-score of -3.53), each pair from one cadaver (four male and three female donors), were acquired from the Maryland Board of Anatomy. Average donors' age, height and weight at the time of death were 81 years, 172cm and 80kg, respectively (Table 1). Computed tomography (CT) scans were acquired from all of the specimens (Aquilion 64 CT System, Toshiba America Medical Systems, Tustin, CA) at 0.5mm slice thickness intervals. Planning consisted of two phases: finite element (FE) optimization of bone cement placement based on the method of Bi-directional Evolutionary Structural Optimization (BESO) (Basafa & Armand, 2013) and matching the optimized pattern using cement diffusion modeling based on the method of Smoothed Particle Hydrodynamics (SPH) (Basafa et al., 2013b).

Cement Placement and Geometry Optimization

To optimize cement pattern inside the femur, we used a modified version of the method of BESO (Querin et al., 1998). The basic idea behind BESO is to gradually remove inefficient elements from a finite element domain and add elements to high load-bearing regions until convergence. Calculations show that if strain energy is used as the criterion for addition/removal of elements, the method tends to maximize the structural stiffness (Tanskanen et al., 2002; Chu et al., 1996). The advantages are no need for gradient calculation, ease of implementation, as well as less sensitivity to the discontinuities in the solution space. We used the CT volumes obtained from the specimens to create FE models, according to the procedure described earlier (Basafa et al., 2013a). Briefly, models consisted of layers of elements, each made of concentric rings of quadratic 20-node brick elements, completed with 15-node wedge elements at the center (Dhondt, 2004). Heterogeneous material properties were assigned to the elements. To this end, each element's average Hounsfield Unit (HU) intensity value was converted to ash density using linear interpolation of known values for plastic phantoms that were placed near the specimens at the time of scanning. Apparent density was found using $\rho_{app} = 1.79\rho_{ash} + 0.0119$ where ρ_{ash} and ρ_{app} are the ash and apparent densities in gr/cm^3 , respectively (van Lenthe et al., 2001). Finally elastic modulus for each element (in MPa) was found using Eq. 1 (Morgan et al., 2003; Keller, 1994). The upper 90mm of the bone model was considered mainly trabecular and the distal part, cortical bone. Also, for each element, if the HU value was less than 100, an elastic modulus of 20MPa and Poisson's ratio of 0.499 was assigned, resembling marrow (Peng et al., 2006).

$$\begin{aligned} E &= 10500\rho_{ash}^{2.29} & \text{Cortical} \\ E &= 6850\rho_{app}^{1.49} & \text{Trabecular} \end{aligned} \quad (1)$$

Boundary conditions similar to a fall to the side on the greater trochanter (Sutter et al., 2010a) were applied to the models and a 500N force was evenly distributed on the surface nodes of the head of the femur.

From each pair of specimens, we randomly chose one for augmentation. We populated the proximal part of the femur, except the outer layer elements, with PMMA cement elements having an elastic modulus of 1200MPa and Poisson's ratio of 0.4 (O'Brien et al., 2010). At the end of each FE iteration, we examined the elements and replaced the properties of PMMA elements of low strain energy values with their original bone properties (cement removal). We also replaced the properties of bone elements that yielded large strain energy values, as well as their surrounding bone elements, with PMMA cement element properties (cement addition). Low and high strain energy elements satisfied $\sigma_e - RR \cdot \sigma_{\max}$ and $\sigma_e - IR \cdot \sigma_{\max}$, respectively, where σ_e is the element strain energy and $\sigma_{\max}$ is the maximum strain energy in the domain. The Rejection Ratio (RR) was computed as $RR = r_0 + r_1 \cdot SS + a_{RR} \cdot ON$ and the Inclusion Ratio (IR) as $IR = i_0 - i_1 \cdot SS - a_{IR} \cdot ON$ where $r_0 = 0$, $r_1 = 0.01$, $a_{RR} = 0.01$, $i_0 = 1$, $i_1 = 0.1$, and $a_{IR} = 0.1$. These values were found empirically to yield the best results. The Steady State number (SS) started with 1 and was increased by one increments whenever no cement element satisfied the removal or the addition conditions. The Oscillation Number (ON) started with 0 and was increased by increments of one when an "oscillation state" condition was reached. We define the oscillation state as a condition in which a group of PMMA elements is added in one step and the same group is removed in the consecutive one. The augmented models were allowed to evolve until their predicted yield load for each specimen reduced to twice as high as its own non-augmented value. Yield load, at the end of each iteration, was predicted by assuming linearity for the resulting strains and scaling the force up until 1% volume of the bone elements reached the yield maximum or minimum principal strain (-0.0427 for compression (minimum) and 0.0299 for tension (maximum) (Basafa et al., 2013a)). The volume of the cement and the list of the cemented elements were recorded throughout the simulations.

