Efficacy of vacuum bone cement mixing systems in reducing methylmethacrylate fume exposure

Comparison of 7 different mixing devices and handmixing

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Background **Polymethylmethacrylate (PMMA) bone cements are mainly used for implant fixation in joint replacement surgery. During cement preparation for application, all staff in the operating theatre are exposed to methylmethacrylate (MMA) fumes, which are known to have toxic side effects.**

Methods and results **In this study we found that vacuum mixing of bone cement with 7 commercially available mixing devices significantly reduced the emission of MMA vapors in the breathing zone when compared with classic hand mixing in an open bowl. Gas chromatography appears to be more sensitive for detection of MMA fumes than Photo Inonization Detection.**

Interpretation **According to present knowledge, even repeated mixing of PMMA bone cement during a normal working day does not seem to constitute an increased health risk, particularly if vacuum mixing is implemented.**

Vacuum mixing of polymethylmethacrylate (PMMA) bone cement is advocated to reduce voids and porosity within the cement mantle, which are suspected to contribute to crack development and prosthesis failure or loosening (Lidgren et al. 1987, Wixson et al. 1987, Geiger et al. 2001). The vacuum mixing devices are connected to specific suction units and are thus also expected to minimise exposure to methylmethacrylate (MMA) monomer fumes evaporating during the mixing procedure (Darre et al. 1988, Bettencourt et al. 2001). MMA is a toxic, highly volatile organic solvent. Cytotoxic effects on human fibroblasts in culture media have been described and attributed to MMA (Vale et al. 1997). Exposure to MMA vapors may have irritating effects on mucous membranes of the respiratory tract and the eyes (Fregert 1983, Nissen and Corydon 1985). Direct contact with PMMA bone cement may lead to toxic dermatitis (Fries et al. 1975), whereas exposure over several years has been suggested to be a cause of toxic encephalopathy (Christiansen et al. 1986). We quantified the emission of MMA fumes in the breathing zone, comparing 7 commonly available vacuum mixing systems with hand mixing in an open bowl. Two detection techniques were applied simultaneously for comparison.

Materials and methods

Set-up

All measurements were performed in a conventional operating theatre with laminar airflow. The total volume of the theatre was 126 m^3 (3 m high × 7 m long × 6.05 m wide). The laminar air flow provided a total exchange rate of 19 times/hour (incoming air 2400 m^3/h, exhaust air 2100 m^3/h). As experiments were carried out, air humidity and temperature were measured and recorded every 2 h. The average humidity was 44% (range 36–55), the average temperature was 22.2°C (range 20.6–23.3). The mixing systems being examined were

positioned on an instrument table situated at typical height (80 cm) near the scrub nurse during joint replacement surgery, next to the operating table. The fume detection systems (see below) were mounted on a second table 65 cm above the lowest level of the mixing devices, thus corresponding to the breathing zone of a nurse during the mixing procedure. A horizontal distance of 15 cm from the upper opening of the systems was kept, while the tips of the two detection systems were positioned 10 cm from each other to prevent interference by suction.

Fume collection and analysis

Over a period of 3 min, air/fume samples were collected using both a Photo Ionization Detector (PID) (RAE-Systems, Sunnyvale, CA, USA) with a suction rate of 0.5 L/min, and at the same time, gas chromatography (GC) with a 1 L/min suction pump (SKC, Eighty Four, PA, USA) and Draeger activated charcoal tubes (Draeger, Luebeck, Germany). GC analysis was performed according to German BIA procedure 7940. Charcoal was extracted with diethyl ether overnight. 1 μL of this solution was then injected into a HP 6890 GC system (Hewlett-Packard, Palo Alto, CA, USA) with helium carrier (1.5 mL/min). The injection temperature was 200 °C, the detection temperature was 230 °C and the column temperature was 180 °C. The lower detection limit was 0.3 ppm for GC and 0.1 ppm for PID. Background measurements with PID were carried out regularly after 5 mixing experiments without ever detecting traces of MMA vapor.

Mixing procedure

7 vacuum mixing systems were included in this study (Table 1). The measurements of fume concentrations were started prior to opening of the cement components. All experiments were performed according to the following standard protocol: loading of the mixing device with monomer and polymer (30 s), application of vacuum (10 s), vacuum mixing (30 s), preparation for application (60 s). For every working step, the time was measured and documented (Table 2). For every mixing process one portion (40 g) of Palamed (Biomet-Merck, Darmstadt, Germany) PMMA-cement was used. Mixing was performed according to the instructions of the manufacturer. For every mixing device, 10 separate mixes were made and measurements done. The option of collecting cement in the cartridge under vacuum was used whenever possible (Table 1).

