

# On stabilization of loosened hip stems via cement injection into osteolytic cavities

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## ABSTRACT

**Background:** Cement injection into osteolytic areas around the cement mantle is a technique for refixation of loose hip implants for patients who cannot undergo standard revision surgery. Preliminary clinical results show the improvement in walking distance, patients' independence and pain relief.

**Methods:** In this study, we use a detailed finite element model to analyze whether cement injection into osteolytic areas contributes to the overall implant stability. We study the effect of various factors, like location and size of osteolytic areas, interface conditions and bone stiffness on bone–cement relative motion.

**Findings:** Presented results demonstrate that the procedure is most effective for the osteolytic areas located in the proximal region of the femur, while factors like a thin layer of residual fibrous tissue around the injected cement, that was not removed during the surgery, combined with reduced bone stiffness reduce the efficiency of the procedure.

**Interpretation:** Cement injection is able to stabilize loosened hip prostheses. However, it is important to remove the fibrous tissue layer completely, as even a thin layer will negatively influence stabilization. We will focus our research efforts on developing fibrous tissue removal techniques in order to optimize this minimally invasive treatment.

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## 1. Introduction

Annually, 154 out of 100,000 population receive cemented and uncemented hip replacement (OECD, 2011). It is believed that this number is going to increase due to longer life expectancy in our aging society. Additionally, this number grows as hip replacement is performed for younger patients. However, within 10 years after primary hip replacement 6–15% of the patients will require revision surgery because of the implant loosening (Hailer et al., 2010).

In case of cemented prosthesis, discussed in this work, loosening starts from debonding at the bone cement interface and subsequent inflammation, caused by polyethylene, cement and metal wear debris (Goldring et al., 1983). Next, inflammation causes bone resorption and formation of a synovium-like fibrous tissue at the interface. Due to very low stiffness of this interface tissue, the implant rotates and migrates into the endosteal medullary canal of the femur which in turn causes pain.

At present, patients with loosened prostheses undergo revision surgery, where the prosthesis, cement and the interface tissue are removed and a new prosthesis is implanted. This is an extensive and

demanding procedure with subsequent blood loss and an infection risk that is substantially higher as compared to primary surgery (Mahadevan et al., 2010; Ong et al., 2009). Patients with severe comorbidity, e.g. angina pectoris, obstructive pulmonary disease or prior myocardial infarction, have a high risk for major complications and are therefore not eligible for revision surgery. In this patient group, revision surgery leads to complications in 51% of the cases and to patient death in 20% of the cases (Donati et al., 2004; Strehle et al., 2000).

A number of studies attempt a non-invasive treatment of prosthesis loosening. They involve inhibition of inflammatory processes within the joint aimed at prevention or slowing of peri-prosthetic osteolysis (Carmody et al., 2002; Sud et al., 2001; Yang et al., 2002). In our group, an approach was developed (de Poorter et al., 2006, 2008) that uses percutaneous gene therapy in order to destroy the interface tissue and subsequently stabilize the prosthesis. The procedure is performed in three steps: injection of a viral vector; injection of a prodrug aimed at killing the infected cells; rinsing the osteolytic cavities with water and refixation of the hip prosthesis with percutaneous bone cement injection under radiological guidance (Fig. 1). The procedure resulted in the improvement in walking distance, patients independence and pain relief.

Despite the promising results with the above non-invasive treatment, important questions remain unanswered. Similar to vertebroplasty, where cement injection is used to treat vertebral osteoporotic fractures

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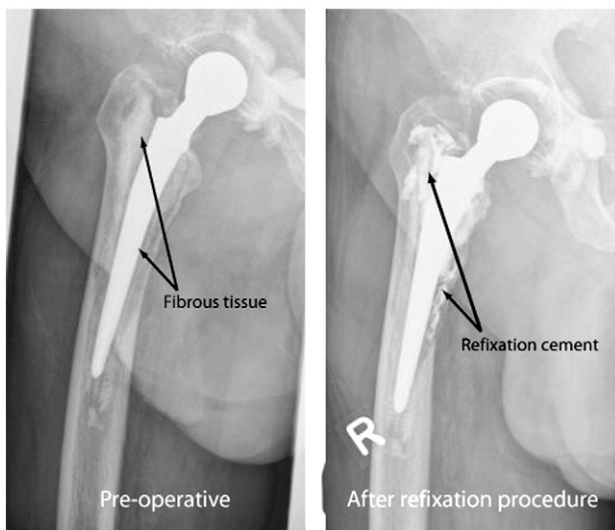


Fig. 1. Example of radiographic results before and after cement injection.

