



Comparison of Ho:YAG laser and coblation for interface tissue removal in minimally invasive hip refixation procedures

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ABSTRACT

Aseptic loosening is the major failure mode for hip prostheses. Currently, loosened prostheses are revised during open surgery. Because of a high complication rate, this demanding procedure cannot be performed in patients with a poor general health. We are developing an alternative minimally invasive refixation procedure that leaves the prostheses in place, but relies on removing the interface membrane and replacing it with bone cement.

The aim of this study was to evaluate two interface tissue removal techniques – Ho:YAG laser and coblation – based on two criteria: thermal damage and the ablation rate.

In vitro a loosened hip prosthesis was simulated by implanting a prosthesis in each of 10 cadaver femora. Artificially created peri-prosthetic lesions were filled with chicken liver as an interface tissue substitute. We measured temperatures *in vitro* at different radial distances from the site of removal. Temperatures during removal were recorded both inside the interface tissue and in the surrounding bone.

This study demonstrated that temperatures generated in the bone do not result in thermal damage (increasing less than 10 °C relative to body temperature). Temperatures inside the interface tissue are sufficiently high to destroy the interface tissue ($T > 50$ °C, duration > 1 min). Using laser instead of coblation for the removal of interface tissue resulted in higher temperatures – thus a faster removal of interface tissue. This is in accordance with the ablation rate test.

Ho:YAG laser is advantageous compared to coblation. We consider Ho:YAG laser a promising tool for interface tissue removal.

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1. Introduction

Worldwide about 1.5 million hip prostheses are implanted annually and this number is growing as people live longer [1]. Within the first ten post-operative years, approximately 10% of these hip prostheses fail because of aseptic loosening [2]. A loosened hip prosthesis is typically surrounded with pockets filled with soft interface tissue which has negligible stiffness and does not provide mechanical stability. During the loosening process bone is resorbed and large displacements of the prosthesis relative to the host bone may occur [3]. This results in very limited functionality and intense pain which makes patients with loosened hip prostheses socially isolated due to decreased ambulation.

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Presently patients can only be treated by complete removal of the loosened prosthesis and interface tissue and insertion of a new prosthesis during open revision surgery. This procedure is highly demanding for the patient as well as the surgeon. In patients with poor general health the complication rate is high, with up to 60% complications in the ASA 3 patient category for elective surgery [4]. For these patients, there is a need for a less invasive alternative to open revision surgery. The first minimally invasive technique used to refixate loosened hip prosthesis was a biological approach in combination with bone cement injection [5,6]. Percutaneous gene therapy was used for interface tissue removal and the resulting cavity filled with bone cement by cement injection. Although these phase 1 and phase 2 studies showed promising results, gene therapy is still experimental and limited to academic centers. For this reason a minimally invasive surgical refixation procedure was proposed. As this new procedure removes interface tissue in a non-biological way, it requires the development of a new surgical instrument, which has to gain access to the periprosthetic area and remove the interface tissue.

Two possible removal techniques were of interest: a Ho:YAG laser and coblation. Laser destroys tissue by transferring photon energy to focused heat as it is absorbed, leading to micro-explosions in tissue cells. Coblation uses high voltage bipolar radiofrequency energy to generate a plasma field which breaks organic molecular bonds to vaporize tissue. During the removal of interface tissue care must be taken. If the temperature in surrounding bone becomes too high, it will result in thermal necrosis; this complication must be avoided. Studies on thermal damage [7–10] indicate that a relationship exists between the rate of thermal damage and temperature. If temperature is above 43 °C, reaction rates double in some cell lines with each further 1 °C increase in temperature [8]. In other words, a temperature level of 49 °C for 2 min may have the same effect as 50 °C for 1 min, or exposure to 51 °C for 1 min may cause twice the damage as 50 °C during the same time interval. This is an advantage when tissue has to be removed since higher temperature will result in a higher ablation rate. Ablation rate is defined as the amount of interface tissue removed in gram per minute. Thermal necrosis in bone occurs when it is exposed to temperatures above 50 °C for more than 1 min [11–13]. De Vrind et al. [14] reported injury to sensory nerves at 45 °C, but only for durations of exposure longer than 30 min. This leads to our risk for thermal damage criterion: a temperature in bone above 50 °C for more than 1 min is considered harmful and has to be avoided [12]. The aim of this study was to investigate whether a Ho:YAG laser and coblation are both suitable for minimally invasive interface tissue removal. Therefore we evaluated these two tissue removal techniques based on two criteria: risk for thermal damage to the bone tissue and the ablation rate (i.e. rate of tissue destruction).

2. Materials and methods

2.1. Tissue removal techniques

For the removal of interface tissue a Holmium YAG (Ho:YAG) laser (Medilas H20, Dornier MedTech, Wessling, Germany) and a VAPR-2 coblation system (DePuy Mitek, Amersfoort, The Netherlands) were used to remove interface tissue around a simulated *in vitro* loosened hip prosthesis. The Ho:YAG laser has a wavelength of 2100 nm with a pulse duration of 350 ms. The energy per pulse was set to 2000 mJ and pulse frequency was set to 8 Hz, which results in a power output of 16 Watts. The laser was equipped with a 0.6 mm fiber. Coblation was performed with a side-effect electrode (diameter 3.5 mm) with a maximum power output of 90 Watts. In routine clinical practice the Ho:YAG laser is used for lithotripsy or in a laserectomy procedure which also removes soft tissue such as nucleus pulposus of the human spinal disc [15–17] and coblation is used for soft tissue repairs in arthroscopies.