Table 1. Vacuum mixing systems being studied

Mixing system	Manufacturer	Possibility of collection under vacuum
ACM	Stryker	–
Cemvac	DePuy J&J	+
Easymix	Mebio	+
MixOR	Smith&Nephew	+
Optimix	Biomet-Merck	+ (prepacked system)
Optivac	Biomet-Merck	+
Vacu-Mix	DePuy J&J	–

Note: Vacuum collection of cement is patented only for Optivac and Optimix

As a control and to mimic a worst-case scenario, handmixing was performed using a standard open mixing bowl and a spatula, following the standard time protocol for adding components and mixing without transfer into a separate cement gun. After mixing, the bowl remained on the table until 2 min 50 sec had been reached. At that time, cement was taken out of the bowl using the spatula and held next to the bowl until measurement was completed at 3 min after mixing.

The systems remained on the table during the mixing process until preparation for nozzle

Table 2. Mean time (SD) in seconds for each step of the mixing procedure

Steps	ACM	Cemvac	Easymix	MixOR	Optimix	Optivac	Vacu-Mix	Handmixing
Filling, sec	38 (4.5)	61 (20.0)	46 (3.6)	44 (41.1)	32 (4.8)	44 (4.5)	56 (4.1)	33 (3)
Vacuum, sec	48 (4.5)	71 (19.6)	56 (3.6)	54 (4.1)	42 (4.8)	54 (4.5)	66 (5.4)	
Mixing, sec	78 (4.5)	101 (19.6)	86 (3.6)	84 (4.1)	72 (4.8)	84 (4.5)	96 (5.4)	63 (3)
Preparation, sec	145 (17.3)	163 (12.6)	146 (3.6)	145 (10.7)	128 (13.8)	144 (4.8)	141 (8.5)	

application with the corresponding cement gun was started. Then the plunger was advanced until a small amount of cement reached the tip of the nozzle. The syringe was placed on the table for the remaining time, with the nozzle tip situated at the same location where the mixing system had been during mixing.

After every single mixing procedure, all material and remnants of mixed bone cement were removed from the theatre. To eliminate residual air contamination, 15-min waiting periods were implemented before measurements were resumed.

Statistics

The primary outcome measure was quantification of MMA fumes in the breathing zone. Differences between 7 mixing systems and manual mixing were tested. Mean, standard deviation (SD) and additional median and interquartile ranges were calculated for the continuous variables. Additionally, as PID software allows quantification of mean values for every second of the mixing process, the concentration curves over time could be calculated. Differences for the outcome parameters gas chromatography GC (ppm) and PID (ppm) were tested in a univariate analysis of variance with mixing system as fixed factor (1 ppm = 4.16 mg MMA/m^3). Post-hoc tests (Tamhane tests) were performed. A two-tailed p-value equal to or less than 0.05 was considered significant. Association between the primary outcome measure and the second method of measurement (two continuous variables) was tested by Pearson's correlation coefficient. Data analysis was performed with SPSS for Windows version 11.0.1 (SPSS Inc., Chicago, IL, USA).

Results

Although a vacuum was applied during the mixing procedure, MMA evaporated continuously from the systems into the breathing zone during mixing (Figure 1). Using gas chromatography (GC) as a detection method, significantly lower concentrations of MMA fumes compared to handmixing were found, when ACM, Cemvac, Easymix, Optimix, Optivac or Vacu-Mix were used for mixing (Table 3). Amongst the vacuum mixing systems, MixOR was associated with the highest fume exposure. With Photo Ionization Detection (PID), significantly lower concentrations of MMA compared to handmixing were seen when ACM, Cemvac, Easymix, or Optimix were used as mixing system (Table 4).

