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Fracture resistance and reinforcement of immature roots with gutta percha, mineral trioxide aggregate and calcium phosphate bone cement: a standardized *in vitro* model

Rita G.E.C. Cauwels[1], Ilse Y. Pieters[2], Luc C. Martens[1], Ronald M.H. Verbeeck[2]

[1]Department of Paediatric Dentistry and Special Care, PaeCaMeD Research; [2]Department of Basic Medical Science, Biomaterials Group, Ghent University, Ghent, Belgium

Correspondence to: Rita Cauwels, Dental School – P8, Ghent University Hospital, De Pintelaan 185, B-9000 Ghent, Belgium
Tel.: +32 9 332 51 04
Fax: +32 9 332 38 51
e-mail: rita.cauwels@ugent.be

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Abstract – Endodontic treatment of immature teeth is often complicated because of flaring root canals and open apices for which apexification is needed. Long-term prognosis for these teeth is surprisingly low because of cervical root fractures occurring after an impact of weak forces. In this study, an experimental model was developed to determine the fracture resistance of immature teeth and to test the hypothesis that endodontic materials succeed in reinforcing them. Compact and hollow bone cylinders from bovine femurs were used as standardized samples. In order to evaluate the experimental model, fracture resistance in both groups was evaluated by determining the ultimate force to fracture (UFF) under diametral tensile stress. Analysis of variance (ANOVA) revealed a statistically significant difference between the mean values of UFF for both groups, independently of the sampling location or subject. In a following setting, the hypothesis that obturation with gutta percha (GP), mineral trioxide aggregate (MTA), or calcium phosphate bone cement (CPBC) reinforces the hollow bone samples was investigated. Obturation resulted in a significant reinforcement for all materials, but the degree of reinforcement depended on the material. The experimental model appeared to be suitable for *in vitro* investigation of reinforcement and fracture resistance in a standardized way.

Endodontic treatment of immature teeth remains a challenge due to open apices and flaring root canals accompanied by thin immature dentinal walls. In case of pulp necrosis, apexification is the treatment of choice inducing a calcified barrier at the apex allowing a more favorable condition for conventional root canal filling with gutta percha (GP) and a root canal sealer. Usually, apexification is performed with calcium hydroxide (CH) as first reported by Granath (1) and later by Frank (2). Mostly, a long-term treatment is required and success is depending on the cooperation of the young patient (3). Although the success rate of apexification is 95%, its long-term prognosis appears to be compromised by cervical root fractures (3, 4). These fractures are strongly related to the stage of root development and defects at the cervical area (4). However, this observation was also explained by the fact that long-term use of CH has a weakening effect on dentin due to a proteolytic reaction. Consequently, with time, this treatment significantly reduces fracture resistance (5, 6). In this respect, calcium phosphate bone cement (CPBC) and mineral trioxide aggregate (MTA) are two promising materials.

Because of the structural and compositional similarity with the mineral component of teeth, CPBC's are highly biocompatible and therefore useful in a variety of dental applications (7–9). Moreover, when used as a root-end filling material CPBC's have shown to promote hard tissue formation at the apex (9, 10).

MTA, which is a powder aggregate containing mineral oxides, has shown to be biocompatible, promoting tissue regeneration in the apical and peri-apical zone. So it has been recommended for apexification (11, 12). According to Andreasen et al. (2006), replacement of long-term CH treatment by a one-visit apexification with MTA prior to filling with GP and sealer could be a good alternative to prevent reduction in fracture resistance (5). Despite the advantageous properties of CPBC's and MTA, no studies have proved their strengthening effect in human immature teeth.

Strengthening non-vital immature teeth has been of concern for many years and different materials and techniques have been examined in this respect (13–17). However, the variability in study design makes the reproducibility and comparability of the results impossible. Some of the investigators used human, bovine or sheep teeth but failed to provide consistent results (18–21). Hence, teeth are unlikely to standardize because of their dissimilarity in shape and structure. In addition, human teeth are available in a limited number. In this respect, the use of standardized samples can reduce the number

of variables and provide a rational and more accurate basis for an initial comparison. The present study aimed to develop an *in vitro* model to assess the fracture resistance of obturated standardized samples, comparing GP, MTA and CPBC.

Materials and methods

Pro analysis chemicals and freshly prepared ultra pure water (Milli-Q system, Millipore, Bredford, MA, USA) were used throughout the experiments.