(Kallmes, 2009), the exact mechanism of action of the cement in achieving pain relief is yet unclear. Whether or not the pain relief correlates with mechanical stabilization has to be studied.

There are many experimental as well as simulation based studies that address stability of uncemented implants (Reggiani et al., 2008; Pettersen et al., 2009; Ong et al., 2009). The stability of the cemented implants, or more specifically, the stability of the cement mantle is a far less studied topic, since in most studies the cement bone interface is assumed fully bonded. This does make sense in the view of experimental studies that show quite small (5–15  $\mu\text{m}$ ) bone–cement relative micromotions (Choi et al., 2010). Nonetheless, there are experimental in-vitro studies (Ebramzadeh et al., 2004; Sangiorgio et al., 2004) that show maximum bone–cement micromotions in the range of 62–138  $\mu\text{m}$ , which is higher than the threshold of 50  $\mu\text{m}$  above which interface fibrous tissue might develop (Søballe et al., 1992). Additionally, recent studies in the microstructure of bone–cement interface (Janssen et al., 2008) suggest friction like interaction, rather than adhesion. The lack of stability of the bone–cement interface was in particular observed in case of the patients admitted for the above mentioned cement injection procedure using fluoroscopy.

In this work, we present a biomechanical analysis of the above hip implant refixation procedure. Using a detailed finite element model we analyze the stability of the cement mantle before and after cement injection. We present results for different configurations of osteolytic areas, material properties and interface conditions.

## 2. Methods

A detailed finite element model of the femur was built based on the geometry of the CT data, obtained from a 76 year old male donor without an implant. First the CT images were manually segmented to obtain slice per slice bone contours and then triangulated surfaces of the femur were generated. The final linear tetrahedral mesh (Fig. 2) with an average element size of 1.2 mm at the bone–cement interface was generated with MSC Patran 2007 (MSC Software, Palo Alto, USA). The analysis was performed using MSC Marc 2008. The quality of the mesh was evaluated by reducing the mesh size at the bone–cement interface twice. The resulting relative interface micromotion of the refined model increased 5.4%. The virtual placement of the hip stem was done according to the surgical manual. A Stanmore Standard Modular Femoral Stem was used (Biomet, Warsaw, USA). Geometry of the cement mantle around the implant was created under supervision of an experienced orthopedic surgeon based on the application of rasp, used to prepare the bone. Three

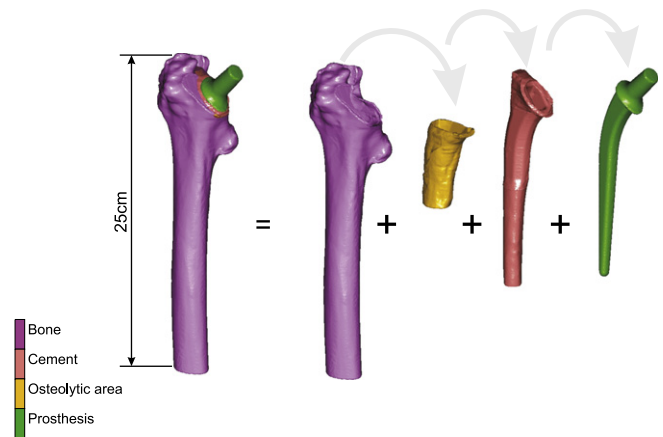


Fig. 2. Finite element meshes of the implanted femur (element edges not shown). The model consists of a femur, which contains cement mantle, which, in its turn, contains the prosthesis. Osteolytic area is located on the bone–cement interface.

geometrical configurations of the osteolytic areas were built (Fig. 3) based on Garcia-Cimbrelle et al. (1997).

The material properties of bone were obtained by a procedure, similar to Gupta et al. (2004). The CT gray value ( $H$ ) was linearly calibrated in terms of apparent density ( $\rho$ ) using the CT numbers for water, i.e. 0, corresponding to bone density of 0  $\text{g}/\text{cm}^3$  and the maximum measured CT gray value of 3375, corresponding to cortical bone. The latter gray value was assigned bone density of 1.42  $\text{g}/\text{cm}^3$ , which according to (Högler et al., 2003) corresponds to average cortical bone density of young adults. The resulting linear interpolation is

$$\rho = 4.2 \times 10^{-4} H. \quad (1)$$



Fig. 3. Three geometries of the osteolytic areas (dark gray) around the cement mantle (light gray). Left–proximal, center–medial, right–distal configurations. The volume of the osteolytic areas is 11.7 mL for the proximal, 15.8 mL for the medial and 8.6 mL for the distal configurations.