Matching Optimized Pattern Geometry using SPH-Based Diffusion Modeling

We then simulated the cement injection to match the ideally optimized cement pattern, while taking into consideration the constraints of intra operative augmentation. The procedure was as follows: The BESO algorithm identified the areas in the neck and trochanter in need of augmentation. We divided the proximal femur into three regions as shown in Figure 1. SPH simulations, using a previously validated method (Basafa et al., 2013b), were run at several locations within each region (4 for regions 1 and 2, 6 for region 3), in a local matching optimization manner. We examined more trial points in the trochanter because of its larger volume compared to the neck and the head. We also tried to keep the number of SPH simulations at a reasonable minimum since they are relatively computationally costly. The SPH method is summarized briefly here: CT volumes of the femora were used to create a porous model for the SPH simulations. Fixed particles were set at the center of the voxels with HU intensity higher than 200 and were given the volume of a voxel (Figure 2). This resulted in an average neck porosity of 90% for the osteoporotic specimens (Loeffel et al., 2008). Drilled path for the needle was simulated by removing particles in the way of the virtual needle (Basafa et al., 2013b). Fluid particles were then introduced into the model as the simulation progressed. Based on our preliminary experiments with bone cement injection inside porous media (Basafa et al., 2013b), 3ml injections were simulated at each location with 0.05ml/s injection rate, resulting in a 60s injection time. We assumed a cement viscosity of 200Pa.s, which increased linearly with time to 270Pa.s after one minute. After

each simulation, the particle information (location and density) were used to update the CT volume (Basafa et al., 2013b): for each voxel, the fluid density was estimated at the center and the HU value of the voxel was increased linearly proportional to that value. The updated CT volume was fed back to the FE user interface. We then determined cement distribution in the FE model by subtracting the pre-injection CT model from the simulated post-injection one and thresholding. We adjusted the threshold so that the FE cement volume matched the one simulated using the SPH method. The cemented element group was compared with the optimal cement pattern and the number of elements overlapping between the two was taken as the “match number” for each injection. After all of the injection simulations in each section (1, 2 or 3) were completed, the simulation with the largest match number was taken as the start point for the next set of simulations in the following bone section. This resulted in three injections overall for each specimen. We then inspected the corresponding locations for these injections to determine the drill path(s): If the third location was close to the line connecting the first two, we fitted a line to the set of the three points as the drill path and the projections of the points on the line were taken as the planned injection points. Otherwise, we determined one drilled path as the line connecting the first two points and another one by assuming a line passing through the supero-posterior part of the greater trochanter to the third point. If necessary, we adjusted the injection path to ensure it was safely away from the neck cortex. After determining the line(s) of injection, we repeated SPH simulation for the final plan followed by FE analysis to determine the outcome of the plan. This planning procedure is summarized below.

- Create and analyze pre-planning FE model.
- Perform BESO simulations and record the final cement pattern.
- Divide the femur into three regions, each containing several “test” points.
- Within each region, for each “test” point, simulate one injection. Select the point that overlaps most with the BESO pattern.
- Repeat the above step for all regions. For each step, use the updated CT of the previous region’s best point to re-create the porous model.
- Examine the points to determine the drill path(s).

3. Results

All BESO optimizations converged to a solution and their results are summarized in Table 2. Figure 3 shows the evolution of the cement pattern for a representative model. The figure shows a rapid removal of the elements from the femoral head, as their contribution to the structure is minimal. The average optimum cement volume (that doubled the yield load of the models) was 13.4ml. A strong correlation ($R^2=0.98$) was found between the intact yield load and the required volume of the cement (Figure 4).