Preparation of bone samples

Eighteen bovine femurs were obtained from a local slaughterhouse immediately after slaughter. Hip and knee heads were removed at two anatomical marks, the lesser trochanter and the nutrient foramen. Approximately 20 mm thick transverse slices were sawn from the middle 2/3 of the diaphysis. Because it was not always possible to prepare samples from the outer slices, only the five central slices were selected. From the hip to the knee, these slices (sampling locations) were numbered from 1 to 5 and stored in 0.5% chloramin T trihydrate (Merck, 8.18705.1000) at room temperature for no longer than 6 days. From the compact bone of each slice, cylinders were cut with a diameter of 7.0 ± 0.1 mm equal to the mean diameter at the cervical area of human central incisors. Subsequently, the cylinders were reduced to a height of 10.5 ± 0.1 mm to obtain a diameter/height ratio = 2/3 according to the norm NBN-EN 24104, 1992. Bone cylinders originating from the same slice were randomized in two groups: compact and hollow cylinders. The hollow samples were obtained by drilling a central canal with a diameter of 3.5 mm in the compact ones. Throughout the experiments, the bone cylinders were stored in water at 4°C until use up to a maximum of 4 weeks. Water was changed twice a week.

Obturation of untreated bone samples

In order to test the hypothesis that obturation strengthens hollow bone samples, two compact and two hollow samples per slice were taken apart and used, respectively, as positive and negative control for each sampling location. The remaining hollow bone cylinders of the slice were obturated either with GP, MTA or CPBC and condensed, holding the sample firmly against a glass plate.

GP

The hollow bone cylinders were obturated either with GP-Points® (Dentsply Maillefer Switserland) (CGP) or with low temperature thermoplasticized gutta percha (Ultrafil®3D–Hygenic, Coltène Whaledent GmbH, Konstanz, Germany) (WGP).

CGP obturation was performed following the lateral condensation technique. Obturation with WGP was performed following the instructions of the manufacturer. Prior to obturation with GP, walls and individual cones were coated with a thin layer of epoxy-resin-based root canal sealer AH 26®silver free (Dentsply DeTrey GmbH, Konstanz, Germany). With respect to the setting time of the root canal sealer, filled specimens were stored at 100% humidity and 37°C for 48 h.

MTA

Obturation with MTA was performed by filling the hollow bone cylinders with grey MTA (Pro Root MTA, Dentsply Tulsa Dental, Tulsa, OK, USA). According to the instructions of the manufacturer, MTA powder was mixed with water in a proportion of 3/1. The obturated samples were stored for 24 h at 100% humidity and 37°C to ensure complete setting of MTA.

CPBC

Preparation of tetra calcium phosphate-based calcium phosphate bone cement. In the present study, a CPBC based on an equimolar mixture of tetracalcium phosphate (TTCP, $Ca_4(PO_4)_2O$) and dicalcium phosphate (DCP, $CaHPO_4$) was used as cement powder.

TTCP was prepared according to the method of Tenhuisen & Brown (22, 23). In brief, equimolar amounts of DCP (Merck, 2144) and $CaCO_3$ (Merck, 2076) were mixed by milling in a Pulverisette 6 planetar ball mill (Fritsch, Idar-Oberstein, Germany). The mixture was heated in platinum vessels for 2 h at 1400°C under a dry nitrogen atmosphere after which it was quenched under vacuum and milled. Phase composition and purity of TTCP were checked with chemical analyses and X-ray diffractometry (Philips PW 1830 diffractometer system, Almelo, The Netherlands). The specific surface area of TTCP was determined as 1.38 $m^2\ g^{-1}$ using the BET method (Monosorb; Quantachrome Corp., Boyton Beach, FL, USA) with an accuracy of 6% (24). A solution containing 0.25 M sodium dihydrogen phosphate (NaH_2PO_4) and 0.25 M disodium hydrogen phosphate (Na_2HPO_4) was used as the cement liquid (25).

The CPBC was prepared by mixing the cement powder with the cement liquid at a powder/liquid ratio of 0.30 ml g^{-1} for 2 min in a small agate mortar with an agate pestle. The cement sets with the formation of calcium hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$, the prototype of the mineral phase in tooth and bone (26, 27). The liquid to powder ratio was chosen to yield cements with a workable consistency and reasonable setting times (28, 29). The initial and final setting times were determined, respectively, as 11 and 37 min using the light and heavy Gillmore needles (30).