Young's modulus of bone was prescribed using the freeware program BoneMat (Taddei et al., 2004; Zannoni et al., 1998). The program calculated the apparent density ( $\rho$ ) for each element using Eq. (1) and assigned corresponding Young's modulus value ( $E$ ) based on the following relation (Keller, 1994):

$$E = 10.5\rho^{2.57}. \quad (2)$$

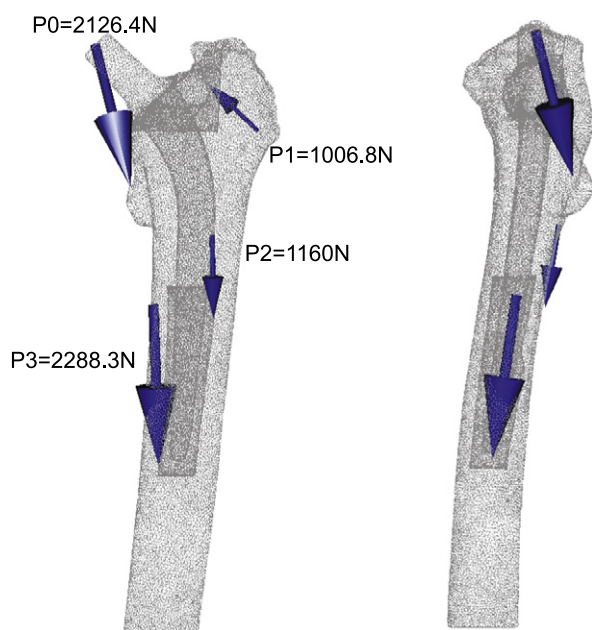
Poisson's ratio of all bone elements was set to 0.3. The properties of the cement mantle were: Young's modulus 2.28 GPa, Poisson's ratio 0.3 (Murphy and Prendergast, 1999). In order to simulate the situation before the refixation, the elastic properties of the osteolytic area were taken as those of fibrous tissue, with Young's modulus 2 MPa and Poisson's ratio 0.167 (Hori and Lewis, 1982). The situation after the refixation was modeled with osteolytic areas having elastic properties of cement.

Boundary conditions simulate a single ramp application of stair climbing load as was measured by Heller et al. (2005). The choice of these loading conditions was based on the results of Pancanti et al. (2003), who concluded that stair-climbing produces the worst conditions for bone in-growth for a femoral component. Hip contact, abductor, vastus lateralis and vastus medialis muscle forces were applied based on the body weight of 847 N (Fig. 4). The displacements of the lower part of the model were fixed.

Contact settings in the models were set similar to Abdul-Kadir et al. (2008). In particular contact zone size was set to 0.025 mm, and in case when friction was modeled, the transition from stick to slip was set to 150  $\mu\text{m}$  while friction coefficient was set to 0.4 for both bone–cement and implant–cement interfaces.

In order to simulate a very thin layer of fibrous tissue or a gap at the bone–cement interface, a numerical technique, described by Viceconti et al. (2001) was used. This technique does not involve a direct modeling of the gap, but rather a modification of the contact area which forces the contact algorithm to behave as if the contact bodies did not fully fit to each other.

All the patients who received the cement injection procedure are of a very senior age (around 80 years old). Ding et al. (1997) and Ding et al. (2001) report around 40% reduction in tibial cancellous



**Fig. 4.** Loading conditions, simulating stair climbing (Heller et al., 2005). P0—hip contact force; P1—cumulative force of ilio-tibial tract (proximal and distal parts) and tensor fascia latae (proximal and distal parts); P2—vastus lateralis; P3—vastus medialis. The lower part of the model is fixed (not shown).

bone stiffness for patients of senior age or patients with osteoarthritis. Additionally, it is known (Blain et al., 2008) that osteoarthritis, osteoporosis and especially osteolysis correlate with thinning of cortex. Given this data we studied the effect of the reduced bone stiffness by reducing the Young's modulus of all bone elements by 40%.

Fourteen models were created for each of the three osteolytic area configurations (Fig. 3),—five that study the pre-operative situation and the other nine study the situation after cement injection.

