Sabri Aydın Ergun Bozdag˘ Emin Sünbüloğlu Halil Ünalan Murat Hanci Önder Aydıngöz Cengiz Kuday

Received: 10 July 2004 Revised: 15 October 2004 Accepted: 30 October 2004 Published online: 24 May 2005 Springer-Verlag 2005

S. Aydın \cdot M. Hanci (\boxtimes) \cdot C. Kuday Cerrahpasa Medical Faculty, Department of Neurosurgery, Istanbul University, Istanbul, Turkey E-mail: murath@istanbul.edu.tr Fax: +90-212-2807630

E. Bozdağ · E. Sünbüloğlu Department of Mechanical Engineering, Istanbul Technical University, Istanbul, **Turkey**

H. Ünalan Cerrahpasa Medical Faculty, Department of Physical Medicine and Rehabilitation, Istanbul University, Istanbul, Turkey

O. Aydıngöz Cerrahpasa Medical Faculty, Department of Orthopeadics and Traumatology, Istanbul University, 792 Sisli, 80220 Istanbul, Turkey

Introduction

Our knowledge regarding the use of self-curing acrylics such as polymethylmethacrylate (PMMA) in spinal surgery has grown constantly over the last few decades. Recent studies have focused specifically on heat produced by the polymerisation of these materials, and the resulting undesired thermal effects [[6](#page-5-0), [8–10](#page-5-0)].

Polymethylmethacrylate is a well-known example of these inorganic chemical substances that have been used

Abstract The objective of this experimental study was to investigate the temperature variations within the spinal cord of calf cadavers during polymethlymethacrylate (PMMA) application for vertebral body reconstruction. Cervical spines including the cervical spinal cord of ten fresh cadavers were used. Corpectomy and laminectomy were performed and dura was exposed at the same level for proper placement of thermal sensors. Sensors were placed in multiple holes in the spinal cord at depths of 3, 6, 9 and 12 mm, respectively. Whether the thermal sensors were placed in the gray or white matter was determined by computerized tomography. The white and gray matters of the spinal cord exhibited different thermal properties. The white matter was

more conductive and absorbed less heat than the gray matter. The heat sensor nearest to PMMA exhibited temperatures of 42–44 °C. The sec-

ond heat sensor placed at 9 mm depth within the gray matter showed 44 °C. The third sensor, which was placed at 6 mm depth within the spinal cord recorded the same temperature as the first, i.e., nearest to location from PMMA demonstrated 37–39 °C. The temperature distribution within the gray matter was inversely proportional to the distance from the heat source. The temperawhich was distant from the heating spinal cord during PMMA applicasignificant in the gray matter when compared with other neural tissues.

Keywords Polymethylmethacrylate \cdot Spinal cord \cdot Thermal injury

In vitro investigation of heat transfer in calf spinal cord during polymethylmethacrylate

application for vertebral body reconstruction

PMMA sensor. The fourth heat sensor, which was at the farthest ture at the dorsal white matter, source, remained nearly constant and was not elevated. Our data suggest that thermal injury to the tion may be expected to be more

for vertebroplasty. These materials undergo polymerisation with an accompanying exothermic chemical reaction, which causes increased temperatures in tissues adjacent to the stabilisation area. This thermal effect may further complicate the clinical picture when the affected adjacent tissue is the spinal cord [[7,](#page-5-0) [8](#page-5-0), [15](#page-5-0)–[17\]](#page-5-0).

An exothermic reaction, which typically occurs during the polymerisation process of PMMA, is a chemical reaction during which energy is released to the environment [\[4](#page-5-0), [12,](#page-5-0) [16,](#page-5-0) [22](#page-5-0)].

