

Original Research Article

Evaluation of agreement between non-surgical management techniques for large periapical lesions

ABSTRACT

Aim: The aim of this study is to evaluate the agreement between three routinely used non-surgical management techniques for large periapical lesions namely the treatments with Calcium hydroxide, Mineralo-Trioxide Aggregate and Bio-dentine.

Methods: Data was collected from 60 patients at the Department of Restorative Dentistry, Faculty of Dental Sciences, University of Peradeniya. The variables age, gender and area of the infected region before and after the treatment and the treatment type were considered. Two homoscedastic and heteroscedastic Mixed-effects models were fitted and the agreement between three treatments were assessed using Concordance Correlation Coefficient (CCC) and Total Deviation Index (TDI).

Results: CCC value calculated for treatment types 1 & 2, 1 & 3 and 2 & 3 are (0.905, 0.909, 0.874) for homoscedastic model and (0.989, 0.990, 0.975) for heteroscedastic model. Further, corresponding TDI values for homoscedastic and heteroscedastic models are (3.148, 4.390, 1.647) and (2.963, 4.388, 1.457) respectively.

Conclusions: Since all the CCC values are close to 1 and TDI values are low, there is a strong agreement between all three treatments and hence they be used interchangeably. Moreover, the agreement between Treatments with Calcium hydroxide and Bio-dentine is higher compared to others.

Keywords: *Agreement, Concordance correlation coefficient, Mixed effects models, Periapical Lesions, Total deviation index*

1. INTRODUCTION

Inflammatory lesions of the pulp and periapical area which are commonly known as periapical lesions are the most common pathologic condition involving teeth. The lesions are caused by a bacterial infection of the dental pulp.¹ Most of the periapical lesions (>90%) can be classified as dental abscesses granulomas or radicular cysts.^{2,3} The occurrence of dental granulomas ranges between (9.3-87.1) % while the incidence of cysts lies within 6-55% and of abscesses between 28.7 and 70.07%.^{4,5} A granuloma is formed when the periapical tissues neutralize and confine the irritating toxic products escaping from the root canal. A radicular cyst has its origin from the cell rests of Malassez which are present in periodontal and periapical ligament, and in periapical granulomas. Most radicular cysts originate from pre-existing granulomas. On the other hand, an apical abscess usually develops from a pulpo-periapical inflammatory condition. It also can arise from a pre-existing granuloma or cyst. Cysts and granulomas may present very similarly and on most occasions are hard to distinguish by simple observation. Only a professional can differentiate them. Periapical lesions are

40 diagnosed either during routine dental radiographic examination or following acute pain in a tooth.⁶ It
41 is accepted that all inflammatory periapical lesions should be initially treated with conservative
42 nonsurgical procedures⁷. Surgical procedures are recommended only in situations where nonsurgical
43 techniques have failed⁸. In most situations endodontic therapy alone is enough to return the infected
44 teeth to a healthy state and function without surgical intervention since surgery has many drawbacks
45 ^{9,10}, which limit its use in management of periapical lesions. Studies¹¹ have reported that a high
46 percentage of 94.4% of complete and partial healing of periapical lesions could be achieved by
47 nonsurgical endodontic therapy.

48 A nonsurgical approach should always be adopted before resorting to surgery. Patients are also
49 psychologically more anxious about surgical treatment than a nonsurgical one. There are several
50 nonsurgical procedures^{12,13}, such as Conservative root canal treatment without adjunctive therapy,
51 Decompression technique, Intra-canal dressing with Calcium hydroxide, Placement of Mineralo-
52 Trioxide Aggregate (MTA) in the apical 4-5mm of the tooth and Placement of Bio-dentine in the apical
53 4-5mm of the tooth.