The first pre-operative model (“original”) assumes that osteolytic areas are filled with fibrous tissue that is connected to both, bone and the existing cement; bone stiffness is as in Eq. (2); no friction at the interfaces. The second pre-operative model is like the original, but the bone stiffness is reduced 40%. The third model is like the original, but friction at the bone–cement (old cement) interface is assumed. The fourth model differs from the original by the presence of friction at the cement–implant interface. The fifth model studies the effect of lytic area thickness, by replacing the whole lytic area with a very thin (0.5 mm) fibrous tissue layer. Given that this thickness is below the resolution of the mesh (element size 1.2 mm) we use the above mentioned technique from Viceconti et al. (2001): the original lytic area is filled with bone material, which is connected to the rest of the bone (as if there is no lytic area) and instead there is a 0.5 mm gap at the original lytic area–cement interface that simulates a thin layer of fibrous tissue; no friction is assumed at the interfaces.

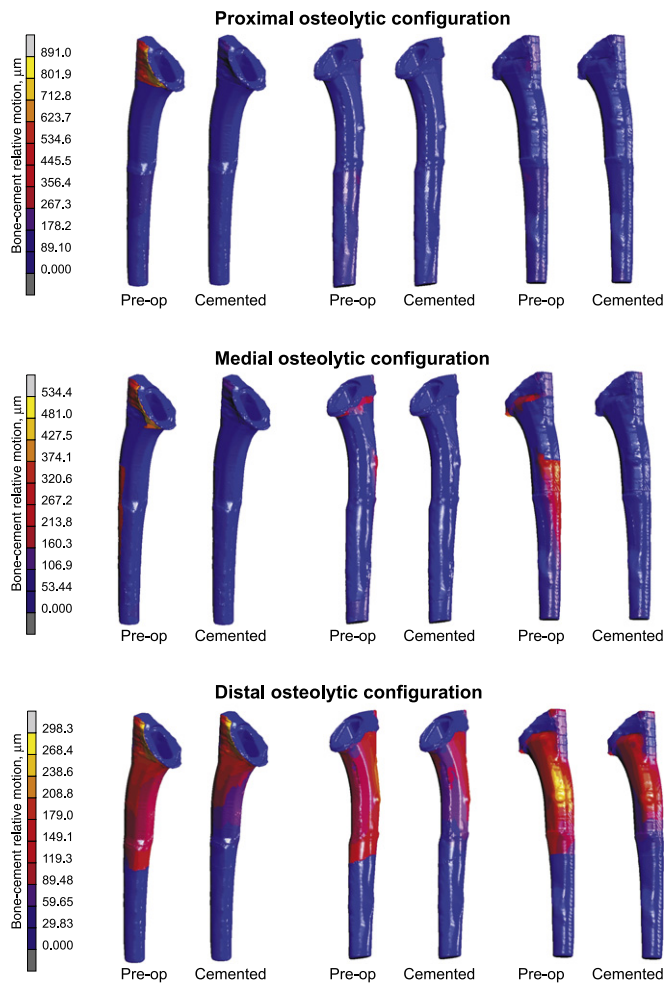
The first post-operative model is identical to the original pre-operative model, except lytic area is filled with cement (lytic area is assigned cement properties) which is connected to the bone and the old cement. The second model differs from the first due to 40% reduced bone stiffness. The third and the fourth differ from the first by the presence of friction at correspondingly bone–cement and implant–cement interfaces (only the old cement, not the newly injected cement in the lytic areas). The fifth model simulates a post-operative scenario for the fifth pre-operative model by removing the gap and bonding the lytic area (which is still filled with bone material) to the old cement. The sixth model differs from the first post-operative model by de-bonding the newly injected cement (in lytic areas) from the bone and the old cement. The seventh is like the sixth, but a 100  $\mu\text{m}$  gap surrounds the newly injected cement. The eighth model simulates unbonded newly injected cement while bone stiffness is reduced 40%. The ninth model simulates the most pessimistic scenario, when the newly injected cement is unbonded, surrounded by a 100  $\mu\text{m}$  gap while bone stiffness is reduced 40%. Table 1 presents a summary of all 14 models. Forty two models in total were created (14  $\times$  3 configurations). Results are presented in terms of relative micromotions at the bone–cement mantle interface. Hence, micromotions between the newly injected cement and the bone are not shown, as those cannot be compared to the preoperative situation. In this study the relative interface micromotions were computed as a magnitude of absolute relative displacement between the surfaces, similar to Pancanti et al. (2003). Given that in the unloaded state the surface nodes at the bone–cement mantle interface were collocated, the interface micromotions were quantified as a distance between those nodes calculated after the loading was applied.

