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ORIGINAL ARTICLE

# X-ray microtomography assessment of Carisolv and Papacarie effect on dentin mineral density and amount of removed tissue

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**ABSTRACT**
**Objective:** The aim of the present study was to directly compare Carisolv and Papacarie regarding the volume of removed tissue (RT) and dentin mineral density (DMD) after excavation.
**Materials and Methods:** Twenty permanent molars were randomized into two groups where caries was excavated using Carisolv or Papacarie followed by removal of softened tissue by a blunt instrument. X-ray microtomography was used to scan teeth before and after excavation generating two- and three-dimensional images that were used to calculate the percentage of RT relative to baseline tooth tissue volume and DMD that was categorized into sound dentin (>1.11 g/cm$^3$) and residual caries (≤1.11 g/cm$^3$). The two groups were compared using *t*-test Fisher exact test.
**Results:** DMD was higher after Papacarie than Carisolv (mean = 1.70 and 1.14, $p = .14$) with higher percentage of cases with sound dentin (70 and 60%, $p = 1.00$). The percentage of RT was lower after Papacarie than Carisolv (7.40 and 8.95%, $p = .31$) with 22.95% less RT in cases that ended with sound dentin after excavation.
**Conclusions:** There was higher DMD, more sound dentin and less RT when Papacarie was used compared to Carisolv.

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## Introduction

Rotary and sharp-edged hand instruments are used to excavate caries and this is associated with problems such as pulp overheating, need for local anaesthesia and discomfort leading to increased patient anxiety. To overcome these drawbacks, minimally invasive alternative methods were developed including chemomechanical caries removal [1–3]. This method depends on softening carious tissue by chemically altering it so that it can be mechanically removed using hand instruments [2]. The agents used in this procedure are either sodium hypochlorite-based or enzyme-based [2]. Agents of the type I degrade collagen in carious dentin to facilitate its removal. Initially, 5% sodium hypochlorite was used but because it lacked selectivity to remove only carious dentin and was unstable, amino acids were added to later formulation. The only commercially available hypochlorite-based chemomechanical caries removal agent [2] is Carisolv (MediTeam, Goteborg, Sweden), launched in 1998. It degrades the organic component of infected dentin so that it can be removed. The only enzyme-based commercially available chemomechanical caries removal agent [2] is Papacarie (Fórmula and Açäo, Sao Paulo, Brazil), introduced in 2003. It is extracted from plants and contains papain; an enzyme similar to human pepsin with proteolytic action [4].

Carisolv and Papacarie action on permanent teeth was directly compared and they were found to have antibacterial effect [5,6] as well as biocompatibility and cytotoxicity [7,8]. Dentin surface after excavation was similarly affected regarding surface morphology [9,10], chemical composition [10] and hardness [10] in addition to time taken to completely remove caries [11] and strength of bond to adhesives [9,12].

The main benefit of the two agents, however, can be proven by comparing the volume of tissue they remove and evaluating the presence of sound dentin after excavation. The amount of tissue removed was previously assessed using calibrated dental probes to measure cavity dimensions and multiplying them to get the volume [13], filling the cavity with silicon impression material of known density and weighing this material [14], using metallic caliper to measure the cavity entrance before and after excavation and calculating the volume using a mathematical formula [15] and using elastomeric impression material to construct a cast then measure with a microscope the entrance to the cavity and calculating its volume [11]. Whether sound dentin or residual caries remain after excavation was previously assessed using caries dye [16], DIAGNOdent [17], mineral content [18] or hardness [10].

X-ray microtomography is non-destructive and can be used to assess in three dimensions the mineral concentration

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at micron level thus differentiating between sound/affected and carious dentin and at the same time assessing the volume of the scanned structure with high accuracy [18,19]. Since the specimens are not destroyed, they can be rescanned to sequentially compare differences before and after excavation. Thus, this technique can accurately measure the mineral density and volume of cavity in the same specimens with reduced errors. X-ray microtomography was used to evaluate Carisolv [20,21], experimental enzyme-based chemomechanical removal agent [21] and Papacarie [22]. Including both agents in the same study avoids problems related to comparisons across different protocols where variations in methods exist. The hypothesis of this study was that Carisolv and Papacarie have similar caries removal effects in terms of excavating equal amounts of tissue to reach sound dentin. The present study aimed to compare Carisolv and Papacarie regarding the percentage of removed tissue (RT) and the dentin mineral density (DMD) in the bottom of the cavity after excavation.