54 Calcium hydroxide is a material widely used in endodontic treatment because of its bactericidal
55 effects. It is thought to create favorable conditions for periapical repair and stimulate hard tissue
56 formation. A high degree of success has been reported by using calcium hydroxide beyond the apex
57 in cases with large periapical lesions.¹⁴ The treatment should be given repeatedly. However this
58 treatment is economical compared to the others.

59 MTA and Biodentine are more novel materials which are recommended to be used for successful
60 apical closure in cases with large periapical lesions. They are considered extremely bio-compatible
61 and have cemento-conductive and osseo-conductive properties. Thus these materials are
62 increasingly used in the management of large periapical lesions. They are considered more
63 advantageous considering the time taken for apical closure and the superior apical seal they offer.¹⁵
64 However, compared with calcium hydroxide the cost of these two treatment modalities are higher. The
65 main advantage of these treatment modalities is that the treatment could be dispensed in one visit.

66 The main objective of this study is to evaluate the agreement between three routinely used non-
67 surgical management techniques for large periapical lesions namely the treatment with Calcium
68 hydroxide (Treatment 1) which serves as the standard reference method, the treatment with Mineralo-
69 Trioxide Aggregate (Treatment 2) and the treatment with Bio-dentine (Treatment 3). If the treatments
70 agree satisfactorily well, then they can be used interchangeably.

71 **2. MATERIAL AND METHODS**

72 The data was collected from the Department of Restorative Dentistry, Faculty of Dental Sciences,
73 University of Peradeniya. Sixty patients were randomly allocated to three groups according to the
74 treatment given. The variables considered in this study are the age and gender of the patient, area of
75 the infected region before and after the treatment and the treatment type. The infected area of the
76 tooth of each patient was recorded under 5-time periods (0, 1, 3, 6, 12 months periods) as realized on

77 periapical radiographs taken using a long cone paralleling technique. The maximum diameter of the
78 lesions was recorded at each review as understood on an illuminated radiograph viewer under x2.5
79 magnification.

80 In this study, the Wilcoxon Rank Sum Test was used to test the significant difference between the
81 Treatment types. The null hypothesis is that there is no significant difference between the two
82 treatment methods while the alternative hypothesis is that there is a significant difference between the
83 two treatment methods. If p-value < 0.05, we reject H_0 and conclude that there is a significant
84 difference between the two treatment methods.

85 At first, the data was modeled using homoscedastic mixed-effects model. Then for the situations
86 where the key assumptions such as constant error variance (homoscedastic error variance) are
87 violated, a multiple heteroscedastic mixed effects model was used to model the data. The fitted model
88 was validated using the 10-fold cross validation technique.^{16,17} In order to assess the agreement
89 between the three treatments, Concordance Correlation Coefficient (CCC) and Total Deviation Index
90 (TDI) were used.¹⁸ Fisher's z-transformation and the log-transformation were used on the CCC and
91 TDI respectively for greater accuracy.

92 The CCC is defined as,

$$P_{ccc} = \frac{2\sigma_{12}}{\sigma_1^2 + \sigma_2^2 + (\mu_1 - \mu_2)^2}$$

93 Here σ_1 and σ_2 are the standard deviations of the two groups being compared while σ_{12} is the
94 covariance between the two groups. μ_1 and μ_2 are the means of group1 and group2 respectively.

95 Total deviation index for the two variables Y_1 and Y_2 is given by,

$$TDI = \sqrt{\chi^{2(-1)}\left(\pi_0, 1, \frac{\mu_d^2}{\sigma_d^2}\right)}$$

96 Here, TDI is the π_0^{th} percentile of $|Y_1 - Y_2|$, for a given large probability π_0 where $0.80 \leq \pi_0 \leq 0.95$.