### 3. Results

Fig. 5 shows distribution of the interface micromotions along the surface of the cement mantle before and after cement injection for the most optimistic scenario, when cement, injected into the osteolytic areas, is rigidly connected to bone. Comparison of preoperative cases shows that osteolytic area in the proximal region causes the highest micromotions, followed by the case with osteolytic areas in the medial and then distal regions. Inspection of the post-operative cases shows that cement injection into proximal region also has the highest effect (approximately four times) on the reduction of micromotions as

**Table 1**  
Summary of fourteen models that were created for each of the three osteolytic configurations.

N	Short model name	Osteolytic area content	Bone stiffness	Bone–cement friction	Cement–implant friction	Ost. area conn. to bone?	Ost. area conn. to cement?	Gap at Ost. area–bone int. (mm)	Gap at Ost. area–cement int. (mm)
<i>Pre-operative models</i>									
1	Original	Fibrous	Normal	–	–	+	+	–	–
2	Soft bone	Fibrous	–40%	–	–	+	+	–	–
3	Bone–cement friction	Fibrous	Normal	+	–	+	+	–	–
4	Implant–cement friction	Fibrous	Normal	–	+	+	+	–	–
5	No lytic	Bone	Normal	–	–	+	–	–	0.5
<i>Post-operative models</i>									
1	Cemented original	Cement	Normal	–	–	+	+	–	–
2	Cem. soft bone	Cement	–40%	–	–	+	+	–	–
3	Cem. bone–cement friction	Cement	Normal	+	–	+	+	–	–
4	Cem. implant–cement friction	Cement	Normal	–	+	+	+	–	–
5	Cem. no lytic	Bone	Normal	–	–	+	+	–	–
6	Cem. cement unbonded	Cement	Normal	–	–	–	–	–	–
7	Cement unbonded and gap	Cement	Normal	–	–	–	–	0.1	0.1
8	Cement unbonded and soft bone	Cement	–40%	–	–	–	–	–	–
9	Cement unbonded, soft bone and Gap	Cement	–40%	–	–	–	–	0.1	0.1



**Fig. 5.** Interface micromotions for the original (pre-operative number 1 in Table 1) and cemented original (post-operative number 1) models for each of the osteolytic configurations from three different views (hence three views for the same pre-op model and three views for the same post-op model for each configuration).

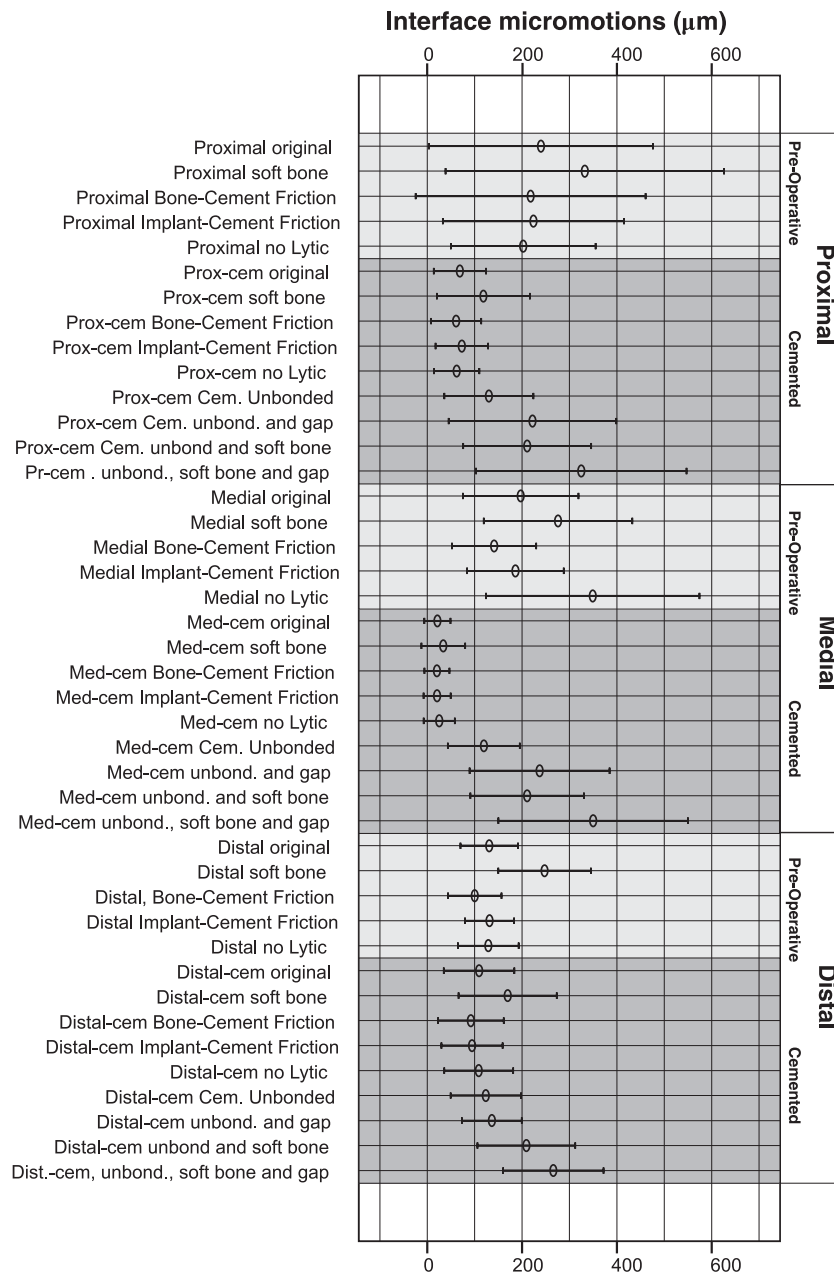
compared to the preoperative cases. Cement injection into the osteolytic area located in the distal region did not contribute to the reduction of micromotions.

