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Seminar Critical Review

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A Novel Planning Paradigm for Augmentation of Osteoporotic Femora

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 and it is desirable to use the minimum amount of cement possible to achieve the goals of augmentation.

Papers selection

Poor cement placement or excessive injection volumes can reduce or eliminate blood supply to healthy bone tissue potentially resulting in osteonecrosis, i.e. death of bone tissue as a result of poor blood supply; therefore, it is essential to study and measure the temperature evaluation caused by bone cement polymerization. Although there is a wealth of research on the effects of augmentation on the vertebral bodies, namely vertebroplsty, there is very limited literature regarding optimal femoral augmentation.

I have chosen three papers regarding temperature evaluation of bone cement polymerization during vertebraplasty which can be categorized in two groups, first group includes two experimental study papers that have measured in vitro and in vivo temperatures, respectively during percantaneous vertebroplasty (PV) using different bone cements. The papers in this group are listed below:

Group 1:

1) Deramond, H., N. T. Wright, and Stephen M. Belkoff. "Temperature elevation caused by bone cement polymerization during vertebroplasty." *Bone* 25.2 (1999): 17S-21S. [4]
2) Anselmetti, Giovanni Carlo, et al. "Temperature measurement during polymerization of bone cement in percutaneous vertebroplasty: an in vivo study in humans." *Cardiovascular and interventional radiology* 32.3 (2009): 491-498. [5]

The third paper studies the thermal analysis and simulation where the distribution of temperature and monomer leftover at the cancellous bone-cement interface during polymerization were simulated, the paper is listed below:

Group 2:

3) Stańczyk, M., and B. Van Rietbergen. "Thermal analysis of bone cement polymerisation at the cement–bone interface." *Journal of biomechanics* 37.12 (2004): 1803-1810. [6]

For each group of papers, I summarize the motivation, methods and key results.

Group 1

Motivation:

Percutaneous vertebroplasty (PVP) was proposed in 1987 to treat painful osteoporotic vertebral compression fracture and osteolytic lesions of the spine. The procedure involves the injection of polymethylmethacrylate (PMMA) cement into the cancellous bone of vertebral bodies (VB) with a cannula inserted through each pedicle. However, thermal necrosis of neural tissue may occur by the heat generated during exothermic polymerization, therefore; study of the thermal effects associated with PVP plays an important role in clinical development of PVP. It has been reported that thermal necrosis occurs in bone tissue exposed to temperatures in excess of 50° C for more than 1 min.

In the first paper, the temperature was measured at three key locations (anterior cortex, center and spinal canal) in excised vertebral body injected with two different bone cements (Simplex P and Orthocomp) to identify the effects of temperature in PVP. Twelve VBs from three elderly female spines were injected with 10cc of one of the two cements and temperatures were measured in a bath (37° C), for 15 minutes after the injection. In the second paper, temperature was measured in-vivo in 22 women with painful osteoporotic vertebral underwent PV on 22 lumbar vertebrae using eleven different bone cements (3 ml each) formulated and approved specially for PV.

Experimental Studies

In this section, I will explain the experimental setup and key results of the experimental studies of the papers I chose.

Paper 1: Experimental Setup

In the first paper, three spines were collected from elderly female cadavers with average t-score -3.8 $\pm$ 3.8, within a given spine vertebral levels T11-T12 and L1-L2 were considered as paired specimen. "Simplex P" was injected in one of each pair and the other was assigned to the "Orthocomp" cement. On the day of testing, VBs were placed in a large path filled with 0.9% saline solution at 37°C and two 10-gauge needles were inserted into the interior of the VB as shown in Figure 1. Also each VB was instrumented with three 30-gauge, butt welded, T-type thermocouples along the midline of the VB at a depth of one-half the VB height. The placement of three thermocouples were as follow: The posterior thermocouple (T1) was placed between the periosteum of the posterior cortex of VB, the central thermocouple (T2) was placed in the geometric center of the VB and the anterior thermocouple (T3) was placed interior to the anterior cortex. Immediately After injection of 10 cc of bone cement, 5 cc through each needle with the VB in the bath, temperatures were measured at the three major locations where thermocouples were placed. The temperatures were recorded every 30 seconds for a period of 15 minutes.