2.2. Specimens

We obtained 10 cadaveric formalin-fixed femora, retrieved from 7 donors (two female and five male, in three cases both femora were included in the study) with mean donor age of 80.7 years (range 67–98). Before implanting a polished tapered femoral stem (Exeter, size 42-2, Stryker, Kalamazoo, USA) all the soft tissues were removed. The femoral neck osteotomy was done with an oscillating saw 1.5 cm above the lesser trochanter and the femoral canal was opened with an osteotome in the fossa piriformis. The medullary canal was reamed with standard, sequentially larger, Exeter broaches. The last broach used was 4 mm oversized compared with the stem. This technique should provide a 2-mm cement mantle if the stem is placed centrally in the reamed medullary cavity. Pulsatile lavage was not used. Bone cement (Palacos, Biomet, Dordrecht, The Netherlands) was hand mixed and injected in a ret-

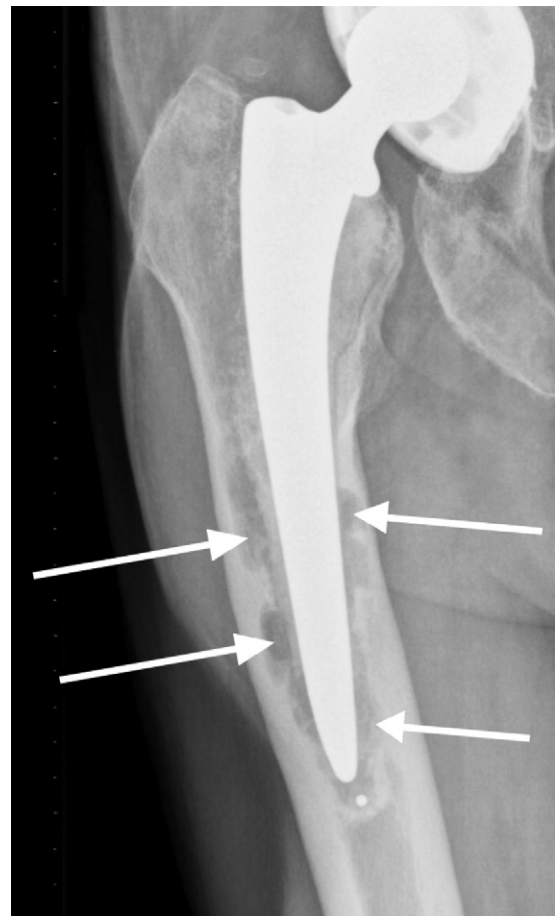


Fig. 1. Frontal radiograph of a patient with an aseptic loosened hip prosthesis. Arrows indicate the presence of interface tissue along the femoral shaft.

rograde manner, 2 min after the start of mixing. The stems were inserted manually in one continuous

movement, 4 min after the start of mixing while attempting to align all prostheses in a neutral position. The prostheses were implanted under supervision of an orthopaedic surgeon (HJLvdH) with experience with this specific implant in patient care. To simulate the *in vivo* environment of a loosened prosthesis, periprosthetic cavities were created according to those described in the literature [18], Fig. 1 shows a typical example of a loosened hip prosthesis with surrounding interface tissue. To this end the polished tapered stem was first removed from the femur without infringing the cement mantle, secondly the femur was cut in two parts with a saw and thirdly cavities were created with a burr between the cement mantle and the bone. These cavities were filled with interface tissue. Depending on the shape of the femur, two or three cavities were created in each femur with mean volume of 2.2 ml (range 1.1–5, SD 1.1)

2.3. Experiments

2.3.1. Substitute for human interface tissue

To guarantee availability and reproducibility we decided to use animal tissue as substitute for fresh human interface tissue. A comparative experiment was performed with human interface tissue as reference and beef mince, beef steak, chicken liver and chicken breast as potential alternatives. During this experiment, temperature was recorded with a K-type (chromel–alumel) thermocouple (RS Components, Haarlem, The Netherlands) while applying the Ho:YAG laser to the different tissues. A schematically drawing of

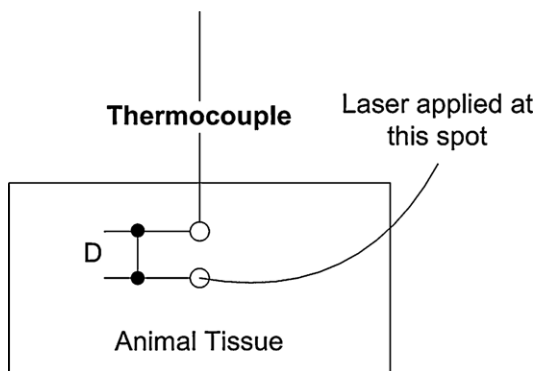


Fig. 2. Schematically overview of the experimental setup for the selection of the human interface tissue substitute. Distance (D) between laser and thermocouple and the depth of the thermocouple in the tissue was kept constant.

this experimental setup is shown in Fig. 2. To compare the different tissues, the slope $\Delta T/\Delta t$ of the temperature rise was determined. An example of a temperature history is presented in Fig. 3.