Fig. 6 shows a summary of micromotions for all 42 models (14 for each of the 3 geometric configurations) presented as standard deviation intervals around the mean for each model. Here we use a statistical method to present a summary of spatial distributions of micromotions, although no statistical information is present in these results. These results also confirm that preoperatively proximal configuration has the highest micromotions and that refixation of the proximal configuration has the highest relative effect on the reduction of the micromotions. Reducing bone stiffness somewhat increases micromotions in the preoperative cases, but they can be reduced with successful cement injection (in the ideal situation where cement is bonded to bone) in proximal and medial configurations. Reducing the size of osteolytic areas (as studied by “no Lytic” models) causes reduction of micromotions for the proximal configuration, while it has no such effect on the medial and distal configurations. All the models with injected cement not connected to bone have higher micromotions while additional presence of a thin (0.1 mm) gap around newly injected cement increases the micromotions even further as compared to the models without gaps (although the micromotion levels are still mostly below the pre-operative levels). Models that study simultaneous effect of the reduced bone stiffness and a thin gap around newly injected cement show micromotions almost equivalent to the preoperative levels.

#### 4. Discussion

In this work, we present a biomechanical analysis of hip implant refixation procedure. Using a detailed finite element model we investigated whether injection of cement into osteolytic areas around cement mantle contributes to the overall implant stability. We used a number of modifications of the finite element model to study the effect of various factors, like location and size of osteolytic areas, interface conditions and bone stiffness on the relative motion between bone and the cement mantle.

The main limitation of the study is the fact that only one femur geometry was used. Viceconti et al. (2006) showed that, for instance, femur size has a significant effect on the level of bone–implant micromotions.



**Fig. 6.** Interface micromotions for all models (see Table 1 for the full description of the models) presented by standard deviation intervals around the mean. The intervals summarize only spatial distribution of micromotion, no statistical data is presented.

However, the conclusions of this work are not based on the absolute levels of the calculated micromotions, but rather on the comparison between pre- and post-operative situations. We find it logical to assume that this comparison is less sensitive to the model size than the absolute levels of micromotions. Additionally, in this work we study the sensitivity of the model to the variations that can be caused by either patient variability or specific surgical techniques. Another limitation of the study is that we considered only one type of loading, based on stair climbing. Perhaps, this type of activity is not very typical for the very senior patients who undergo refixation procedure, however it is considered as a worst case scenario which allows to obtain a conservative estimation. And, again, given that we draw our conclusion only based on the comparison between pre- and post-operative situations, this type of loading can be considered appropriate.

The level of micromotions in our study (up to 1 mm) can be compared to the levels obtained by Ong et al. (2009). That work studies uncemented stems subjected to stair climbing based loading, while

bone-implant interface conditions are assumed similar to the conditions at the bone-cement interface, used in our models. Additionally, the results of our work show the same effect of bone stiffness as Wong et al. (2005), who observed higher implant stability in case of stiffer bone.

The results of the study allow for several conclusions. First, cement injection into proximal area has the highest effect on micromotion reduction as compared to medial and especially distal areas. In fact, even in case of the best possible outcome of the surgery (the ideal case, when cement firmly bonds to bone) cement injection into the osteolytic area located distally does not reduce micromotions caused by stair climbing. Second, reduced bone stiffness is a reason for increased micromotions, but these micromotions can be substantially reduced if good connection between bone and cement, injected into osteolytic area in proximal region can be established. Third, size of an osteolytic area does not always have a negative effect on the micromotions; for instance, smaller osteolytic area causes smaller

micromotions if located in proximal region, larger micromotions if located in medial region and has almost no effect if located in distal region. Fourth, lack of connection between the newly injected cement and bone has a very negative effect on the refixation procedure. And last, cement injection has almost no effect on the reduction of micromotions in case of reduced bone stiffness (like in severe cortical bone thinning or even cortical bone defects) and simultaneous presence of even a thin fibrous tissue layer around the newly injected cement.