Exothermic reaction of inorganic compounds used for stabilisation in spinal surgery may result in two distinct thermal injuries regarding the spinal cord. One of these major injuries is due to local warming of the spinal cord, and the other is secondary to the elevated overall body temperature. It was reported in previous studies that a body temperature of 42°C for an average time of 60 min may result in histopathological changes in the spinal cord, and is closely related to neurological deterioration [[3](#page-4-0), [8,](#page-5-0) [13](#page-5-0), [18,](#page-5-0) [17](#page-5-0), [19\]](#page-5-0). Local rise of temperature to the range of $40-43^{\circ}$ C for the same period, however, does not cause any obvious damage in the

[8](#page-5-0), [11,](#page-5-0) [15,](#page-5-0) [18](#page-5-0), [17](#page-5-0), [19,](#page-5-0) [23\]](#page-5-0). Experimental studies on mice suggest that the highest temperature without any unwanted effect at the epidural level is 44°C; temperatures above this level may result in some electrophysiological alterations in the spinal cord. Most of the previous studies have focused on the epidural temperature variations and how temperature changes affect the neural tissue is not precise [\[6,](#page-5-0) [10,](#page-5-0) [18](#page-5-0), [20](#page-5-0), [23\]](#page-5-0). The local variation of temperature within the medulla spinalis and the potential harm that might be triggered by overheating seems to be of great concern for those who are engaged in PMMA application for vertebral body reconstruction.

spinal cord except for some physiological alterations [\[5](#page-5-0),

The present experimental study was designed to investigate the temperature variations within the spinal cord during PMMA vertebroplasty, considering various durations, and the effect of the position of the material (PMMA).

Materials and methods

In the present experimental study, cervical spines and spinal cord tissues of ten fresh calf cadavers were used. Vertebrectomy cavity was filled with bone cement and the temperature variations observed in spinal cord and at the adjacent tissues due to the exothermic reaction, during the whole reaction process, were noted. Threeyears-old calf cadavers were used. Decapitation was performed at the atlanto-occipital region according to routine procedures; anatomical contiguity of the cervical spine was preserved. All preparations were stripped of overlying muscles immediately following decapitation with special attention to bony structures and the spinal cord tissue adjacent to the area under investigation. The experimental specimen were preserved in 0.9% isotonic sodium chloride solution at 37°C and then transferred to the laboratory within a maximum of 4 h. The temperature of the laboratory room was kept constant at 23°C.

The specimens were then taken out of the saline bath and a one-level corpectomy was performed using routine surgical techniques. The volume of the corpectomy cavity was 12 cm^3 .

In the next step, laminectomy was performed and dura was exposed at the same level for proper placement of the intramedullary thermal sensors. Dura was punctured at the laminectomy site by leaving 4 mm space in between. The probes (TT-K-36-SLE Type-K Thermocouple wire OMEGA Engineering) were placed in different holes in medulla spinalis at the depths of 3, 6, 9 and 12 mm respectively (Figs. 1, 2). Proper placements of the probes were confirmed by computerized tomography and following this procedure the probes were fixed in the dura by cyanoacrylate adhesive. The other probes, which will be used to detect the temperature variations in bone tissue and the epidural space, were placed. During all these procedures, the temperature of the saline bath, which consisted of 20 l 0.9% isotonic sodium chloride, was kept constant at 37°C using a temperature stabiliser (Neslab RTE-300 instruments inc./

Fig. 1 Illustration of localization of thermal probes

Fig. 2 Dorsolateral view of the specimen showing the localization of the sensors in spinal cord (asterisk spinal cord)

- differentiation Electronic Controlled Constant-Temperature Water \blacktriangleleft
- **Discharging Unit**

Fig. 3 Schematic for the experimental setup

[Nevington - NH, 03801-USA model RTE-300 D\). The](#page-1-0) [specimens, with the probes in proper places, were then](#page-1-0) [suspended in the thermostatically controlled saline bath.](#page-1-0) [For temperature measurements, the free ends of the](#page-1-0) [probes were combined with a data acquisition system](#page-1-0) [\(Keihtley model 2,700 multimeter\), which was con](#page-1-0)nected via interface to a recording computer (Fig. 3).