2.3.2. Thermal damage experiment

Temperatures were measured (accurate to 0.5°C) with K-type thermocouples, at a sample rate of 3 Hz. Two groups of three thermocouples were placed in each femur. The first group was placed in the outer surface of the cortical bone and the second group was placed inside the interface tissue volume. A schematic view of the locations of the thermocouples is shown in Fig. 4. In both groups the thermocouples were located at a radial distance of 1, 3 and 5 mm with respect to the centerline of the applicator. The bone surface temperatures were measured to determine the risk of thermal damage to the bone. Interior temperatures were measured to determine whether temperatures were high enough to destroy the interface tissue.

After preparation, the instrumented femora were placed in a temperature-regulated (37°C) 0.9% saline solution bath and allowed to reach thermal equilibrium (Fig. 5). Data was acquired with an USB-9211 device from National Instruments (National Instruments Netherlands BV, Woerden, The Netherlands).

To avoid a learning curve effect, laser and coblation were randomly used at the cavities around the simulated loosened prostheses. Each measurement cycle consisted of three intervals during

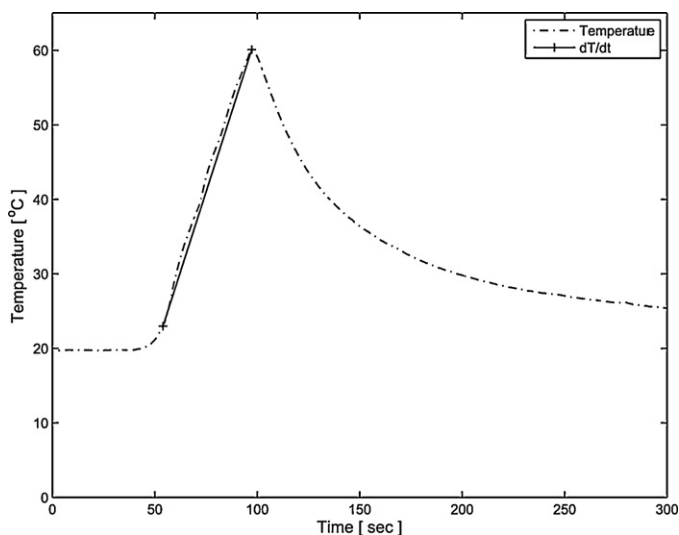


Fig. 3. Temperature recorded while applying the laser to beef steak. The slope of the temperature rise was determined in order to compare the different tissues.

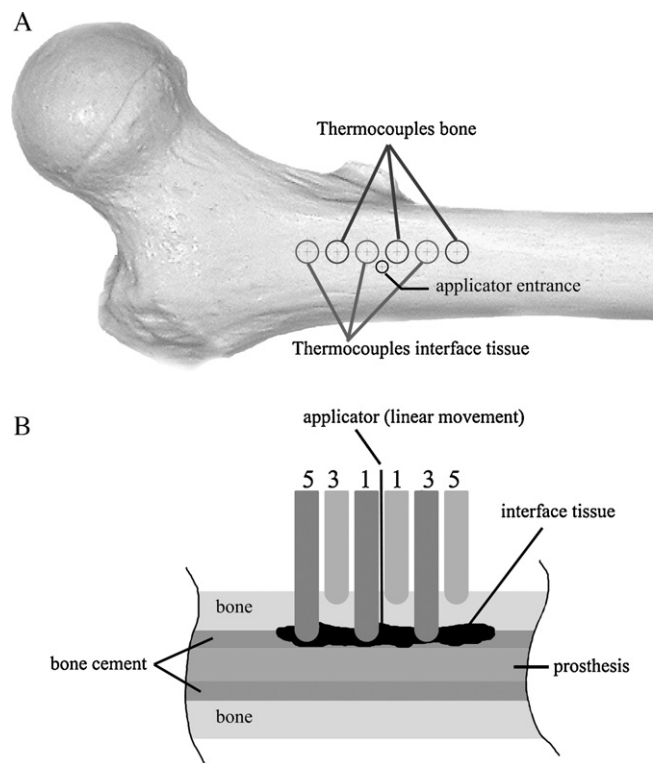


Fig. 4. Schematic overview of the placement of the thermocouples. (A) Top view of the thermocouple placement. (B) Cross sectional view, the numbers indicate the radial distance in mm between the applicator and the thermocouple.

which the removal technique was activated for 30 s. Each interval was started 2 min after the previous interval or when the temperature returned to 37°C . This measurement cycle was repeated for all cavities in the 10 femora.

To determine the risk for thermal damage, peak temperatures, area under the temperature curve and durations of temperatures above 50°C were identified for each measurement, taking into account the used removal technique, the material in which temperature was measured and the distance between thermocouple and removal applicator. The area under the measured temperature curve, corrected for the area under the body temperature (37°C) line is a measure of the energy deposition rate. According to the thermal damage criterion (a temperature of 50°C for 1 min) limited energy deposition is allowed before thermal damage will occur. The area representing this allowed energy deposition is subtracted from the area under the temperature curve, resulting in the AUC value. If the $\text{AUC} < 0$ (the energy added was less than needed for thermal damage), the AUC was considered to be zero. A risk for thermal damage exists if $\text{AUC} > 0$, with an increasing risk for a higher AUC.