Figure 1 - radiographs of cannula and thermocouple placement in a VB injected with Simplex P

Paper 1: Key Results and conclusion

In the first experiment, it is shown that the spinal cord and nerve roots are not at the risk of thermal damage. Temperatures liberated at thermocouples T2 and T3 in some VB might be significantly high and long in duration, potential of causing thermal necrosis of bone tissue. Figure 2, demonstrates thermocouples surrounded by the bone cement. On average temperature histories for VBs injected with Simplex were

greater than Orthoconp. In summary, the temperature monitoring results of thermocouple were shown in Table 1 which indicates that

- There was no substantial difference in peak temperature at T1 between two cements and it never exceeds 41°C.
- At T2, the peak temperature was significantly greater and longer in duration for temperature above 50°C with Simplex cement than Orthocomp
- At T3, there was no significantly difference between peak temperatures however it experienced temperatures above 50°C for significantly longer period for VBs injected with Simplex than those injected with Orthocomp.
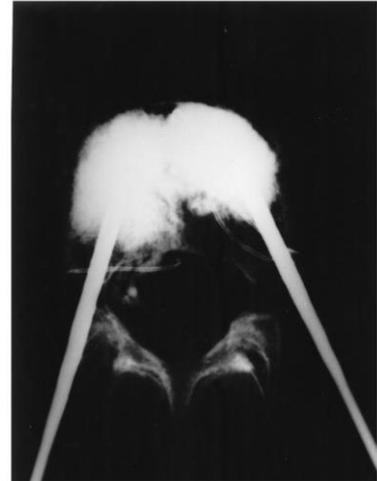
Figure 2 – Peak temperatures occurred at the central thermocouple in all VBs except one injected with Orthocomp

Bone Cement/Thermocouple	Peak Temperature			Temperature over 50° C		
	T1	T2	T3	T1	T2	T3
Orthocomp	40.1±0.8°C	51.2±6.2°C	45.2±4.9°C	-	1.3±1.4 min	0.2±0.6 min
Simplex P	38.5±1.4°C	61.8±12.7°C	50.3±9.8°C	-	3.6±2.1 min	1.2±1.6 min

Table 1 - Average temperature histories for two different bone cements

Furthermore, evaluation of cement pattern in T12 VB verified that the T3 thermocouple was embedded in cement, consequently, the cement fill pattern and subsequent contact with the thermocouple plays an important role in temperatures recorded.