Obturation of the hollow cylinders was performed with an amalgam carrier and a home-made condenser. The obturated samples were stored for 24 h at 100% humidity and 37°C before determination of the UFF.

Determination of the Ultimate force to fracture (UFF)

The bone cylinders were loaded diametrally at a crosshead speed of 1 mm min^{-1} in a Lloyd's mechanical testing machine (model LR 50K, Hampshire, UK) at a temperature of 22°C until failure occurred. The maximum force (kN) that a sample can withstand before it fractures, was taken as the UFF.

Evaluation of the results

The dependency of the UFF on the sampling location (level in the femur), the treatment (compact, hollow and/or obturated bone cylinder) and the subject (cow) was investigated using ANOVA based on a General Linear Model (GLM). The UFF was taken as the dependent variable, the sampling location and the treatment as fixed factors and the subject as random factor. Significant differences among the means were detected with the Bonferroni multiple comparison test at the 95% confidence level.

Results

In the first part of the experiment, the accuracy of the bone sampling and preparation procedure was checked by comparing the homogeneity of the UFF of compact ($N = 158$) and hollow ($N = 161$) bone cylinders. The GLM with the sampling location and the treatment (compact vs hollow) as fixed factors and the subject as random factor demonstrated that the UFF of the bone cylinders was independent of the subject ($P = 0.318$) and the sampling location ($P = 0.722$), but significantly differed between compact and hollow samples ($P < 0.001$) (Table 1). Moreover, there was no interaction between the compact and the hollow samples and the subject ($P = 0.249$) or the sampling location ($P = 0.723$) (Table 1). Hence, all the samples with the same treatment could be pooled. The global mean and corresponding 95% confidence interval of the UFF then amounted to 2.90 ± 0.10 kN for the compact and 0.48 ± 0.02 kN for the hollow bone samples. In the second part of the experiment, the effect of obturation on the fracture resistance of hollow bone cylinders was investigated. In order to detect possible differences of sampling location and subject on the UFF, the data for the compact and hollow bone cylinders obtained in the first part of the study were included in the analysis. The GLM with the sampling location and the treatment (compact bone cylinder, hollow bone cylinder, hollow bone cylinder obturated with CGP, hollow bone cylinder obturated with WGP, hollow bone cylinder obturated with MTA, hollow bone cylinder obturated with CPBC) as fixed factors and the subject as random factor demonstrated that the UFF of the bone cylinders was independent of the subject ($P = 0.255$) and the sampling location ($P = 0.111$), but depended significantly on the treatment ($P < 0.001$) (Table 2). Moreover, there was no interaction between the factors treatment, subject and sampling location indicating that the UFF of compact, hollow and the differently obturated samples was only affected by the treatment and not by the subject or the sampling location. Hence, the data of the samples with the same treatment could be pooled and resulted in the global means represented in Fig. 1. The global mean and corresponding 95% confidence interval of the UFF then amounted to 2.87 ± 0.05 kN for the compact bone cylinders, 0.47 ± 0.05 kN for the hollow bone cylinders, 0.77 ± 0.06 kN for the CGP obturated bone cylinders, 0.68 ± 0.06 kN for the WGP obturated bone cylinders, 1.31 ± 0.10 kN for the MTA obturated bone cylinders and

Table 1. Results of the ANOVA based on a General Linear Model (GLM) of the Ultimate Force to Fracture (UFF) as a function of treatment (compact and hollow bone cylinder), sampling location of the femur (level), subject and the interaction (×) among these factors

Source	df	MS	F	P
Intercept	1	818	2420	**<0.001**
Factor				
Treatment	1	422	1815	**<0.001**
Level	4	0.077	0.520	0.722
Subject	7	0.346	1.629	0.318
Interaction				
Treatment × level	4	0.087	0.518	0.723
Treatment × subject	7	0.234	1.408	0.249
Level × subject	23	0.144	0.867	0.632
Treatment × level × subject	23	0.166	0.779	0.757

Probability (*P*) of a significant effect on the UFF according to the *F*-value based on the calculated mean square (MS) and corresponding degrees of freedom (df).
P-values considered as statistically significant are indicated in bold.