### Conflict of interest statement

None of the co-authors of the manuscript has a financial or personal relationship that could inappropriately influence this work.

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### References

- Abdul-Kadir, M.R., Hansen, U., Klabunde, R., Lucas, D., Amis, A., 2008. Finite element modelling of primary hip stem stability: the effect of interference fit. *J. Biomech.* 41, 587–594.
- Blain, H., Chavassieux, P., Portero-Muzy, N., Bonnel, F., Canovas, F., Chammas, M., 2008. Cortical and trabecular bone distribution in the femoral neck in osteoporosis and osteoarthritis. *Bone* 43, 862–868.
- Carmody, E.E., Schwarz, E.M., Puzas, J.E., Rosier, R.J., O'Keefe, R.N., 2002. Viral interleukin-10 gene inhibition of inflammation, osteoclastogenesis, and bone resorption in response to titanium particles. *Arthritis Rheum.* 46, 1298–1308.
- Choi, D., Park, Y., Yoon, Y.S., Masri, B.A., 2010. In vitro measurement of interface micromotion and crack in cemented total hip arthroplasty systems with different surface roughness. *Clin. Biomech.* 25, 50–55.
- de Poorter, J., Hoeben, R.C., Hogendoorn, S., Mautner, V., Ellis, J., Obermann, W.R., et al., 2008. Gene therapy and cement injection for restabilization of loosened hip prostheses. *Hum. Gene Ther.* 19, 83–96.
- de Poorter, J.J., Obermann, W.R., Huizinga, T.W.J., Nelissen, R.G.H.H., 2006. Arthrography in loosened hip prostheses. Assessment of possibilities for intra-articular therapy. *Joint Bone Spine* 73, 684–690.
- Ding, M., Dalstra, M., Danielsen, C.C., Kabel, J., H.I., Linde, F., 1997. Age variations in the properties of human tibial trabecular bone. *J. Bone Joint Surg. Br.* 79-B, 995–1002.
- Ding, M., Danielsen, C.C., Hvid, I., 2001. Bone density does not reflect mechanical properties in early-stage arthrosis. *Acta Orthop. Scand.* 72 (2), 181–185.
- Donati, A., Ruzzi, M., Adario, E., Pelaia, P., Coluzzi, F., Gabbanelli, V., et al., 2004. A new and feasible model for predicting operative risk. *Br. J. Anaesth.* 93, 393–399.
- Ebramzadeh, E., Sangiorgio, S.N., Longjohn, D.B., Buhari, C.F., Dorr, L.D., 2004. Initial stability of cemented femoral stems as a function of surface finish, collar, and stem size. *J. Bone Joint Surg.* 86, 106–115.
- García-Cimbrelo, E., Madero, R., Blasco-Alberdi, A., Munuera, L., 1997. Femoral osteolysis after low-friction arthroplasty. *J. Arthroplasty* 12 (6), 624–634.
- Goldring, S.R., Schiller, A.L., Roelke, M., Rourke, C.M., O'Neill, D.A., Harris, W.H., 1983. The synovial-like membrane at the bone–cement interface in loose total hip replacements and its proposed role in bone lysis. *J. Bone Joint Surg. Am.* 65, 575–584.
- Gupta, S., van der Helm, F.C.T., Sterk, J.C., van Keulen, F., Kaptein, B., 2004. Development and experimental validation of a three dimensional finite element model of the human scapula. *Proc. Inst. Mech. Eng. H* 218, 127–142.
- Hailer, N.P., Garellick, G., Kärrholm, J., 2010. Uncemented and cemented primary total hip arthroplasty in the Swedish hip arthroplasty register. *Acta Orthop.* 81, 34–41.
- Heller, M.O., Bergmann, G., Kassi, J.-P., Claes, L., Haas, N.P., Duda, G.N., 2005. Determination of muscle loading at the hip joint for use in pre-clinical testing. *J. Biomech.* 38, 1155–1163.
- Högler, W., Blimkie, C.J.R., Cowell, C.T., Kemp, A.F., Briody, J., Wiebe, P., et al., 2003. A comparison of bone geometry and cortical density at the mid-femur between pre-puberty and young adulthood using magnetic resonance imaging. *Bone* 33, 771–778.
- Hori, R., Lewis, J., 1982. Mechanical properties of the fibrous tissue found at the bone cement interface following total joint replacement. *J. Biomed. Mater. Res.* 16, 911–927.