Paper 2: Experimental Setup

In the second paper, in which temperatures were measured in vivo, 22 women with mean age of 75 years suffering from painful osteoporotic vertebral collapse were selected to undergo PV and polymerization temperature monitoring using 11 different bone cements. Each cement was tested in two patients to obtain two measurement for 11 different bone cements. The treated vertebrae were L1(2 cases), L2 (7 cases), L3 (11 cases) and L4 (2 cases), similar to the first paper, two 10-gauge needles were inserted into the interior of the VB through the pedicles; however, for temperature measurement, a 16-gauge radiofrequency thermoablation (RFA) needle with nine deploying hooks carrying five thermocouples was coaxially inserted into the VB through the left pedicle. Thermocouples were placed clockwise in odd order as shown in Figure 3 and the hooks were opened in order to locate each thermocouple as desired positions as follows: within the anterior third (T5), and in the mid part of the vertebral body (T2), close to the superior (T1) and inferior (T3) endplates, and near the lateral left wall (T4). Thermocouples T2 and T5 were embedded in the cement while T1, T3, T4 were in the bone-cement interface. 3 ml of cement ware injected in each treated vertebrae and after PMMA consolidation, RFA needle were pulled out by cutting edges of the hooks. The temperatures were recorded every 30 seconds until temperature on every thermocouple dropped below 45° C.
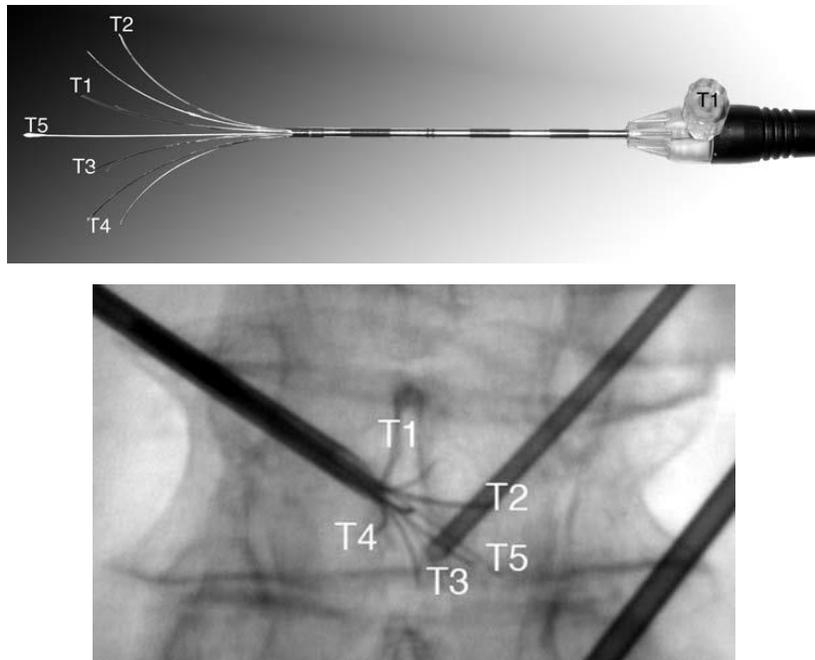
Figure 3 – RITA radiofrequency thermoablation (RFA) needle carrying five thermocouples (Top), Bilateral transpedicular approach with RFA needle through the vertebroplasty needle on the left pedicle (Bottom)

Paper 2: Key Results and conclusion

Bone cements used in this experiment is categorized in three groups depending on the peak temperatures. Similar to the previous experiment, the result confirms that a higher temperature depends on the injected volume and concentration of the cement where longer dwell time recorded for thermocouple T2 and T5 located in the medial and anterior parts of VB. Figure 4 demonstrates thermocouples completely surrounding by the bone cement and complete withdrawal of the RFA needle. In summary the temperature monitoring results of thermocouple were shown in Table 2 which indicates that Peak temperature values for vertebrae injected with Group A were significantly higher than those injected with Group B and C bone cements. From Table 2, we can see that in Group C temperatures did not reach 50°C and the average dwell time was less than 1 min, thereby using Group C cements can significantly reduce or eliminate the possibility of thermal necrosis.
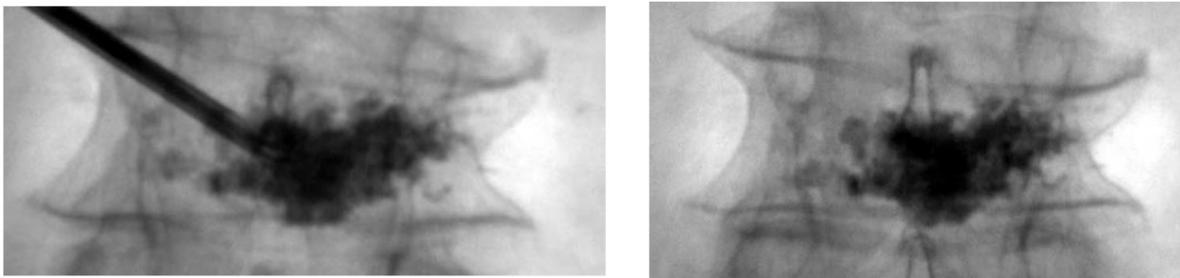
Figure 4 - Posteroanterior view demonstrating the thermocouples com- pletely surrounded by the bone cement (Left), Final check showing good technical results and complete withdrawal of the RFA needle (Right)

	Thermocouple T2		
Bone Cement Group	Group A mean peak temperature >60°C	Group B 50°C < mean peak temperature < 60°C	Group C mean peak temperature <50°C
Peak temperature	86.7±10.7°C	60.5±3.7°C	44.8±2.6°C
Temperature over 50°C	Average of all : 2 min 25s±1 min 17s Longer in Osteopal-V :5 min 7s±28s		42s±1 min 33s in Osteofirm