2.3.3. Ablation rate experiment

To test ablation rate, laser and coblation were applied to the interface tissue substitute for five 2-min intervals each. Tissue mass was measured before and after each interval, from which the ablation rates were determined.

2.4. Statistical analysis

In view of, e.g. the continuous outcome variables, e.g. peak temperature with main predictor techniques and co-predictors material and distance and the repeated measures nature within femora of the experiment we used a linear mixed (regression) model with femur as random factor and, e.g. techniques as fixed

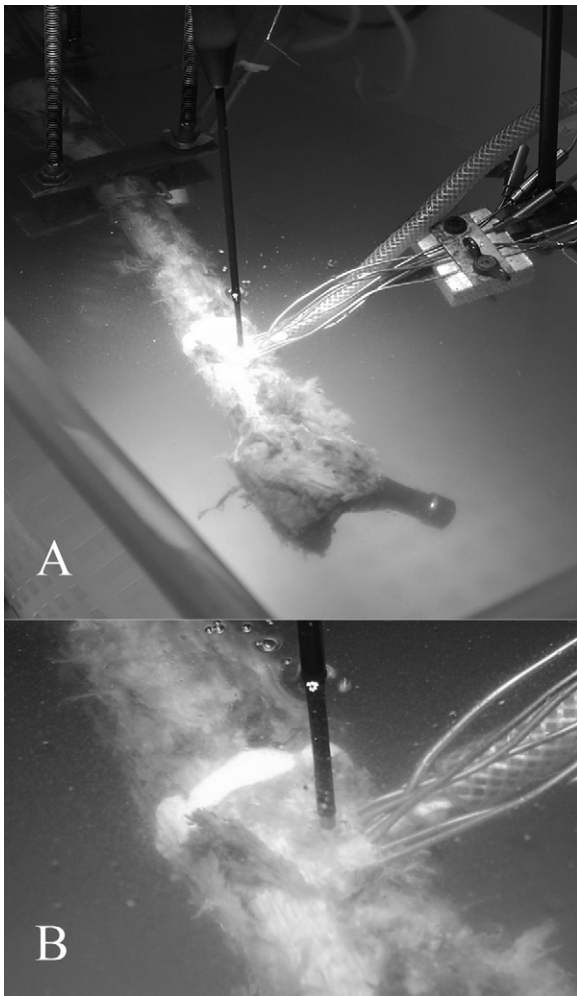


Fig. 5. Example of a femur equipped with thermocouples, (A) placed in a saline solution at 37 °C while using coblation and (B) a close up of the measurement location.

factors. *P*-values less than 0.05 were considered significant. SPSS 18 was used for the analysis.

3. Results

3.1. Substitute for human fibrous tissue

Values found for the $\Delta T/\Delta t$ coefficients are presented in Table 1. Visible reaction to the laser, structure and color of the tissue were also taken into account. From Table 1 we determined that $\Delta T/\Delta t$ for mince and chicken liver were close to the $\Delta T/\Delta t$ of human interface tissue. It was decided to use chicken liver as substitute based on the results in Table 1, the observation that the structure and color of chicken liver were closest to human interface tissue and that it reacted similarly to laser light.

Table 1
Values for $\Delta T/\Delta t$ for interface tissue and substitutes.

Tissue	$\Delta T/\Delta t$ [°C/s]	
	Mean	Range
Human interface tissue	0.3	0.1–0.48
Mince	0.1	0.09–0.17
Steak	0.4	0.17–0.87
Chicken liver	0.2	0.13–0.23
Chicken breast	0.04	0.01–0.08

Table 2

Mean durations (SD) of temperatures above 50 °C, measured in seconds, in interface tissue and bone at three distances from application site.

	Interface tissue		Bone	
	Laser	Coblation	Laser	Coblation
1 mm distance	52.2 (24)	39.6 (8.3)	– ^a	6.7 (1.4)
3 mm distance	54.3 (40)	27.8 (19)	– ^a	– ^a
5 mm distance	52.8 (31.7)	39 (24.2)	– ^a	– ^a

^a Temperature did not exceed 50 °C.

3.2. Thermal damage experiment

A typical result of measured temperatures is presented in Fig. 6, showing decreasing temperature with increasing distance. For each interval the peak temperature and the duration above 50 °C were determined.

3.2.1. Peak temperatures

Peak temperatures are presented in Fig. 7. Values were excluded from the analysis when thermocouple became dislodged (two cases). Furthermore, during three measurements a thermocouple was destroyed when its tip was hit by direct laser light resulting in measured temperatures as high as 800 °C. These measurements were not included in the analysis. In three instances a short circuit, due to physical contact between the coblation electrode and a thermocouple, resulted in unusable measurement cycles. According to our linear mixed model, generated peak temperatures given in Fig. 7 were significantly higher for laser than for coblation. Temperatures in the interface tissue were also significantly higher compared to temperatures in bone and with increasing radial distance peak temperatures decreased significantly.

3.2.2. Duration of temperatures above 50 °C

In Fig. 8 the duration of temperature in interface tissue and bone above 50 °C is shown. *P* indicates the percentage of the samples with temperatures above 50 °C. Temperatures in the bone exceeded 50 °C in two out of a total of 214 measurements. The durations of temperatures above 50 °C for laser and coblation are shown in Table 2 (mean, SD). According to the linear mixed model, durations of temperatures above 50 °C were significantly higher for laser than with coblation, and significantly higher in the interface tissue, but not significantly different with changing radial distance.