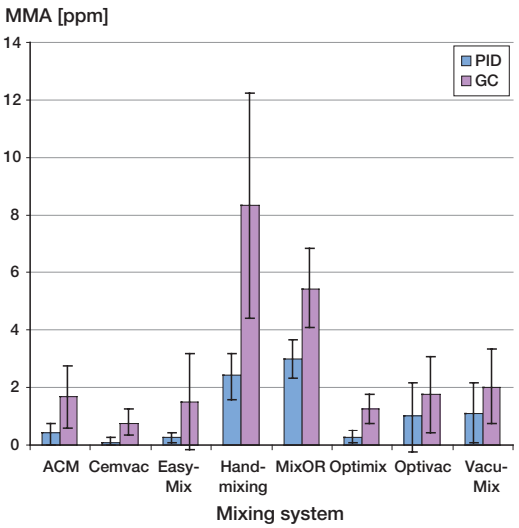

Figure 1. Mean (and standard deviation) MMA concentration in the breathing zone over 3 min using Photo Ionization Detection (PID) and gaschromatography (GC) in 80 mixing procedures.

As no standard detection method has been defined for MMA vapors to date, we used classic GC and PID simultaneously to cross-check reliability of the measured values and give additional information about sensitivity and correlation. Pearson's correlation coefficient for the two detection systems was calculated to be r = +0.78. The mean MMA concentrations detected with the PID for every second of the mixing process were calculated for every mixing device separately (Figure 2). The concentrations measured differed between the different systems examined. Thus, we focused on the major emission peaks within single systems. These results showed that the initial loading of the mixing systems with cement resulted in major emission peaks with ACM, Cemvac, Easymix, MixOR, Optivac and Vacu-Mix. Mixing led to additional peaks when the Optimix and VacuMix systems were used, or when handmixing was used as preparation method. Preparation for application resulted in further MMA concentration peaks with the ACM, Cemvac and the VacuMix Systems.

Table 3. Comparison of outcome data (GC) for the different mixing systems used: p-values from the Tamhane test

	ACM	Cemvac	Easymix	Hand-mixing	MixOR	Optimix	Optivac	Vacu-Mix
One-Way-ANOVA F = 70, df = 7, p<0.001, R-square: 0.69:								
ACM	–	0.6	1.0	0.009	<0.001	1.0	1.0	1.0
Cemvac	–	–	1.0	0.004	<0.001	0.7	0.8	0.3
Easy-Mix	–	–	–	0.007	0.001	1.0	1.0	1.0
Hand-mixing	–	–	–	–	0.7	0.007	0.01	0.01
MixOR	–	–	–	–	–	<0.001	<0.001	0.001
Optimix	–	–	–	–	–	–	1.0	0.9
Optivac	–	–	–	–	–	–	–	1.0
Vacu-Mix	–	–	–	–	–	–	–	–

Using gas chromatography (GC) as detection method, significant differences between handmixing and ACM, Cemvac, Easymix, Optimix, Optivac and Vacu-Mix are shown underlined. The data show results from cement collection under vacuum, except for ACM and Vacu-Mix, which cannot collect under vacuum.

Table 4. Comparision of outcome data (PID) for the mixing systems used: p-values from the Tamhane test

	ACM	Cemvac	Easymix	Hand-mixing	MixOR	Optimix	Optivac	Vacu-Mix
One-Way-ANOVA F = 25, df = 7, p<0.001, R-square: 0.71:								
ACM	–	0.6	1.0	<0.001	<0.001	1.0	0.1	0.8
Cemvac	–	–	0.4	<0.001	<0.001	0.6	0.7	0.3
Easy-Mix	–	–	–	<0.001	<0.001	1.0	1.0	0.5
Hand-mixing	–	–	–	–	0.9	<0.001	0.2	0.2
MixOR	–	–	–	–	–	<0.001	0.009	0.006
Optimix	–	–	–	–	–	–	0.1	0.6
Optivac	–	–	–	–	–	–	–	1.0
Vacu-Mix	–	–	–	–	–	–	–	–

Using Photo Ionization Detection (PID) as detection method, significant differences between handmixing and ACM, Cemvac, Easymix and Optimix are shown underlined. The data show results from cement collection under vacuum, except for ACM and Vacu-Mix, which cannot collect under vacuum.

Overall, all vacuum mixing systems significantly reduced MMA fume exposure, by approximately 50–75%, compared to open-bowl mixing.