Table 2 - Average temperature histories of thermocouple T2

Group 2

Paper 3: Motivation

In this paper, the distribution of temperature for possibility of thermal necrosis during polymerization and monomer leftover which may cause chemical necrosis were simulated and investigated at the cancellous bone-cement interface. In this study, the finite element model has been created for realistic microstructure bone-cement architecture and realistic temperature-dependent polymerization kinetics behavior where the transient temperature field throughout the interface along with the polymerization fraction distribution in the cement domain were calculated.

Paper 3: Technical Approach

The temperature field equations resulting from the cement polymerization supplementing with an additional kinetic equation for the polymerization fraction w that were employed in the simulation are shown below:

$$\frac{\partial T(\mathbf{x}, t)}{\partial t} = a_i \nabla^2 T(\mathbf{x}, t) + q_v(\mathbf{x}, t) \quad \text{in } \Omega_i,$$

$$\frac{\partial w(\mathbf{x}, t)}{\partial t} = a \exp\left(-\frac{E_a}{RT(\mathbf{x}, t)}\right) P(T(\mathbf{x}, t), w(\mathbf{x}, t)),$$

It is noticeable that polymerization was modelled as temperature independent and only steady state solution was considered. A cube of bovine trabecular bone was used for this study where the cement was mixed and placed directly on the bone surface within a rubber ring and a load of 150 N was applied to the top surface while it was curing which is shown in Figure 5.

After curing for 1 hour, micro CT scans of the specimen was obtained and a 1.75mm×1.75mm×5.95mm sob-volume with its longest edge perpendicular to the bone-cement
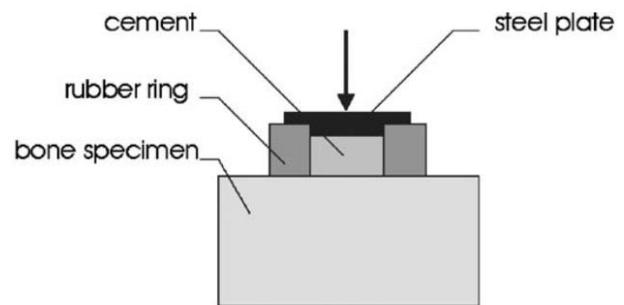
Figure 5 - Experimental setup used to pressurize the bone–cement

interface was selected for further processing. using two-level threshold, the domains of marrow, cement and bone were identified and segmented and 3-D computer model of bovine cancellous bone were created by assigning different colors to the bone, cement and marrow domain which is shown in Figure 6. Using Abaqus Software, the transient temperature problem formulated in the equations above, was calculated. The finite element model consists of 27% bone tissue, 29% cement and 44% bone marrow.
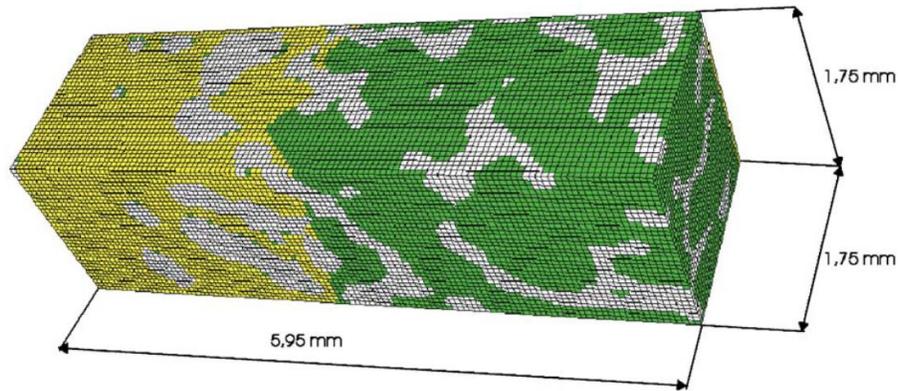
Figure 6 - The 3-D model of the bone–cement interface. White denotes bone, yellow (light gray) is cement and green (dark gray) is void and marrow