- Janssen, D., Mann, K.A., Verdonschot, N., 2008. Micro-mechanical modeling of the cement–bone interface: the effect of friction, morphology and material properties on the micromechanical response. *J. Biomech.* 41, 3158–3163.
- Kallmes, D.F., 2009. Vertebroplasty and kyphoplasty. *Bone* 44 (Supplement 1), S46.
- Keller, T.S., 1994. Predicting the compressive mechanical behaviour of bone. *J. Biomech.* 27, 1159–1168.
- Mahadevan, D., Challand, C., Keenan, J., 2010. Revision total hip replacement: predictors of blood loss, transfusion requirements, and length of hospitalisation. *J. Orthop. Traumatol.* 11, 159–165.
- Murphy, B.P., Prendergast, P.J., 1999. Measurement of non-linear microcrack accumulation rates in polymethylmethacrylate bone cement under cyclic loading. *J. Mater. Sci.* 10, 779–781.
- Ong, K.L., Day, J.S., Manley, M.T., Kurtz, S.M., Geesink, R., 2009. Biomechanical comparison of 2 proximally coated femoral stems. *J. Arthroplasty* 24 (5), 819–824.
- Pancanti, A., Bernakiewicz, M., Viceconti, M., 2003. The primary stability of a cementless stem varies between subjects as much as between activities. *J. Biomech.* 36, 777–785.
- Pettersen, S.H., Wik, T.S., Skallerud, B., 2009. Subject specific finite element analysis of implant stability for a cementless femoral stem. *Clin. Biomech.* 24, 480–487.
- Reggiani, B., Cristofolini, L., Taddei, F., Viceconti, M., 2008. Sensitivity of the primary stability of a cementless hip stem to its position and orientation. *Artif. Organs* 32 (7), 555–560.
- Sangiorgio, S.N., Ebramzadeh, E., Longjohn, D.B., Dorr, L.D., 2004. Effects of dorsal flanges on fixation of a cemented total hip replacement femoral stem. *J. Bone Joint Surg. Am.* 86, 813–820.
- Søballe, K., Hansen, E.S., Rasmussen, H.B., Jørgensen, P.H., Bunger, C., 1992. Tissue ingrowth into titanium and hydroxyapatite-coated implants during stable and unstable mechanical conditions. *J. Orthop. Res.* 10, 285–299.
- Strehle, J., DelNotaro, C., Orler, R., Isler, B., 2000. The outcome of revision hip arthroplasty in patients older than age 80 years. *J. Arthroplasty* 15, 690–697.
- Sud, S., Yang, S.Y., Evans, C.H., Robbins, P.D., Wooley, P.H., 2001. Effects of cytokine gene therapy on particulate-induced inflammation in the murine air pouch. *Inflammation* 25, 361–372.
- Taddei, F., Pancanti, A., Viceconti, M., 2004. An improved method for the automatic mapping of computed tomography numbers onto finite element models. *Med. Eng. Phys.* 26, 61–69.
- OECD, 2011. *OECD Indicators: Health at a Glance*. <http://dx.doi.org/10.1787/888932524754>.
- Viceconti, M., Brusi, G., Pancanti, A., Cristofolini, L., 2006. Primary stability of an anatomical cementless hip stem: a statistical analysis. *J. Biomech.* 39, 1169–1179.
- Viceconti, M., Monti, L., Muccini, R., Bernakiewicz, M., Toni, A., 2001. Even a thin layer of soft tissue may compromise the primary stability of cementless hip stems. *Clin. Biomech.* 16 (765–775).
- Wong, A.S., New, A.M.R., Isaacs, G., Taylor, M., 2005. Effect of bone material properties on the initial stability of a cementless hip stem: a finite element study. *Proc. Inst. Mech. Eng. H* 219, 265–275.
- Yang, S.Y., Mayton, L., Wu, B., Goater, J.J., Schwarz, E.M., Wooley, P.H., 2002. Adeno-associated virus-mediated osteoprotegerin gene transfer protects against particulate polyethylene-induced osteolysis in a murine model. *Arthritis Rheum.* 46, 2514–2523.
- Zannoni, C., Mantovani, R., Viceconti, M., 1998. Material properties assignment to finite element models of bone structures: a new method. *Med. Eng. Phys.* 20 (10), 735–740.