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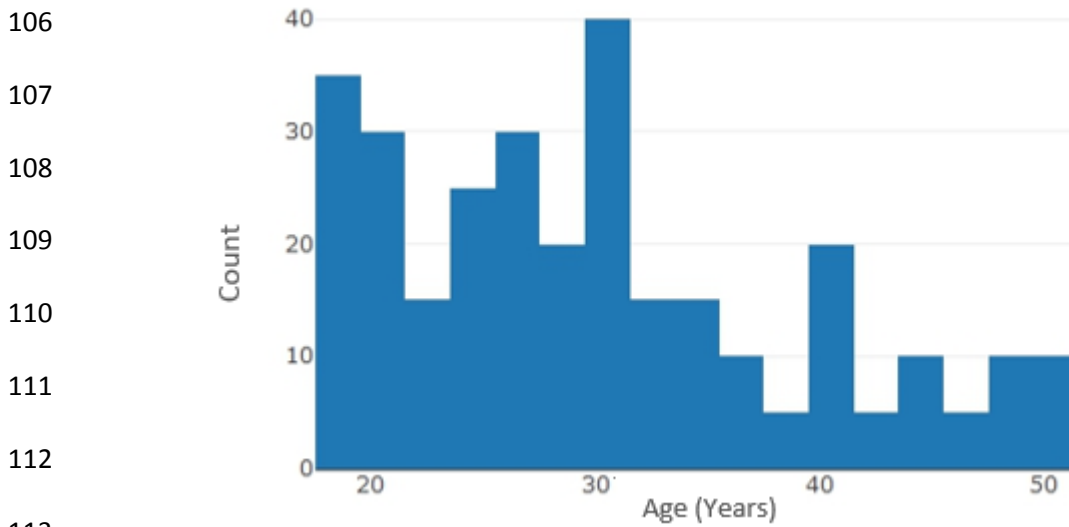
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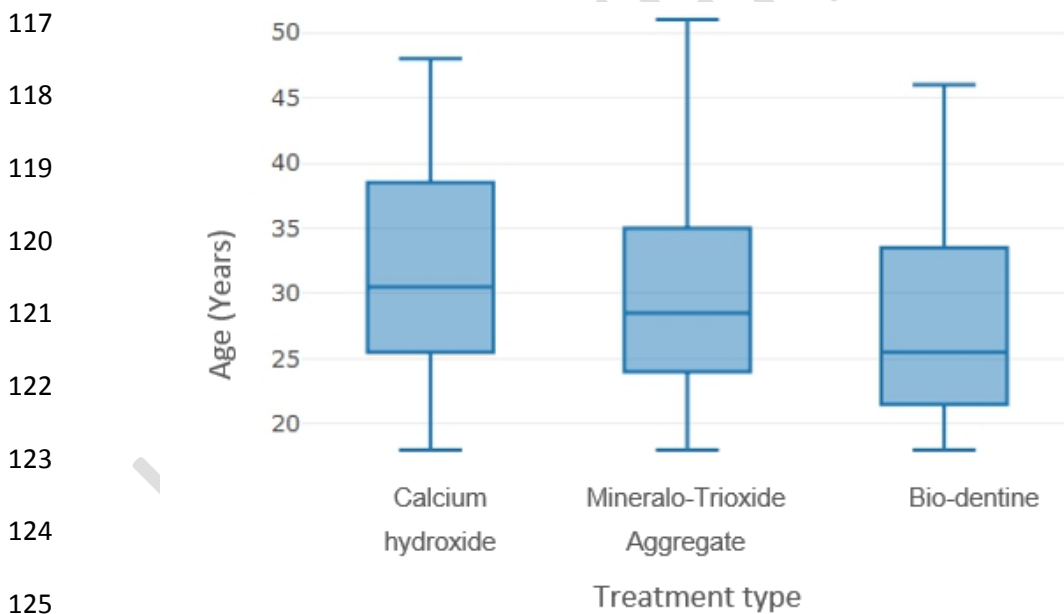
104 **3. RESULTS**

105 Most patients with periapical lesions belonged to the below 30 year age group (Figure 1).



114 **Fig 1: The Plot of count based on the age of the participants**

115 Figure 2 implies that Treatment 1 was mostly given to the patients above 30 years, while the other two
116 treatments (Treatment 1 and Treatment 2) were given to the patients who are below 30 years.