A 12-ml (Codman cranioplastic Type 1-slow set) cement was placed into the vertebrectomy cavity and a no 7 probe was placed. Then the entire system was immersed once again into the saline bath and measurements were acquired. The temperature variations were continuously recorded for 1,800 s and data points were collected at a frequency of 1 Hz. All data obtained by this procedure were transferred to Microsoft Excel 2000.

The differences between mean temperature values of probes was analysed by using non-parametric Wilcoxon Signed Rank test and $p < 0.05$ was considered as statistically significant.

The raw data obtained from all measurements were processed using Microsoft Excel software. Non-linear curve-fitting operations have been applied to the collection of data from ten samples to express a best-fit

- PC Computer & Data Management $8)$
- 9) Plotter

curve demonstrating the thermal behaviour of each probe. Curve-fitting procedure was performed using MATLAB engineering software.

Results

Measurement point 1 was located in the spinal cord and was the nearest point to the PMMA filling the corpectomy cavity. It was observed that the thermal effects on the spinal cord tissue started to be significant within 200–400 s following the placement of PMMA and began to diminish thereafter as the 800-s threshold had been passed. The temperature values in this location were found to be at the critical level of $42-44$ °C for five specimens. In one of those five specimens the temperature more than 44° C was noted. The data obtained from measurement point 2 which was located at 9 mm depth were similar to those obtained from measurement point 1. The temperature rise at this location began at the 200th second of the experiment and lasted for 800 s. At measurement point 2, the critical level of 44° C was exceeded in five specimens and the high temperature plateau lasted longer.

Results obtained from the third location showed similar characteristics to data acquired from measurement point 1. At this location, critical temperature levels were exceeded only in one experiment. Temperature variations at measurement point 4, which was the farthest location from the PMMA region, ranged between 37° C and 39° C, and were not within the critical range. When compared with all recording sites, the dorsal white matter exhibited the lowest temperature $(p < 0.05)$ (Fig. 4).

Temperature variations obtained from the thermal probe, which was in contact with the saline bath and located at the ventral epidural surface of the corpectomy cavity ranged between 40° C and 45° C throughout the whole experiment. Temperature rise at this point began within 200 s of the experiment, remained constant between 400 s and 600 s, and progressively diminished within 800 s after the start of the experiment.

High temperature values were recorded from sensor 6, which was located in the trabecular portion of the vertebral body and in the vicinity of the corpectomy region filled with PMMA. Although the average temperature recorded from the bone was 45°C, temperature increases as high as 60°C were observed in some cases. The evolution of the values was similar to those recorded at location 5.

Sensor number 7, located in the core of the PMMA filling region, was used to determine the behaviour of PMMA during the polymerisation process. The core

Fig. 4 Temperature variations recorded from the thermal sensors. GM gray matter, WM white matter

temperature of cement increased as high as 130°C, with an average of 80°C. A sharp peak was recorded in temperatures during the 200 s and 400 s time interval, which diminished in a short time to reach the temperature of the saline bath. The temperature of the saline bath remained constant at 37°C, and provided an optimal in vitro environment throughout the whole experimental procedure.

Discussion

Polymethlymethacrylate has been used as bone cement in previous studies in order to secure fixation of metal and polyethylene prosthetic materials into living bone tissue [[2\]](#page-4-0). PMMA is a well-known polymer with its extensively studied chemical and physical characteristics; it is also a stabilisation material that is commercially available.

Since the first introduction of PMMA, its thermal effects due to polymerisation have been of great concern to researchers and physicians. The exothermic reaction, which occurs during the in vitro polymerisation of PMMA, has been reported to cause a temperature rise that may reach 100° C [\[2\]](#page-4-0).

In orthopaedic surgical procedures, such thermal effects have been implicated as a cause of excessive bone

necrosis, and, loosening or failure of the implants. It has been widely accepted that temperature at the bone-cement interface during polymerisation of the cement mass is often greater than 70° C, and is responsible for bone necrosis observed at this location [2, [13,](#page-5-0) [14,](#page-5-0) [17](#page-5-0), 1].