Discussion

Vacuum mixing of bone cement is considered to be beneficial, as reduced porosity and improved physical properties of acrylic bone cements are achieved (Alkire et al. 1987, Lidgren et al. 1987, Schreurs et al. 1988). Also, vacuum mixing devices are expected to reduce exposure to MMA vapours, as the mixing process is performed under vacuum. Interestingly, there are apparently different permissable exposure limits in Europe (Table 5). British, Swedish and German law allows a maximum concentration of 50 ppm MMA during a normal working day of 8 h in a 40 h week. These legally valid limits, however, may not necessarily reflect the occupational hazards created by exposure to MMA. Inhalation or skin contact with even lower

Table 5. PMMA limits in Europe

Country	8 hour (ppm)
UK	50
Belgium	100
Denmark	75
Finland	100
France	100
Germany	50
Sweden	50

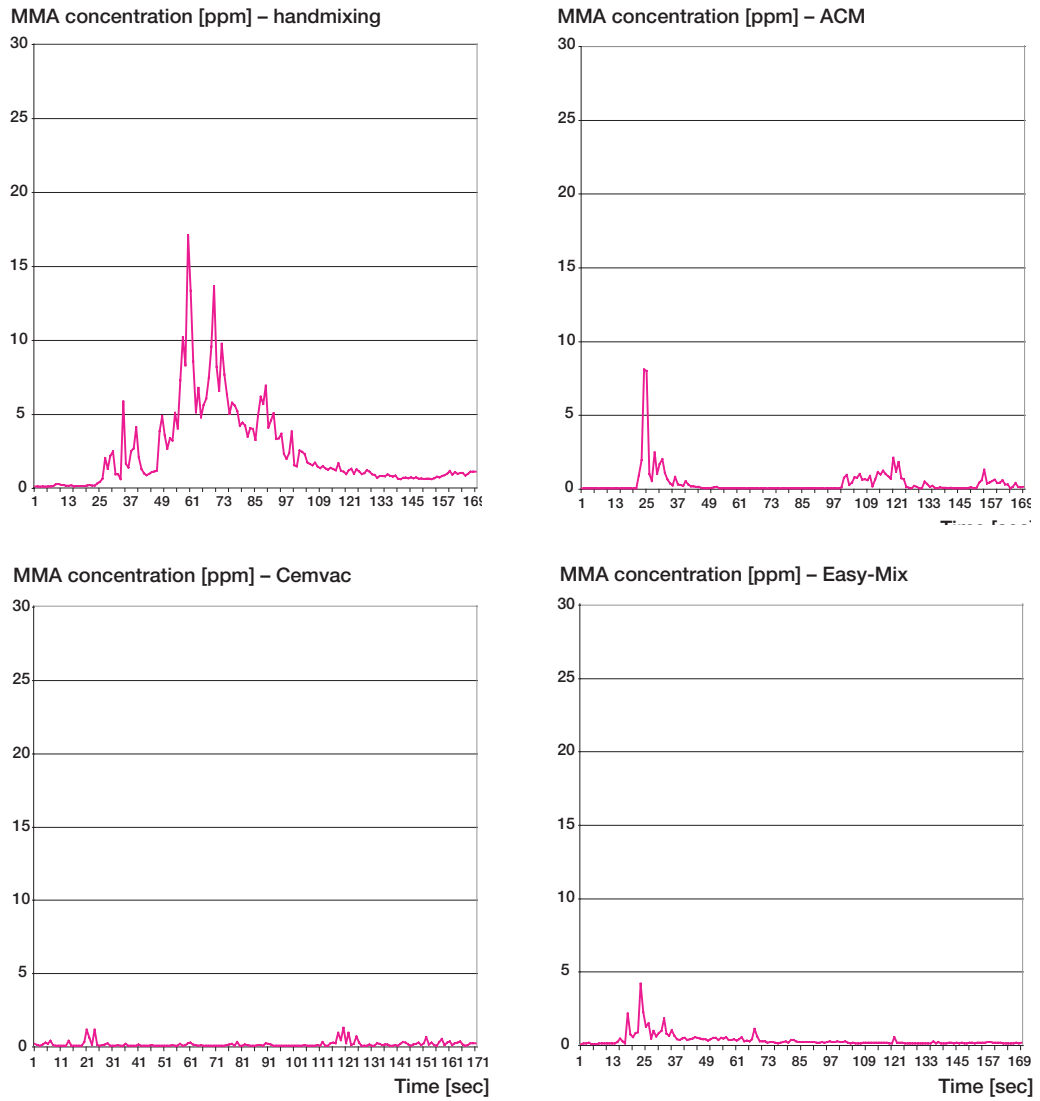

Figure 2. Mean concentrations of MMA from 10 mixes, calculated for every second of the mixing procedure.

concentrations may lead to the specific symptoms in particularly sensitive individuals.