3.2.3. Area under temperature curves (AUCs)

The AUCs for bone we all found to be zero. For the interface tissue the AUC for each location is shown in Fig. 9. The same trend can be seen as with peak temperatures and durations. According to our linear mixed model, a significantly higher AUC is found for laser compared to coblation. Also with increasing radial distance, the AUCs decreased significantly.

3.3. Ablation rate experiment

The ablation rate test for removal of the interface tissue showed that Ho:YAG laser had a mean ablation rate of 0.25 g/min (SD 0.014) while coblation had a mean ablation rate of 0.09 g/min (SD 0.065).

4. Discussion

This study was performed to evaluate whether Ho:YAG laser or coblation may be alternatives for gene directed peri-prosthetic interface tissue removal, and whether either technique is suitable for minimally invasive soft tissue removal. The ablation rate, a measure of the amount of tissue removed, was about 2.5 times higher for the laser compared to coblation. Temperatures and AUC

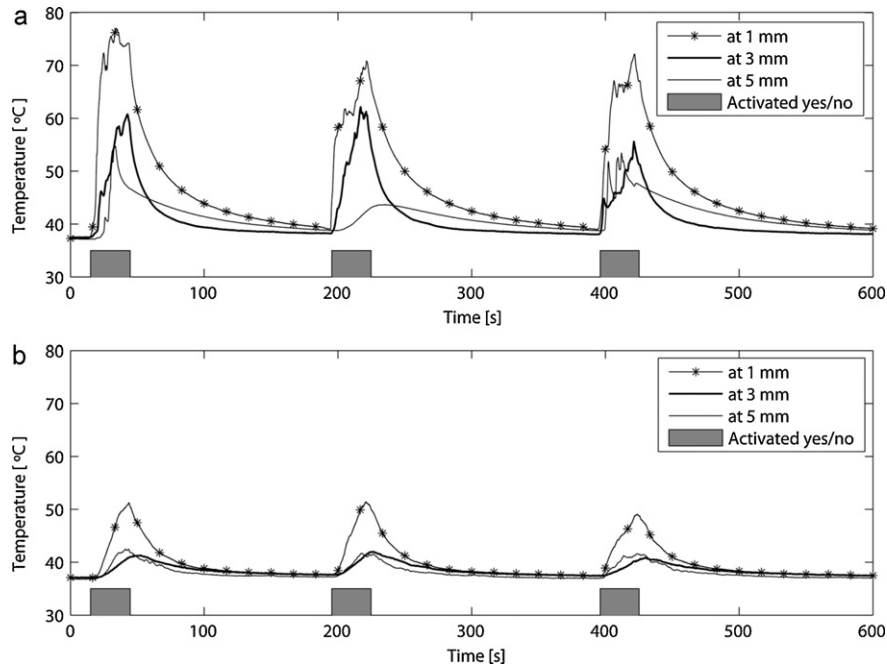


Fig. 6. A typical temperature history during coblation (A) in interface tissue and (B) in bone. Activated yes/no indicates whether coblation was active or not. Temperature peaks can be seen during the activated interval.

in the interface tissue were also higher with the laser technique than with the coblation technique. Based on our temperature criterion where a temperature above 50°C for more than 1 min is considered harmful, laser will also thermally damage interface tissue at a faster rate than coblation. However, temperatures and AUC measured at a radial distance of 5 mm with respect to the centerline of the applicator might indicate a risk of necrosis to surrounding bone while removing interface tissue by laser. Fig. 7 shows that the temperatures in the interface tissue may exceed 50°C at 5 mm radial distance, both for laser and coblation. Fig. 8 shows that, in interface tissue at 5 mm radial distance, about 7% of the used samples for laser and coblation reach temperatures

above 50°C for a duration longer than 1 min. Although this is not often, it does occur and thus surrounding bone can be damaged as a side effect while removing interface tissue close to the bone. Fig. 7 shows that peak temperatures measured at the bone surface of the femur do not exceed 50°C except for two outliers when performing coblation at 1 mm radial distance; this represents 6% of the measurements at this distance. However, Fig. 8 shows that those peak temperatures have a duration of only 8 s and the AUC for all measurements in bone equal to zero. This suggests that bone at the outer surface is not at a substantial risk for thermal damage while using coblation. The higher temperatures for laser can be explained by the working principles of both techniques.