Polymethlymethacrylate application has been considered as an efficient method in the surgical treatment of spinal stabilisation disorders. Some important indications of PMMA use in spine surgery may be summarized as follows:

- (1) When maximum post-op stability is crucial to the survival of the patient,
- (2) In conditions when auto and/or allograft substitutes are not available
- (3) Stabilization requirement in an extremely ill patient $[12–14, 20]$ $[12–14, 20]$ $[12–14, 20]$ $[12–14, 20]$ $[12–14, 20]$.
- (4) Augmentation of osteoporotic compression fractures [\[19\]](#page-5-0).

As mentioned previously, PMMA undergoes a spontaneous transformation, which changes its initial monomer molecular structure to a polymer with an accompanying exothermic chemical reaction that results in undesired thermal effects in the surrounding tissues.

Temperature elevations reached during PMMA application depend on several variables such as the amount of the reacting monomer, the rate of heat dissipation, and, the thermodynamic properties of PMMA such as its specific heat capacity and thermal conductivity [[12](#page-5-0)]. The most important of these variables seems to be the amount of monomer used which yields an average of 13 kcal thermal energy per 100 g of monomer [\[12](#page-5-0)]. The second most important variable is the surface area over which the heat dissipates. The rate of temperature elevation in a substance is primarily dependent on two physical properties: the heat capacity of the substance and its ability to transport heat [[12\]](#page-5-0).

It is a well-known fact that the histological characteristics of substantial alba and substantia grisea of the medulla spinalis are different. Due to the histological properties of the spinal cord, thermal conductivity may be expected to be different at different regions within the spinal cord. The present study demonstrates that the temperatures recorded from the vicinity of the heat source i.e. PMMA, were higher and increased earlier. The temperature recorded from the gray matter was higher compared to the white matter, and also, the peak temperatures were reached faster in the gray matter. The lower temperature values and the longer duration for heating as recorded from the peripheral white matter may partly be explained by the different thermal conductivity characteristics of the tissue. However, the temperature variations observed in the gray matter of the anterior horn and the ventral white matter showed no significant difference in our study ($p > 0.05$). On the other hand, the temperatures recorded from the dorsal side of the gray matter were significantly lower than the ventral side ($p < 0.05$). According to these results it can be suggested that:

- 1. The white and the gray matters of the spinal cord exhibit different thermal properties; the white matter seems to be more conductive and absorbs the heat less than the gray matter.
- 2. The temperature distribution within the gray matter is inversely proportional to the distance from the heat source, i.e., PMMA.
- 3. The inverse proportion between the distance from PMMA and the temperature is more profound in the gray matter.
- 4. The temperature of the dorsal white matter remains almost constant and does not elevate as it absorbs less heat than the other parts and is distant from the heating source.

All experiments in the present study were carried out in a 0.9% isotonic sodium chloride bath and measurements from the spinal cord indicated that the existence of water within the PMMA application region is not insulative enough and did not prevent thermal overloads.

Conclusion

We conclude that thermal injury to the spinal cord due to PMMA application might be more profound in the gray matter compared with other neural structures. In order to minimize complications related to PMMA application, it may be advisable to place an insulating material between the PMMA and the neural tissue, or to substitute PMMA with a material that dissipates less heat during polymerisation.