126 **Fig 2: The variation of the treatment type with age**

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128 The p-values obtained using the Wilcoxon Rank Sum Test are given in Table 1. This suggests that
129 there is no significant difference between the three treatments.

130 **Table 1: The results of the Wilcoxon Rank Sum Test for checking the significance difference**
 131 **between the Treatment types.**

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134 Several models were obtained using different variance function classes provided in *nlme* library in the

	Treatment-1 and Treatment-2	Treatment-1 and Treatment-3	Treatment-2 and Treatment-3
w-value	209.5	227.5	213.5
p-value	0.8065	0.2943	0.514

135 statistical software R. AIC and BIC values obtained for the fitted models are given in Table 2.

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137 **Table 2: AIC and BIC values for homoscedastic and heteroscedastic models**

		AIC	BIC	Log Likelihood
Homoscedastic Model	Model A	2962.31	2999.25	-1471.16
Heteroscedastic Model	Model B	2962.53	3006.85	-1469.26
	Model C	2948.87	2985.81	-1464.44
	Model D	2951.38	2999.39	-1462.69
	Model E	2937.23	2977.86	-1457.61
	Model F	2957.14	2997.77	-1467.57
	Model G	2959.53	3000.16	-1468.76
	Model H	3100.65	3141.28	-1539.33
	Model I	2963.32	3003.95	-1470.66
	Model J	2644.27	2699.68	-1307.14

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140 Model A was selected as the best homoscedastic model (Table 2). This model was fitted using the
 141 variables time, age, treatment type and their two-variable interaction terms.

142 Fixed effect for model A is the area of the infected region which is explained by time, treatment and
 143 age with the interaction between time and treatment (interactions between only 2 variables) while the
 144 random effect is explained for each group where grouping is given by the patient number.

145 Model J was selected as the best model. It can be concluded that the area of the infected region
 146 depends on the age of the patient, time periods, treatment type and their two-variable interaction
 147 terms. There is a positive impact on the area of the infected region by the interaction between the
 148 treatment type and age. There are negative impacts on the area of the infected region by the
 149 treatment type, age, time and the interaction between the treatment type and time. According to the
 150 model summaries, the highest negative impact on the area of the infected region is caused by the
 151 treatment type.

152 In order to assess the agreement between three treatment types, CCC and TDI values were obtained
 153 (Table 3). From both CCC and TDI values given in Table 3, a strong positive agreement is observed
 154 between all three treatments.

155 **Table 3: CCC and TDI values for models**

Homoscedastic Model				156
	Treatment 1 and Treatment 2	Treatment 1 and Treatment 3	Treatment 2 and Treatment 3	
CCC values	0.905	0.909	0.874	159
TDI values	3.148	4.390	1.647	
Heteroscedastic Model				161
CCC values	0.989	0.990	0.975	161
TDI values	2.963	4.388	1.457	162
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165 **4. DISCUSSION**

166 In the present study, the data of 60 patients who were subjected to endodontic treatment for anterior
 167 teeth was investigated. They have selected the patients exhibiting well circumscribed periapical
 168 lesions of more than 5mm in diameter on a pre-operative periapical radiograph. Akinyamoju et al ¹⁹
 169 found that the age range of the patients having periapical lesions was 9 to 80 years with a peak at
 170 age group of 20-29 years. In the present study, we obtained the similar results reconfirming the fact
 171 as given in Figure 1. Furthermore they have found that, females were more frequently affected by this
 172 condition. The present study has been reported the similar observations as in Figure 3.