Interestingly, little information has been published to date regarding exposure of the scrub nurse to MMA fumes during vacuum mixing or handmixing of bone cement. Former studies concentrated more on monomer detection during handmixing and found values from 200–500 ppm at a maximum distance of 10 cm from the bowl (Darre et al. 1988a), whereas cementing of the actetabular component is known to cause concentrations of 50–100 ppm in the breathing zone of the surgeon (Darre et al. 1992). Another study found MMA concentrations of 87 ppm when measuring over a period of 10 min next to a Vacu-Mix System (Darre et al. 1988a). These studies used gas chromatography as the detection method. According to current publications, no gold standard for detecting MMA vapor has been defined. Using Photo Ionization Detection (PID) and gas chromatography (GC) simultaneously in this study allowed us to compare both methods. With GC, fume collection and analysis are difficult and time-consuming, but GC was more sensitive for measurement of MMA fumes,

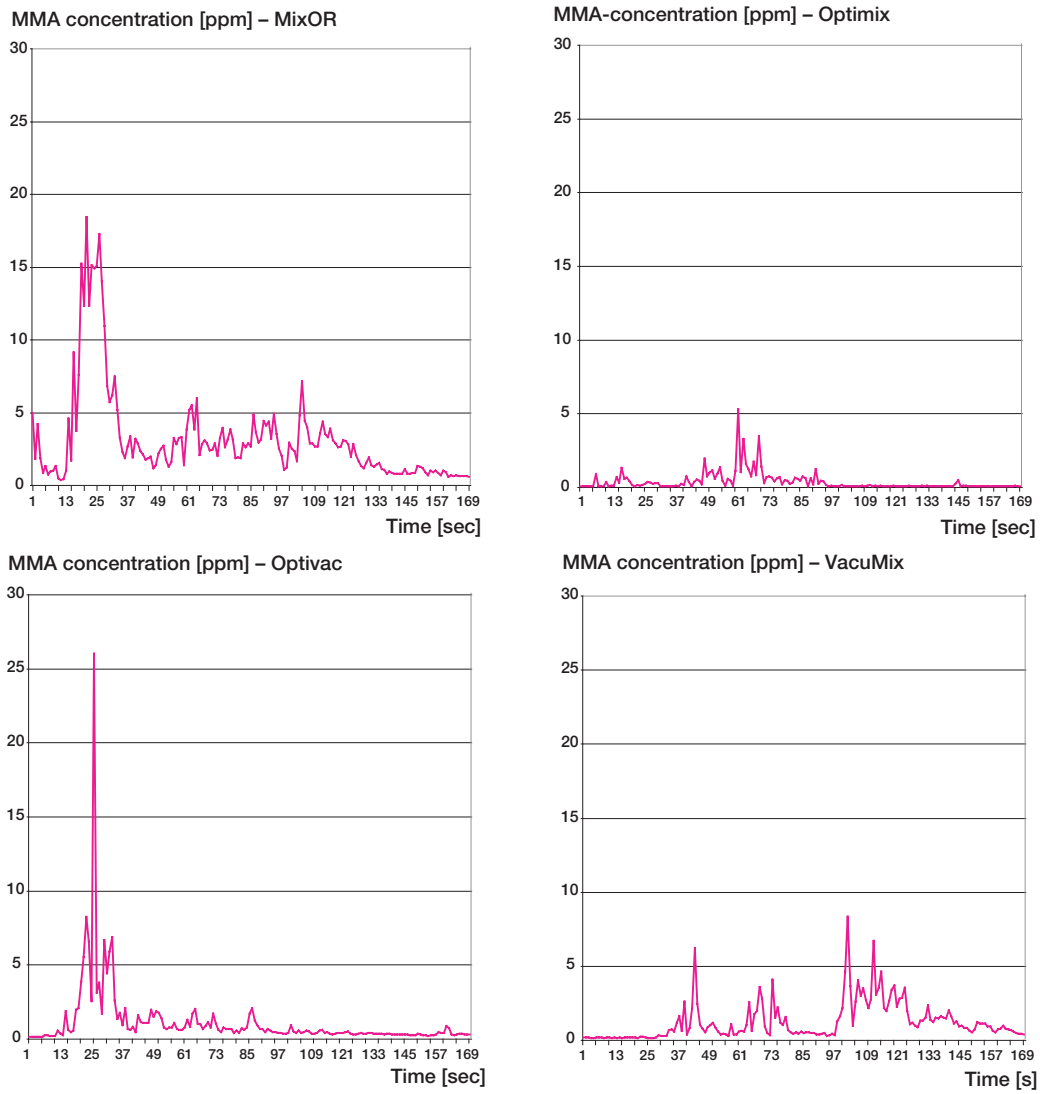

Figure 2 continued.

as concentrations were usually higher than those measured with PID. In contrast, PID allows easy data collection and gives the possibility of checking MMA concentrations at any point in time whilst the measurement is still in progress. Although less sensitive, we found PID to be a useful and effective alternative to the classical GC. The characteristic smell of MMA was present with all systems, which is not surprising, as concentrations as low as 0.2 ppm lead to this sensation.

Our data have shown that the vacuum mixing systems in this study reduced exposure to MMA vapors significantly as compared to handmixing. Buchhorn et al. (1992) reported MMA concentrations lower than 50 ppm at a distance of 20 cm from the open mixing bowl. Mixing in an open bowl in their study had resulted in maximum mean MMA concentrations of 8.3 ppm (GC) in the breathing zone. This may be due to the fact that the distance from the upper opening of the mixing bowl to the tips of the detection systems was greater than for the vacuum mixing systems, so that air turbulence could easily take away a proportion of the released fumes before measurement. Also, no transfer of

the handmixed cement into an application gun was carried out, which contributes to higher measured concentration levels, as handling of the cement leads to further emission of MMA vapors. At a distance of 65 cm, most systems in our study resulted in less than 4 ppm/^{3} min. Further exposure after that can be expected to be low, as shown in our continuous recordings.