References

- 1. Belkoff SM, Molloy S (2003) Temperature measurements during polymerisation of polymethylmethacrylate cement used for vertebroplasty. Spine 28:1555– 1559
- 2. Berman AT, Reid SJ, Daniel RY, Sih GC, Zimmerman MR (1984) Thermally induced bone necrosis in rabbits. Clin Orthop 186:284–293
- 3. Depuy Instruction Book Leaflet (1997) CMW Ortopaedic Bone Cements De-Puy Int Ltd. Cornford Road Blackpool, Lancashire FY4 4QQ, England, pp 2–4
- 4. Douglas MA, Parks LC, Bebin J (1981) Sudden myelopathy secondary to therapeutic total body hyperthermia after spinal cord irradition. N Engl J Med 304:583–585
- 5. Greenberg MS (2001) Handbook of neurosurgery. Thieme Greenberg Graphics Inc. Lakeland, p 726
- 6. Herman HJ, Sowder WG, Anderson D, Appel AM, Hopson CN (1989) Polymethylmethacyrlate-induced release of bone resorbing factors. J Bone Joint Surg 71-A:1530–1541
- 7. Hız M, Elazıg N, Bilgili MG (2000) In vivoanalysis of thermal changes in sheep model followingapplication ofwater at various temperatures and different volumes of bone cementto bony cavitiesfrom variable distances to the cavity wall, with and without the usage of turniquet. Thesis, Istanbul University
- 8. Jasty M (1995) Polymehylmethacrylate. Orthopaedic knowledge update. Hip and knee recostruction. AAOS Publication Edited by Callaghan, JJ 6300 North River Road Rosement, IL, pp 43–48
- 9. Jefferis CD, Lee AJ, Ling RMS (1975) Thermal aspects of self-curing polymethlymethacylate. J Bone Joint Surg 57B:511–518
- 10. Kaammerlen P, Thiesse P, Jonas P (1989) Percutaneous injection of orthopaedic cement in metastatic vertebral lesions. N Engl J Med 70:557–562
- 11. Konno S, Olmarker K, Byrod G, Nordborg C, Strömqvist B, Rydevic B (1994) Acute thermal nerve root injury. Eur Spine J 3:299–302
- 12. Leeson MC, Lippitt SB (1993) Thermal aspects of the use of polymethlymethacrylate in large metaphyseal defects in bone. Clin Orthop 295:239–245
- 13. Lin PS, Wu A, Ho K (1987) Stability of heating temperature on cytotoxicty. Int J Radiat Oncol Biol Phys 13:869–873
- 14. Panjabi MM, White A (1991) Clinical biomechanics of spine: biomechanical considerations in the surgical management of the spine. JP Lippincott Co, Philadelphia, pp 570–579
- 15. Park JK, Allen MJ, Shoonmeker J, Juan O, Bani B, Yuan HA (1994) Gelfoam as a barrier to prevent polymethylmethacrylate-induced thermal injury of the spinal cord in vitro and in vivo studies in pigs. Eur Spine J 386:299–302
- 16. Sminia P, Troost B, Hervenzanj (1989) Histopathological changes in the spinal cord after 434 mhz microwave hyperthermia in the cervical region of the rat. Int J Hyperthermia 51:85–89
- 17. Sminia P, Van der Zee J, Wondergem J, Heneman J (1994) Effects of hyperthermia on the central nervous system: a review. Int J Hyperthermia 10:1–30
- 18. Sminia P, Hendriks JJ, Van der Kracht A, Rodernand H, Honveman J, Jansen W, Koedoodur K, Franken NA (1995) Neurogical observations after local irraditions and hyperthermia of rat lumbosacral spinal cord. Int J Radiat Oncol Biol Phys 32:165–174
- 19. Snell R (1998) Clinical neuroanatomy for students. Lippincott Williams and Wilkins, Washington, pp 125–133
- 20. Stuecklschweiger G, Shad KS, Kapp DS, Handl-Zeller L, Hackl AG (1993) Analysis of temperature distrubutions of interstitial hyperthermia using a hot water system. Int J Radiat Oncol Biol Phys 26:891–895
- 21. Takahashi S, Tanaka R, Watanebe M, Takahashi H, Kakinuma K, Suda T, Yamade M (1999) Effects of whole body hyperthermia on the canine central nervous system. Int J Hyperthermia 15:203–216
- 22. Wegner M, Markwalder M (1999) Surgically controlled, transpedicular methylmethacrylate vertebroplasty with flouroscopic guidance. Acta Neurochir 141:625–663
- 23. Wilkes RA, Maccinnon JG, Thomas WG (1993) Neurological deterioration after cement injection into a vertebral body. J Bone Joint Surg 76-B:155–158