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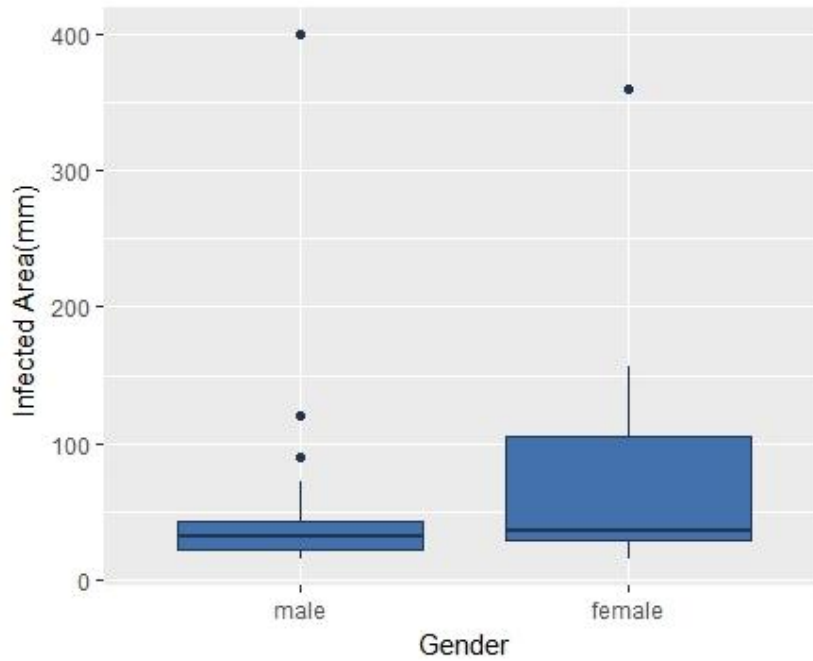


Fig 3: Variation of Infected area with gender

A similar study was carried out by Dexon et al²⁰ and the three treatments they compared are Photo Activated Disinfection(PAD), triple antibiotic paste and the calcium hydroxide where all three were used as root canal disinfectant. Moreover, in their study they have found that there is a significant change between calcium hydroxide and PAD using Kruskal-Wallis Test and Bonferroni post hoc test. In the present study the two treatments being compared with the treatment 1 (calcium hydroxide) differ from the previously mentioned study. Although the above-mentioned study has reported a significant difference between the two treatments, no significant difference was found among any of the treatments we considered. As denoted in the Table 1, the p-values obtained using the Wilcoxon Rank Sum Test which are greater than 0.05 suggests that there is no significant difference between the three treatments. Therefore, the present study has used mixed effects model analysis to compare the three treatment types.

The standard mixed-effects model is successful in explaining the data set, in accordance with the literature. The presence of heteroscedasticity is indicated by the situations where the key assumptions such as constant error variance (homoscedastic error variance) are violated. Therefore, in the present study, a multiple heteroscedastic mixed effects model is proposed to model the data and this fitted model is then used to assess the agreement between multiple methods of measurements. This methodology has been indicated by Nawarathna et al ^{21,22} as a way of measuring agreement in method comparison studies with heteroscedastic measurements.

Bland et al²³ affirmed that use of correlation is misleading in comparison of a new measurement technique with an established one. Furthermore they have suggested an alternative approach based on graphical techniques and simple calculations. In the current study this evaluation was done using

208 Concordance Correlation Coefficient and Total Deviation Index where the correlation coefficient is
209 taken into account.

210 In this study, we only considered 60 patients for the analysis. The results would be more accurate, if
211 the sample size had been increased. Further, simple random sampling was used with no specific
212 attention to the gender. Therefore, future studies may include responsiveness of the treatment
213 conditional on gender.

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215 5. CONCLUSION

216 The two treatments; with Mineralo-Trioxide Aggregate and Bio-dentine agreed sufficiently well with the
217 standard reference method with Calcium hydroxide and hence all three treatments can be used
218 interchangeably. Moreover, the agreement between the treatments using Calcium hydroxide and Bio-
219 dentine is higher compared to other treatments.

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