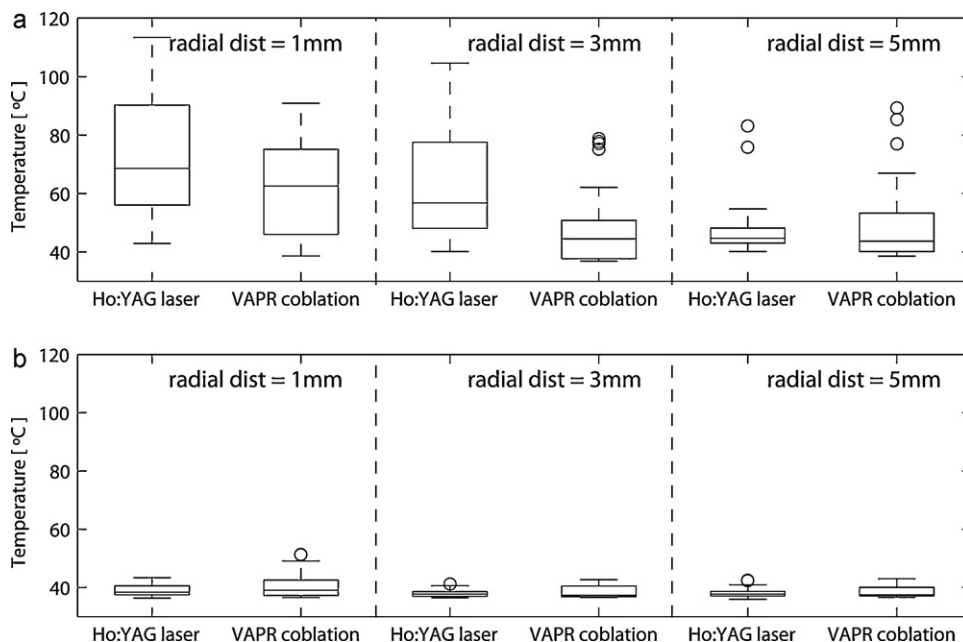


Fig. 7. Box plots of maximum measured temperature during removal of interface tissue in (A) interface tissue and (B) bone. Outliers are indicated with "o".

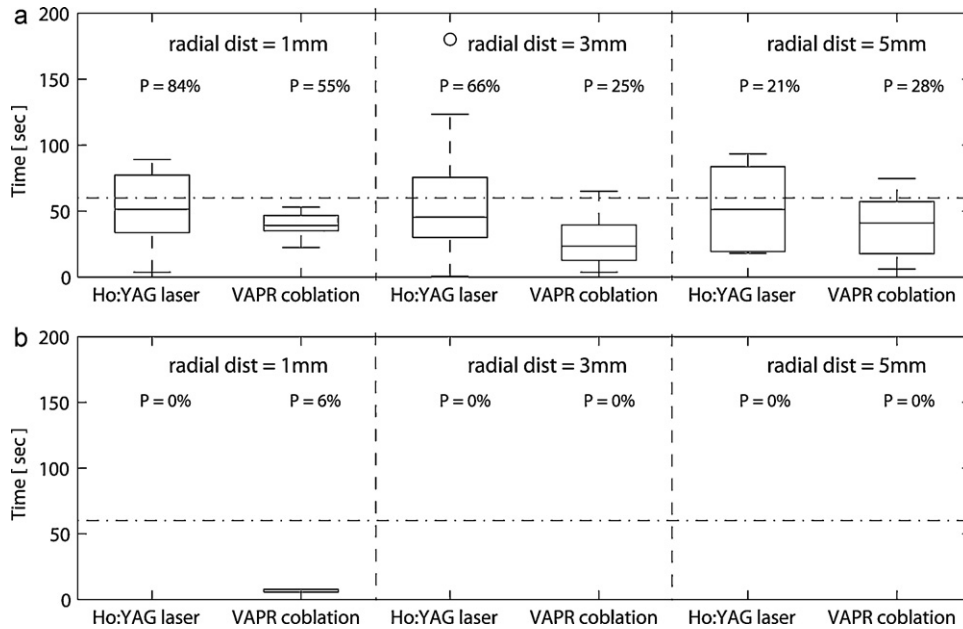


Fig. 8. Box plots of temperature duration exceeding 50°C in (A) interface tissue and (B) bone. *P* indicates the percentage of samples where temperatures exceeded 50°C. Outliers are indicated with “o”. The horizontal line marks the “50°C for 1 min” threshold.

Laser destroys tissue by transferring photon energy to focused heat as it is absorbed, leading to micro-explosions in tissue cells. Coblation uses high voltage bipolar radiofrequency in a conductive medium to generate a plasma field which breaks organic molecular bonds to vaporize tissue. Most of the heat is consumed in the plasma layer, or in other words, by the ionization process [19]. Tissue is dissolved and not destroyed by micro-explosions which requires heating of the tissue, thus lower tissue temperatures.

This study has some limitations in applicability to real patients. Although physiological conditions were simulated by placing the femora in a saline bath maintained at 37°C, it is unknown how this environment compares to the in vivo environment in which substantial heat transfer results from blood perfusion. Secondly, formalin fixed femora were used, which might influence the results since thermal properties can be affected by this preservation

method. Thirdly, chicken liver was used as a substitute for interface tissue. Although tissue characteristics were comparable to interface tissue, real interface tissue might result in slightly different temperatures.

In future work it will be useful to visually monitor the removal process. In this study the removal site inside the bone was not visible while applying the described techniques. A drawback of the flexible laser fiber is that the tip of the fiber was in some cases perturbed from the specified radial distances of 1, 3 and 5 mm to the applicator. There could also have been some variation in the distance between the coblation electrode, shown in Fig. 10, and its intended position. The side effect electrode is designed in such a way that tissue is removed at one side of the electrode tip. If the electrode is rotated, the active part is aimed in another direction, influencing the distance between the thermocouples and the