For specimens #1, #2, #3, #5, and #7, the following augmentation was inferred from the optimization for the applied loading conditions: reinforce the neck area by adding a “ring” of cement around the neck and reinforce the greater trochanter by placing cement in the supero-posterior and the lateral parts of the trochanter. Figure 5(A) shows the cross section

of the model for specimen #2 for a better inside view of the optimized pattern. For specimen #4 (Figure 5(B)), only the superior aspect of the neck and the supero-posterior aspect of the trochanter were augmented. Finally, for specimen #6, most of the cement was populated in the superior neck area and almost none of the greater trochanter was cemented (Figure 5(C)).

Figure 6 illustrates the evolution of cement volume and yield load of a sample model. There is a substantial drop in those quantities in the first step, as there are a large number of unnecessarily cemented elements discarded. The evolution is terminated when the predicted yield load drops to twice its value for the intact femur model.

Based on SPH simulations and subsequent FE analyses, we decided on two paths of injections for specimens #4 and #6 and one path of injection for the rest of the models. For specimens #1, #2, #5, and #7 the line was directed from the supero-anterior aspect of the neck to the posterior of the greater trochanter. For specimen #3 the line was directed from the supero-posterior aspect of the neck to the posterior of the trochanter. The first line of injection in specimens #4 and #6 was directed from the superior aspect of the neck toward the lateral side of the trochanter. Figure 7 shows example planned injection paths.

FE analyses on the models predicted an average yield load of 2343N for the control group while the average load for the models selected for augmentation was 2457N before augmentation. No difference was found between the two intact groups ($P=0.379$). The load for augmented specimens increased to 3226N and the increase was significant compared to both the control group (+38%, $P=0.002$) and the intact augmented group (31%, $P=0.008$). Table 3 summarizes these results.

A strong correlation ($R^2=0.86$) was found between the “degree of augmentation”, here defined as the ratio of the planned load over the BESO optimized load, and the ratio of the planned cement injection (9ml) over the volume of cement suggested by BESO. Figure 8 shows this relation.

4. Discussions

Femoroplasty can reduce the risk of fracture in the elderly with highly osteoporotic hips. However, the procedure is still in its research stages and mostly performed on cadaveric specimens, mainly because of its unknown complications. These include the risk of thermal necrosis caused by large quantities of cement injections, leakage of the cement, and premature fractures as a result of stress concentration. In this paper, as a proof of concept, we showed that computational models can be used for simulating the biomechanics of the femur for effective planning of femur augmentation. We first used an optimization technique to find the optimum location for placement of the cement. However, there are numerous practical limitations that prevent the surgeon from achieving the optimum plan. Among the limitations are the need for a pre-drilled needle insertion path to inject the cement in the desired location, irregular dispersion pattern of cement into the porous cancellous bone, cortical weakening as a result of multiple drilled paths (Beckmann et al., 2011), limited volume available for each injection, and limited number of possible injections as each

injection limits the space available for the following cannula insertions and injections. Therefore, we employed a particle-based model for simulating cement infiltration of the cancellous bone that we had developed earlier for realistic simulations of cement injection. Results showed that, by employing less than 10ml of PMMA bone cement, it is possible to increase the yield load of osteoporotic femora by more than 30%. This is comparable to the outcomes reported in earlier experimental studies of femoroplasty (Heini et al., 2004; Beckmann et al., 2007, Sutter et al., 2010a) where, instead, gross filling of the entire neck and trochanter areas were done using 40–50ml volumes of cement. Our study shows that it is possible, through subject-specific modeling and optimization, to limit the injection volume and potentially avoid the risk of thermal necrosis and stress concentration.