Table 2. Results of the ANOVA based on a General Linear Model (GLM) of the Ultimate Force to Fracture (UFF) as a function of treatment (compact, hollow, CGP, WGP, MTA and CPBC obturated bone cylinder), sampling location of the femur (level), subject and the interaction (×) among these factors

Source	df	MS	F	P
Intercept	1	819	3130	**<0.001**
Factor				
Treatment	5	114	515	**<0.001**
Level	4	0.285	1.960	0.111
Subject	9	0.303	1.410	0.255
Interaction				
Treatment × level	19	0.196	1.200	0.270
Treatment × subject	24	0.254	1.499	0.089
Level × subject	32	0.145	0.860	0.678
Treatment × level × subject	75	0.175	1.383	0.020

Probability (*P*) of a significant effect on the UFF according to the *F*-value based on the calculated mean square (MS) and corresponding degrees of freedom (df).
P-values considered as statistically significant are indicated in bold.

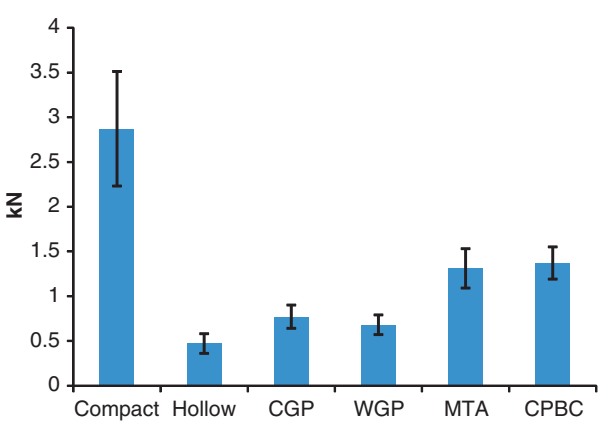

Fig. 1. The global mean and corresponding SD of the Ultimate Force to Fracture (UFF) for the different treatments (compact, hollow, lateral gutta percha condensation CGP, thermoplasticized gutta percha WGP, MTA and calcium phosphate bone cement CPBC).

Table 3. Bonferroni multiple comparison test

	Compact	Hollow	CGP	WGP	MTA	CPBC
Compact		0.000	0.000	0.000	0.000	0.000
Hollow	0.000		0.000	0.000	0.000	0.000
CGP	0.000	0.000		**0.856**	0.000	0.000
WGP	0.000	0.000	**0.856**		0.000	0.000
MTA	0.000	0.000	0.000	0.000		**1.000**
CPBC	0.000	0.000	0.000	0.000	**1.000**	

No significant difference is seen between the UFF of CGP and WGP and between the UFF of MTA and CPBC as indicated in bold.

1.37 ± 0.06 kN for the CPBC obturated bone cylinders. Apparently, obturation with GP, MTA or CPBC resulted in a significant reinforcement of the hollow bone cylinders ($P < 0.001$) (Table 3). However, the UFF of the obturated samples remained drastically lower than that of the compact samples ($P < 0.001$). Moreover, the difference between the UFF of CGP and WGP obturated samples was not significant ($P = 0.856$) neither that between MTA and CPBC filled samples ($P = 1.000$). When testing fracture resistance of MTA and CPBC filled bone samples, it was remarkable that, in contrast with GP, both materials adhered well to the walls (Fig. 2a–c).