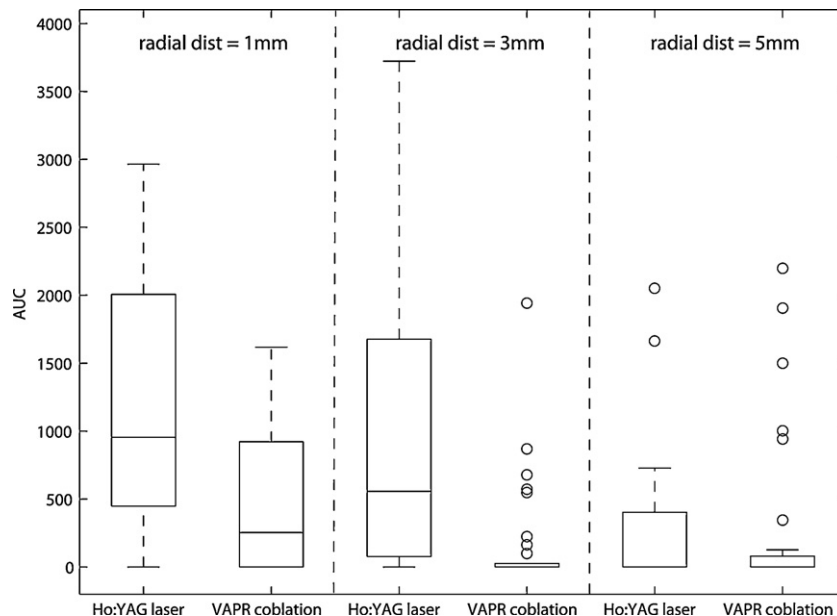


Fig. 9. Box plots of AUC in interface tissue. AUC in bone was equal to zero in all cases.

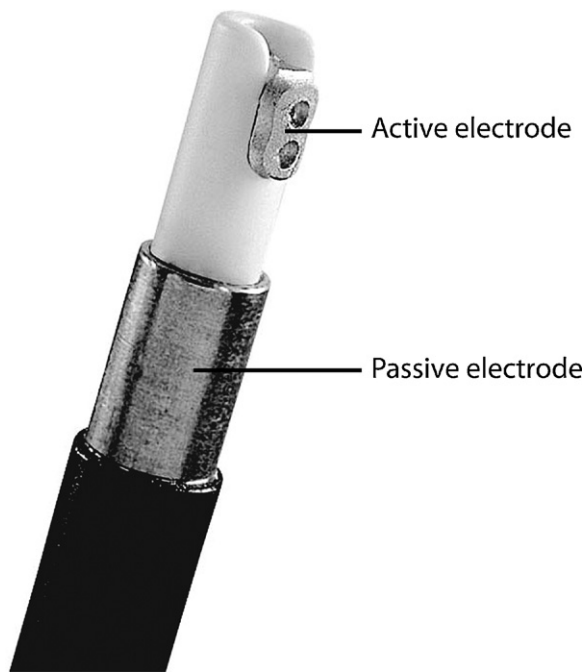


Fig. 10. Detail of the tip of the VAPR coblation electrode. Radio Frequency current flows between the active and passive part, resulting in tissue removal at this side of the electrode.

active part of the electrode. This can clarify the outliers shown in Fig. 7.

Since no literature is available regarding minimally invasive tissue removal around loosened hip prostheses using either laser or coblation, no comparison can be made except to the technique of minimal invasive interface tissue removal by gene therapy [20]. Gene therapy carries no thermal risk but is also experimental, and performed at the cost of requiring much time and specialized laboratory facilities.

Thermal side-effects after applying laser or coblation were measured in other studies. In a technical case report Kobayashi et al. [21] describe a case of nerve root heat injury induced by percutaneous laser disc decompression. Intra-operative findings in this case include carbon spots in the dura mater of the nerve root and a disc herniation strongly adherent to the nerve roots. These findings indicate that the area adjacent to the nerve roots was damaged by excessive heat during laser irradiation [21]. Coblation can also be used for percutaneous disc decompression. An evaluation of temperature distributions in a cadaveric lumbar spine while using coblation during nucleoplasty was performed by Nau and Diederich [22]. They measured the temperature at different radial distances from an applicator in a human cadaver spine which was placed in a temperature-regulated (37 °C) saline water bath. After 5 sec of power application with a stationary applicator the maximum temperature change (ΔT) was 19.7 ± 7.2 °C. Significant temperature rises (>10 °C) were measured within 1.5 mm of the applicator [22]. Although our setup differs from these studies we encountered the same phenomena: laser can induce thermal damage at larger distances than coblation, as evidenced by temperatures which could exceed the safe zone even at 5 mm. Temperatures at 3 mm and 5 mm radial distances remained in the safe zone while using coblation.

In this *in vitro* study we found that coblation met our thermal damage criterion. The Ho:YAG laser met our thermal damage criterion in 93%, but not all, cases. The ablation rate of Ho:YAG laser is about 2.5 times the ablation rate of coblation. It is important to realize that the removal technique must be integrated with a

new surgical instrument for minimally invasive tissue removal. This instrument has to be small in diameter in order to navigate through the limited available space in the peri-prosthetic area. In this respect laser is advantageous, because its fiber can have a small diameter (0.6 mm) and is flexible. The coblation electrode is rigid with a diameter of 3.5 mm, and would take more effort to integrate into a steering mechanism compared to a laser fiber. This advantage together with the higher ablation rate makes the Ho:YAG laser a promising removal tool, although its usage needs to be optimized in order to meet the thermal damage criterion.