Despite their differences in details, the BESO simulations “sculpted” the cement in the same qualitative manner. They suggest augmentation of the postero-superior aspect of the greater trochanter and the neck areas close to the cortical shell. This is in agreement with the recent experimental findings of Palumbo et al. (2014). By closer examination, one can notice the thicker augmentation in the superior of the neck, compared to the inferior aspect. Specifically for one specimen, there was no cement populated in the inferior aspect of the neck. This agrees with the experimental studies on femur (de Bakker et al., 2009; Dragomir Daescu et al., 2010) that found the initial failure happens at the superior aspect of the femoral neck when loaded in a fall to the side loading configuration.

The method of BESO, albeit similar to gradient-based approaches and relatively successful for our application, is a heuristic method and its results are sensitive to the chosen parameters. Future work involves using gradient-based optimization techniques and investigating the similarity between those and the current findings.

Hip fractures can occur during normal daily activities such as walking and sitting as well as trauma such as backward falling. Ideally, the planning should take into account a number of different loading conditions and try to minimize the overall risk. In this study, we only considered fall to the side only since those are reportedly the main cause of hip fracture (Parkkari et al., 1999). This study, therefore, cannot draw conclusions regarding the effect of augmentation on preventing fracture due to the other type of falls. This will be the focus of future studies.

BESO terminated when there was a 100% increase in the predicted yield load of the osteoporotic femur model. This was decided based on the findings of Courtney and colleagues (Courtney et al., 1994; Courtney et al., 1995) who observed that bone strength, on average, reduces by half due to osteoporosis and aging. This, however, does not ensure that the risk of all fall-to-the-side fractures is completely eliminated. The impact load on the femur depends on several other factors including height of the fall, floor covering, body weight etc. (Parkkari et al., 1997; Kannus et al., 1999). To improve the optimization, one can benefit from a patient-specific fall model, e.g. a spring-dash system (Robinovitch et al., 1991; Robinovitch et al., 1997), that can more accurately predict the impact loads exerted on the femur and set the planning goal accordingly. Of note, the main objective of this study was to show that with the proposed planning strategy, the yield load can be improved with

significantly less amount of PMMA injection when compared to the amount applied in the previous literature.

We employed an ad-hoc procedure to match the BESO results using SPH simulations. To that end, as discussed before, we had to consider the constraints that the surgeon is facing at the time of surgery. Considering all those limitations, there are possibly a number of other methods of approaching the problem of pattern matching that could, potentially, reduce the time needed for planning. Furthermore, reducing SPH simulation times will allow examining more points in the design space and, therefore, improving the planning strategy.

In this study we only allowed a limited volume of cement for the second phase of planning but, as BESO suggested, some specimens needed volumes more than 20ml of cement to achieve the goal of augmentation. Performing multiple injections or larger volume injections pose challenges such as excessive pressure required for injecting high viscosity cement and/or leaking of cement into unwanted regions. Robotics technologies can be employed to realize pre-drilling/milling of the target regions inside the bone so that cement can be delivered exactly as the optimized plan (Kutzer et al., 2011).

The particle model for cement modeling used here included simplifying assumptions which likely were the source of differences between the modeled and actual cement behavior (Basafa et al., 2013b). These include the unmodeled viscoelastic behavior of the cement, especially at large viscosities, as well as interaction of the cement with the surrounding soft tissue (bone marrow, blood, etc.). For the latter, however, similar experiments (Heini et al., 2004; Beckmann et al., 2007; Sutter et al., 2010a; Sutter et al., 2010b) as well as our own tests (Basafa et al., 2013c) have shown that displacing the bone marrow does not pose a practical issue, especially in the case of osteoporotic femora where a major portion of bone density is lost due to osteoporosis. Also, since we are aiming for injection volumes much less than the “conventional” femoroplasty, this will be a less pressing issue. Of note, the purpose of developing the particle model was to predict the shape of the cement profile at the end of the injection. The model was used earlier to simulate experimental PMMA injections into porous materials and the resulting shapes differed by only about 1mm. Therefore, despite inaccuracies in the modeling, the method performs well in predicting cement profiles. Furthermore, the overall planning is independent of the particular method of cement modeling and that module can be replaced with a more accurate/efficient method, e.g. the recent study of Widmer Soyka et al. (2013) in modeling the injection of nonlinear viscoelastic bone cement in the context of vertebroplasty.