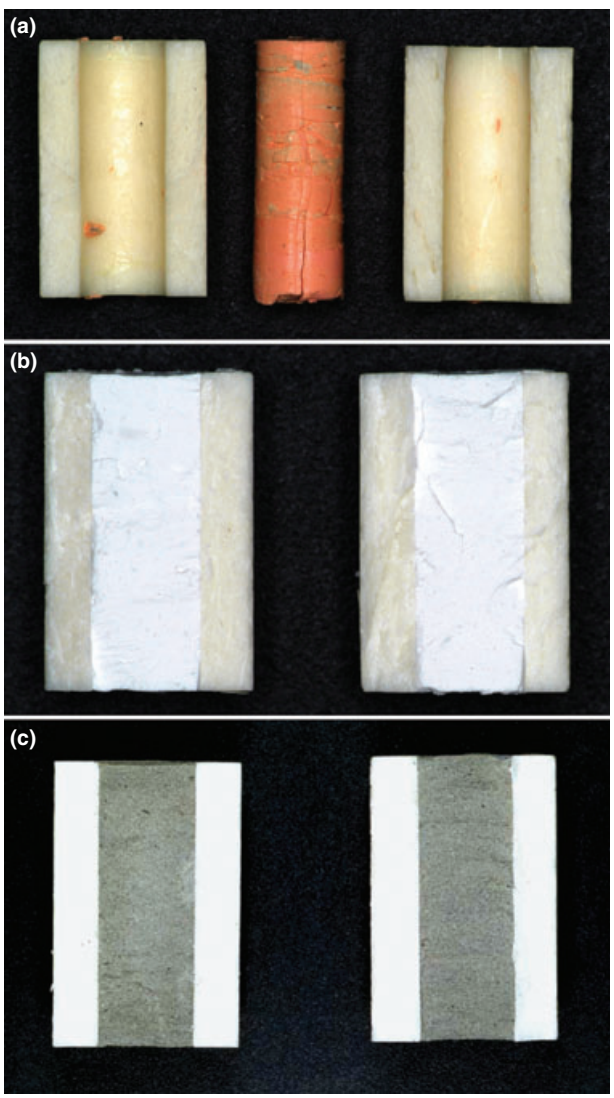

Fig. 2. Fractured samples of a thermoplasticized gutta percha (WGP) obturated bone cylinder (a), a calcium phosphate bone cement (CPBC) obturated bone cylinder (b) and a MTA obturated bone cylinder (c). Gutta percha (GP) detaches completely while CPBC and MTA adheres to the bone surface following pressure until ultimate force to fracture (UFF).

Discussion

In the present study, bovine bone samples were investigated for standardization and different endodontic materials were tested for their strengthening effect. Bone samples were preferred to teeth or dentin samples to exclude concomitant factors. Moreover, the main components of mineralized hard tissue such as bone and dentin are comparable. They both consist of inorganic material (calcium phosphate of the hydroxyapatite type), organic material (mainly type-I collagen) and of water (31). The most striking difference between both is found in the dentinal tubules giving rise to an anisotropic microstructure, which significantly influences mechanical properties (32–35). Although most studies measured fracture resistance to compressive stress or impact forces, consistent with dental traumatic injuries, the samples in the present study were subjected to tensile stress until fracture occurred. In order to approach the dimensions of an immature tooth at the cervical area, the hollow bone samples obtained a central canal of 3.5 mm diameter resulting in a cylindrical wall thickness of 1.75 mm, comparable to the cervical dentinal wall in immature teeth. Earlier investigation revealed that the reinforcement of a canal with a diameter less than 1.5 mm seems not to be necessary, while wall thickness of 2.63 mm is insufficient to weaken tooth structure (36).

To test the validity of this model, in the first part of this study the UFF under tensile stress of compact bone samples was compared with that of hollow samples. As expected, the fracture resistance was significantly higher for the compact samples compared to the hollow ones, but most important, this difference did not depend on the sampling location or the subject. Consequently, this experimental model was suitable for reproducible measurements of UFF of bone cylinders.

In the second part of this study, the model was used to test the assumption that obturation with endodontic materials (GP, MTA and CPBC) increases the fracture resistance of the hollow samples. Gutta percha combined with a root canal sealer is currently the material of choice for root canal filling and can be seen as the standard. Two different techniques, CGP and WGP, used with an epoxy-resin-based root canal sealer were tested. Upon fracture, WGP and CGP detached completely from the walls of the bone samples as is illustrated in Fig. 2a. The UFF, representing the fracture resistance, depended on the treatment (compact, hollow, GP obturated hollow samples) regardless of the subject or sampling location. Although the UFF of CGP obturated samples tended to be slightly higher compared to the WGP ones, the difference was not significant. Obturation with GP, regardless of the technique used, resulted in a small,

although significant reinforcement of the hollow samples. When testing fracture resistance of MTA and CPBC filled bone samples, in contrast with GP, both materials adhered to the walls (Fig. 2a–c), suggesting a chemical interaction between the material and the bone wall. Sarkar et al. (2005) investigated the fundamental physicochemical interactions at the MTA-dentin interface (37). These authors suggested that initially, the bond between these materials is mechanical and, with time, becomes chemical because of a diffusion-controlled reaction between MTA and dentin. MTA in contact with dentin undergoes a gradual dissolution inducing a nucleated growth of hydroxy apatite crystals at its surface. Such so-called bioactive material, in proximity to calcified tissues, forms a chemical bond with the latter (37). Because bone and dentin have a similar mineral composition, this may explain the interaction of MTA and CPBC with the bone surface following fracture. The fracture resistance of the MTA and CPBC filled samples was significantly higher than that of the hollow and GP filled samples. When comparing the UFF of MTA- and CPBC-filled samples, no significant difference was found.