Following initial and boundary condition were applied to solve the finite element model.

$$T|_{t=0}(\mathbf{x}) = 300 \text{ K}, \qquad w|_{t=0}(\mathbf{x}) = 0.01.$$

Adiabatic condition $\frac{\partial T}{\partial n} = 0$ is applied on all the walls perpendicular to the interface and leftmost wall where assumed to be position at the center of the cement mantle where the peak temperature is reached; on the other hand, free convection condition is applied on the rightmost wall. $\lambda \frac{\partial T}{\partial n} = h(T_0 - T)$ where $T_0 = 310 \, K$ and $h = 5 \, W/m^2 K$. Approximately it took 52 hour to solve the finite element model.

Paper 3: Key Results and Conclusion

The simulation results have confirmed that modelling the bone microstructure is indeed essential for accurate calculation of the temperature and monomer leftover profiles. Figure 7 shows the temperature and polymerization fraction distribution in the bone and cement domain . The results demonstrated that temperatures in the cement embedded trabeculae regions were much higher than those in the bone-marrow region adjacent to the bone-cement interface; furthermore, the bone tissue with highest temperature is also subjected to high leftover monomer concentration. The summary of results is described as below:

(a)   (b)
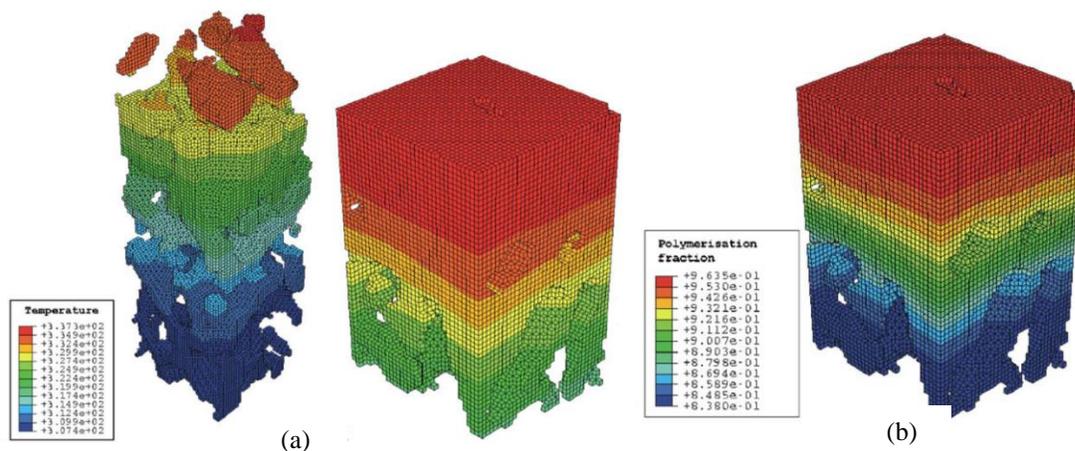
Figure 7 – (a) Temperature distribution when reaching the peak temperature in the bone (at t=112 s). Left: Bone domain. Right: Cement domain. (b) polymerization fraction distribution in the cement domain

- The peak bone temperature was reached at t=112 s and it has shown that maximum temperature in the bone or cement (337 K) is much higher than temperature in the bone/marrow region (307 K). From

Figure 8, it can be seen that all the bone is exposed to a temperature higher than 45°C from t=140 s until the end of analysis; however only 10% of the bone were subjected to temperatures higher than 70° C and dwell time to these high temperatures is 50s.