The relative amount of cement volume used correlated very well with the amount of augmentation in the augmented group. This further emphasizes the importance of subject-specific planning as, for any desired augmentation outcome, different specimens require different volumes of cement augmentation. The volume and cement injection profile needed depends, among other factors, on the size of the femur and the severity of the osteoporosis and anatomy of the internal trabecular structure of individual specimen. Rough measures such as the average bone mineral density (BMD) or T-score do not contain enough detailed information for making decisions on the location and volume of the cement to be injected. Finite element modeling and optimization, on the other hand, take into consideration the

inhomogeneity and irregular geometry of the bone and can provide more detailed information about the regions of stress or strain concentration in need of reinforcement.

The main purpose and contribution of this study is to introduce a patient-specific planning of femoral augmentation using validated individual simulation components (Basafa et al., 2013a; Basafa et al., 2013b). As part of ongoing research, the same femora are used for the augmentation experiments based on the proposed planning approach, and the results are compared to the simulations. The partial results of those experiments were briefly presented recently (Basafa et al., 2013c) and showed to be promising. Future work will involve reporting the detailed experimental tests and results.

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Figure 1.
Trial points (blue) for injection. The red dots represent head and neck center points.

Figure 2.
Sample cross section of fixed particle (cyan) and fluid particles (yellow) arrangements for SPH simulations. The red line represents the cannula path.

Figure 3.
From left to right: evolution of the cement placement (green elements) in a representative model.

Figure 4.

Correlation between the intact yield load of the augmented models and the volume required to increase the load by 100%.

Figure 5.
Cross sections of optimized models for specimens #2 (A), #4 (B) and #6 (C). Only the cemented and the outer most bone elements are shown for clarity.

Figure 6. Evolution of cement volume (A) and predicted yield load (B) for a sample model. The dashed line in (B) indicates the target yield load.

Figure 7.
Planned paths of injection and placed cement elements for specimen #2 (A) and #4 (B). The dashed lines represent the paths of injection.

Figure 8.
Degree of augmentation in the augmented group vs. relative volume of injection.

Table 1
Specimens' measurements. "Control" denotes the side kept as control and "Plan" denotes the side chosen for planning

Specimen Number	Age (years)	Gender	Weight (Kg)	Height (cm)	Neck T-Score	
					Control (side)	Plan (side)
1	76	M	75	175	-4.10 (L)	-3.90 (R)
2	83	M	127	188	-3.50 (R)	-3.30 (L)
3	68	M	70	175	-4.90 (L)	-4.30 (R)
4	93	F	73	163	-3.70 (R)	-3.70 (L)
5	85	F	66	160	-3.10 (L)	-3.10 (R)
6	87	M	91	183	-2.90 (L)	-2.90 (R)
7	74	F	59	160	-3.10 (R)	-2.90 (L)
Mean(±SD)		81 (±9)	-	80 (±23)	172 (±11)	-3.61 (±0.70) -3.44 (±0.54)

Table 2

Summary of BESO optimization end results

Specimen Number	# Iterations	Cement Volume (cm ³)	Final Yield Load (N)	Intact Yield Load (N)
1	19	11.8	4470	2250
2	12	20.5	6510	3420
3	2	26.2	7460	3905
4	41	5.6	3380	1670
5	36	10.8	4590	2290
6	55	6.3	3590	1485
7	17	12.3	4210	2180
Mean ($\pm$ SD)	26 ($\pm$ 19)	13.4 ($\pm$ 7.5)	4887 ($\pm$ 1524)	2457 ($\pm$ 888)

Table 3

Summary of the planning results

Specimen Number	Control Group Yield Load (N)	Augmented Group		
		Augmented Yield Load (N)	%Increase Compared to Control	%Increase Compared to Self
1	2105	2540	20.7	12.9
2	3300	3655	10.8	6.87
3	3495	4550	30.2	16.5
4	2215	3080	39.1	84.4
5	1890	2880	52.4	25.8
6	1320	3040	130	105
7	2075	2840	36.9	30.3
Mean	2343	3226	37.7*	31.3*
(±SD)	(±779)	(±675)		