Several mechanisms must be considered. Generally, monomer liquid and polymer powder are filled into the system, then the device is closed and a vacuum is applied. Mixing is then performed with an integrated paddle connected to an exterior handle. The collection of the cement can be achieved by vacuum or by pushing the plunger up mechanically. The latter option should theoretically lead to more monomer loss than in vacuum collected samples, which was observed in the ACM and Vacu-Mix systems. However, recordings over 3 min for MMA exposure were higher when using the Mixor system (collection under vacuum) compared to ACM and Vacu-Mix (collection without vacuum). This may be due to the fact that the vacuum collection process with this system (Mixor), after having released the plunger, occurs very rapidly, thus probably liberating even more fumes during this phase. Additionally, increased monomer loss during the mixing process, i.e. leakage, may have contributed to the high concentrations of MMA observed with this system (Figure 6).

In our opinion, continuous stirring with the mixing paddle seems to lead to forced monomer loss in some of the mixing devices via the upper opening for the paddle in the lid of the mixing system, and brings it up to the breathing zone. Vacuum mixing systems apparently differ in their ability to reduce MMA exposure. Exhaust air from the system that has already passed the filter in the vacuum pump does not seem to contribute further to air contamination in the breathing zone, as background measurements after the mixing procedure in this study never showed evidence of MMA in the air of the theatre.

All vacuum-mixing systems tested, and even handmixing, were within the European legal limits, but significant differences were found. Most vacuum systems resulted in a maximum of 4 ppm per mix of 40 g cement in the first 3 min. According to the lowest European limit of 50 ppm per 8 h, which does not refer to cumulative exposure, but to the maximum at any given point during the 8-h working period, handmixing would only exceed the limit if 3 mixes (120 g) were mixed simultaneously, which may be required when cementing a large femur to allow for appropriate cement pressurization. However, if 50 ppm is taken as a cumulative exposure then, extrapolated, this would mean that 3 to 4 total hip replacements (using 120 g each) can be performed in a working day without the lowest European legal limits being reached when using vacuum, but only 2 when handmixing in an open bowl.

It is still important to note that most vacuum mixing systems in this study reduced methylmethacrylate exposure significantly compared to handmixing. In any case, keeping a maximum distance and leaving the system or bowl on the instrument table during mixing is a simple but important step for reducing exposure to MMA.

Bone-cement and vacuum-mixing systems were provided by the companies mentioned in the study.

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