- At t=300 s the polymerization has completed and it has shown that polymerization fraction has increased between t=70 and 100s; furthermore, cement polymerization fraction is 96% in the centre which is higher than that in the region near the bone (84%) which demonstrated that polymerization at the centre of the cement occurs earlier and is more complete that that near the bone interface.
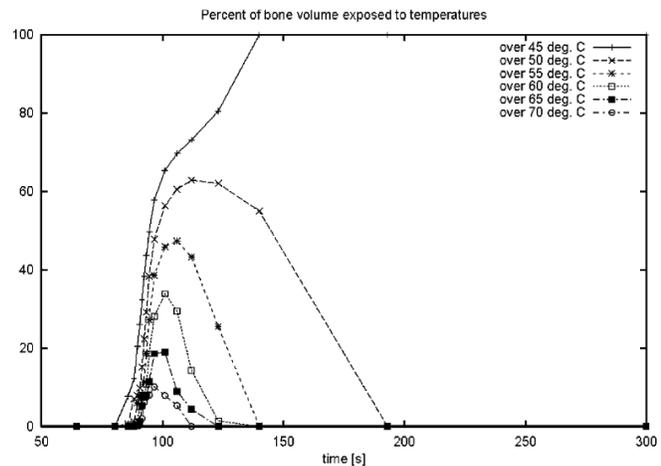
Figure 8 - Percentage of tissue exposed to a temperature exceeding each of the 6 indicated levels

Analysis and Relevance

I have reviewed three papers on the subject of temperature evaluation of bone cement polymerization during vertebraplasty which can be also a valuable asset for thermal analysis of femoroplasty. First two papers measure and evaluate in vitro and vivo temperatures during bone cement polymerization in which we utilize similar in vitro measurement to evaluate temperature during bone cement polymerization in femoroplasty. For each of injection experiments, we have recorded surface temperature of the bone using three k-type thermocouples placed at neck, greater trochanter and trochanteric crest for femur. Thermal evaluation of these two paper also suggested that thermal damage to the intraosseous neural tissue may not be excluded as a potential mechanism in the clinical results of PV such as pain relief; however, it does not consider explicitly as a main factor either. On the other hand, augmentation of osteoporotic femoral neck, femoroplasty, utilizes a larger volume of PMMA, consequently inducing greater temperature gradients and a higher risk of thermal necrosis to surrounding tissue; therefore, the effects of bone cement injection causing risk of thermal necrosis must be taken into consideration. Overall these papers develop an informative insight to measurement and evaluation of bone cement polymerization during procedures of bone augmentation; on the other hand, in vitro measurements may not be completely accurate due to the fact that the injection of 10 cc cement is not conducted at the same time and vivo temperature were not matched by histologic findings. It would also be beneficial to include more detail for the patients that underwent the PV.

It has been reported that thermal necrosis due to high heat generation during polymerization and chemical necrosis due to unreacted monomer release are considered as major complications of the cementation procedure. In the third paper, the finite element (FE) modeling scheme for distribution of temperature and monomer leftover after cementation have been developed to investigate the significance consequences of PMMA cementation. Similar to this study, we have aimed to develop the heat transfer finite element model capable of bone temperature estimation prior to augmentation during bone cement polymerization in femoroplasty. We will use the method described here to segment bone and cement as homogeneous continuum materials and simulate the heat transfer model using temperature field equations. Unlike other previous simulations models, this paper provided a realistic temperature dependent polymerization FE model that can account for the micro-structure of cancellous bone; however, it is not clear that the bone-

cement interface model can be relied for cemented implants or after vertebroplasty since the cement was placed directly on bone surface and scanned afterwards to create 3D finite element model. This paper has also increased the accuracy of the FE model by separating the bone and marrow and assigning different mechanical and thermal properties to each element group, but the model can be further improved by using inhomogeneous elements to reflect the real bone more truly. Moreover, all this three papers were well written in describing the workflow of experiments and simulation.

Reference:

[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] Deramond, H., N. T. Wright, and Stephen M. Belkoff. "Temperature elevation caused by bone cement polymerization during vertebroplasty." *Bone* 25.2 (1999): 17S-21S.

[5] Anselmetti, Giovanni Carlo, et al. "Temperature measurement during polymerization of bone cement in percutaneous vertebroplasty: an in vivo study in humans." *Cardiovascular and interventional radiology* 32.3 (2009): 491-498.

[6] Stańczyk, M., and B. Van Rietbergen. "Thermal analysis of bone cement polymerisation at the cement–bone interface." *Journal of biomechanics* 37.12 (2004): 1803-1810.