Further research on laser settings and removal strategy are necessary before this technique can be applied for the removal of interface tissue. In this study, measurements were conducted during 30 s of activation time and rest intervals of 2 min. It should be investigated if the length of the active and rest periods have a large effect on the procedure's success and risks. It should also be investigated whether *in vivo* conditions, such as blood perfusion, influence heat transfer and resulting temperature build-up. Settings in this study were chosen based on typical values and were not changed during the experiments. Despite the higher ablation rate for laser, it still takes a lot of time to remove the interface tissue. Measurements should be done with different equipment settings (pulse frequency, pulse energy, power output and activated time) in order to find the most suitable settings for the specific purpose of removing interface tissue around loosened prostheses. Before this tissue removal technique can be applied to clinical practice, it will be necessary to perform *in vivo* experiments to assess its effectiveness and safety.

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Conflict of interest statement

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

References

- [1] Looney RJ, Boyd A, Totterman S, Seo GS, Tamez-Pena J, Campbell D, et al. Volumetric computerized tomography as a measurement of periprosthetic acetabular osteolysis and its correlation with wear. *Arthritis Res* 2002;4:59–63.
- [2] Malchau H, Garellick G, Herberts P. The evidence from the Swedish hip register. In: Breusch S, Malchau H, editors. *The well-cemented total hip arthroplasty*. New York/Berlin/Heidelberg: Springer; 2005. p. 291–9.
- [3] Hori RY, Lewis JL. Mechanical properties of the fibrous tissue found at the bone-cement interface following total joint replacement. *J Biomed Mater Res* 1982;16:911–27.
- [4] Strehle J, DelNotaro C, Orler R, Isler B. The outcome of revision hip arthroplasty in patients older than age 80 years. *J Arthroplasty* 2000;15:690–7.
- [5] de Poorter JJ, Hoeben RC, Hogendoorn S, Mautner V, Ellis J, Obermann WR, et al. Gene therapy and cement injection for restabilization of loosened hip prostheses. *Hum Gene Ther* 2008;19:83–95.
- [6] de Poorter JJ, Hoeben RC, Obermann WR, Huizinga TW, Nelissen RG. Gene therapy for the treatment of hip prosthesis loosening: adverse events in a phase 1 clinical study. *Hum Gene Ther* 2008;19:1029–38.
- [7] Dewey WC. Arrhenius relationships from the molecule and cell to the clinic. *Int J Hyperthermia* 2009;25:3–20.

- [8] Field SB, Morris CC. The relationship between heating time and temperature: its relevance to clinical hyperthermia. *Radiother Oncol* 1983;1:179–86.
- [9] Lumry R, Eyring H. Conformation changes of proteins. *J Phys Chem* 1954;58:110–20.
- [10] Rastegar S, Chard AM, Azeemi A. Analysis of the kinetics of single-rate and multi-rate thermal damage in laser irradiation of biological tissue. In: Proceedings of the 1993 ASME winter annual meeting. American Society of Mechanical Engineers, Heat Transfer Division, (Publication) HTD 268; 1993. p. 137–40.
- [11] Eriksson AR, Albrektsson T. Temperature threshold levels for heat-induced bone tissue injury: a vital-microscopic study in the rabbit. *J Prosthet Dent* 1983;50:101–7.
- [12] Eriksson RA, Albrektsson T, Magnusson B. Assessment of bone viability after heat trauma. A histological, histochemical and vital microscopic study in the rabbit. *Scand J Plast Reconstr Surg* 1984;18:261–8.
- [13] Rouiller C, Majno G. Morphological and chemical studies of bones after the application of heat. *Beitr Pathol Anat* 1953;113:100–20.
- [14] de Vrind HH, Wondergem J, Haveman J. Hyperthermia-induced damage to rat sciatic nerve assessed in vivo with functional methods and with electrophysiology. *J Neurosci Methods* 1992;45:165–74.
- [15] Ranu HS. The use of lasers in orthopaedic procedures. *J Bone Joint Surg Am* 1994;76:633–4.
- [16] Ranu HS. Laserectomy of the human nucleus pulposus and intradiscal pressure measurements: an in vitro and in vivo study. In: Proceedings of the 14th southern biomedical engineering conference. 1995. p. 257–9.
- [17] Ranu HS. Multipoint determination of pressure-volume curves in human intervertebral discs. *Ann Rheum Dis* 1993;52:142–6.
- [18] Garcia-Cimbreló E, Madero R, Blasco-Alberdi A, Munuera L. Femoral osteolysis after low-friction arthroplasty. A planimetric study and volumetric estimate. *J Arthroplasty* 1997;12:624–34.
- [19] Sergeev VN, Belov SV. Coblation technology: a new method for high-frequency electrosurgery. *Biomed Eng* 2002;37:22–5.
- [20] de Poorter JJ. 2009. Gene therapy and cement injection for the treatment of hip prosthesis loosening in elderly patients. Thesis/Dissertation. Leiden University Medical Center, Leiden, The Netherlands.
- [21] Kobayashi S, Uchida K, Takeno K, Yayama T, Nakajima H, Nomura E, et al. A case of nerve root heat injury induced by percutaneous laser disc decompression performed at an outside institution: technical case report. *Neurosurgery* 2007;60:171–2.
- [22] Nau WH, Diederich CJ. Evaluation of temperature distributions in cadaveric lumbar spine during nucleoplasty. *Phys Med Biol* 2004;49:1583–94.