MTA has an alkaline pH, comparable to that of CH. During setting, MTA changes from pH 10.2 to pH 12.5 in 3 h (38). It has been shown that, because of an interaction between MTA or CH and the organic phase of dentine resulting in a degradation of type-I collagen, the microhardness of dentine is altered (5, 18). Alkalinity is known to denature the organic matrix of dentin, i.e. the collagen. On the contrary, an alkaline pH and calcium release is needed to stimulate mineralization. According to Santos et al. (2005), during the setting of MTA, pH increases within the first 24 h because of the hydroxide-ion release and remains alkaline after 360 h (39). This is in contrast with TTCP-based CPBC which creates a neutral pH during setting (7). In spite of this, CPBC revealed to have the capacity to promote hard tissue formation at the apex (10, 40). As root canal sealer/filler, this material showed to be highly adaptable and adhering to the root canal surface, to be dimensionally stable and easily to handle (41). It was concluded that CPBC could be seen as an adequate root canal cement because it sets to hard consistency, has reasonable high compressive strength, adheres to the canal walls and is pH stable (42). Of course, it needs further investigation whether this neutral pH in CPBC could be advantageous concerning the strengthening effect in immature teeth.

According to Torabinejad et al. (1995), the compressive strength of MTA increased from 40 MPa after 24 h to 67.3 MPa after 3 weeks (38). In contrast, one *in vitro* study investigated the possible reduction in fracture resistance of bovine dentin filled with MTA (6). The results showed a significant mean decrease in strength after only 5 weeks of exposure to CH (32%) and MTA (33%) compared to the control group (6). Andreasen et al. (2006) reported that MTA, compared to CH, strengthens the cervical fracture resistance of immature sheep incisors (5). According to Roberts et al. (2008), this result is promising but it should be considered that the sample number was low (< 10) and the sample dimensions were not standardized which includes possible biological variations (43). In a recent *in vitro* study (18), Hatibović-Kofman et al. (2008) compared the influence of MTA and CH on the fracture resistance in sheep teeth. Over a period of 1 year, MTA was responsible for a decrease in fracture resistance of only 2% which was significantly different from the CH filled and untreated samples which showed a decrease of 28% and 47%, respectively. On the basis of a histological investigation, it was thought that this result could be related to a change in the dentin matrix as a result of a biological interaction in 1 year between MTA and dentin, inhibiting destruction of the organic matrix of dentin (18, 44). Yet, according to Tjäderhane (2009), these results are, also because of a discrepancy between the methods and the results, at least questionable (45).

The present *in vitro* study provides evidence that MTA and CPBC have an important and equal strengthening effect on hollow bone samples when compared to GP. According to the literature, they are biocompatible and have an excellent sealing ability when used as a root-end filling material. Because they are structurally and compositionally different, it is necessary to investigate both materials for the effect of dynamic loading in human teeth and the long-term reaction *in vivo*.

The results of this study have to be interpreted within the limitations of an *in vitro* study. Moreover, in the proposed model, bovine bone was used. The authors are aware that biological variations as tooth morphology, periodontal condition and trauma force direction will influence the *in vivo* situation in the human dentition. On the contrary, results from this model using standardized bovine samples can give indications for the *in vivo* application in humans. The investigation on strengthening immature teeth is a multifactorial process in which the above-mentioned limitations are important influencing factors. The present study developed a model in which these factors have been excluded. Although this could be a limitation, it certainly is a first step in the development of a multifactorial model in which the strengthening effect of different materials can be compared.

Conclusion

In the present study, a model was developed to investigate fracture resistance of standardized bone samples. Under the condition of this model, it was concluded that samples obturated with GP, MTA or CBPC showed a significantly higher fracture resistance when compared to unfilled samples. Moreover, MTA and CPBC filled samples showed mutually no significant difference but, compared to GP obturated samples, a significantly higher reinforcement.

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