## Materials and methods

### *Selection of teeth and caries excavation procedures*

The study included teeth extracted from adult patients in the Oral Surgery Clinic of the University of Dammam. Patients' consent was secured. Approval to conduct the study was obtained from the Research Unit, College of Dentistry and the study was conducted in accordance with the Declaration of Helsinki. Twenty permanent molars with open lesions and no overhangs were randomly selected. They were immersed in 0.1% thymol solution at room temperature for 2 weeks followed by distilled water at −4 °C and used within 3 months after extraction. Soft tissues remnants and calculus were removed with ultrasonic scaler. Teeth were embedded in self-cured acrylic resin blocks, with their long axes perpendicular to occlusal surfaces, which were in one plane with the acrylic resin blocks to facilitate manipulation. All teeth were subjected to X-ray microtomography scan before and after caries removal to record the volume of RT and DMD.

Teeth were equally and randomly divided into two groups according to caries removal agent; the first group using Carisolv whereas Papacarie was used in the second group. Carisolv comes in twin syringes: one containing a colorless gel and the other a transparent fluid. The materials are mixed automatically in the correct proportions in the tip of the static mixer of the syringe prior to application. Papacarie comes in a single syringe that is used to apply the gel in the cavity. In either group, the gel was left in the cavity for 30 s then dentine was excavated using a blunt instrument #4 provided with Carisolv. After excavation, the cavity was rinsed with distilled water for 20 s and the process was repeated until the material remained clear and unaltered and there was no more softened tissue to remove.

### *Scanning and image processing*

Teeth were scanned using a MicroCT Skyscan 1172 scanner system (Bruker Micro-CT, Kontich, Belgium). The parameters used were: source voltage (kV) = 100, source current (μA) = 100, image pixel size (μm) = 13.73, filters = 0.5 mm Al and 0.5 mm Cu placed in the path of the beam to filter out the low energy radiation to increase the accuracy of the subsequent beam hardening correction [23], image format = TIFF, exposure (ms) = 2550, rotation step (°) = 0.400, frame averaging = 3, random movement = 10 and 360 rotation. Raw images were reconstructed with NRecon software (Bruker microCT, Belgium version 1.6.4.8, Skyscan 2011) for the cross sections of micro CT scan images (Figure 1) with smoothing = 5, smoothing kernel = 2 (Gaussian), ring artifact correction = 10 and result file type = BMP. The CTAn software (Bruker microCT, Belgium version 1.11.10.0 + 64-bit, Skyscan 2003–11) was used to calculate the volume and mineral density. CTVol software (Bruker microCT, Belgium version 2.2.1.0 64-bit, Skyscan 1983–2010) was used for visualization of 3D images (Figure 1). Calibration of grey values into mineral density values was done as described by Neves. et al [22]. We followed the method of Neves et al. [24] in applying the multi-level Otsu threshold to the tri-dimensional histograms of the scans before and after excavation. It is a modification that uses mathematical algorithms to separate the different groups (enamel and dentin, sound and carious). We also used a lookup table applied to tooth volume and calibrated with mineral density values.

### *Analysis*

The two agents were compared regarding:

1. DMD: Adjusted means, standard deviations and 95% confidence intervals were calculated and compared after controlling for baseline DMD values using linear regression analysis. DMD after excavation was dichotomized using the cutoff point (1.11 $g/cm^3$) [20,22,24] into sound dentin (average DMD $>$1.11 $g/cm^3$) and residual caries (average MD $\leq$1.11 $g/cm^3$). The percentage of cases in each group after excavation with sound or with residual caries was compared between the two agents using Fisher exact test.
2. RT: The percentage of RT to tooth tissue volume at baseline was calculated as: [(tooth tissue volume after excavation − tooth tissue volume at baseline)/tooth tissue volume at baseline] × 100. Baseline tooth tissue volume, volume after excavation and volume of RT were compared between the two agents using *t*-test. *T*-test was also used to compare the percentage of RT between the two agents after splitting the cases into those where sound dentin or residual caries was left after excavation. The difference in the percentage of RT in one agent compared to the other was similarly calculated as [(percentage of RT in Papacarie cases − percentage of RT in Carisolv cases)/percentage of RT in Carisolv cases] × 100. This was calculated for all cases, as well as those with sound or carious dentin after excavation. Means, standard deviations and 95% confidence intervals were calculated. Significance was set at the 5% level. Statistical analysis was performed using SPSS version 22.0 (IBM Corp., Armonk, N.Y., USA).

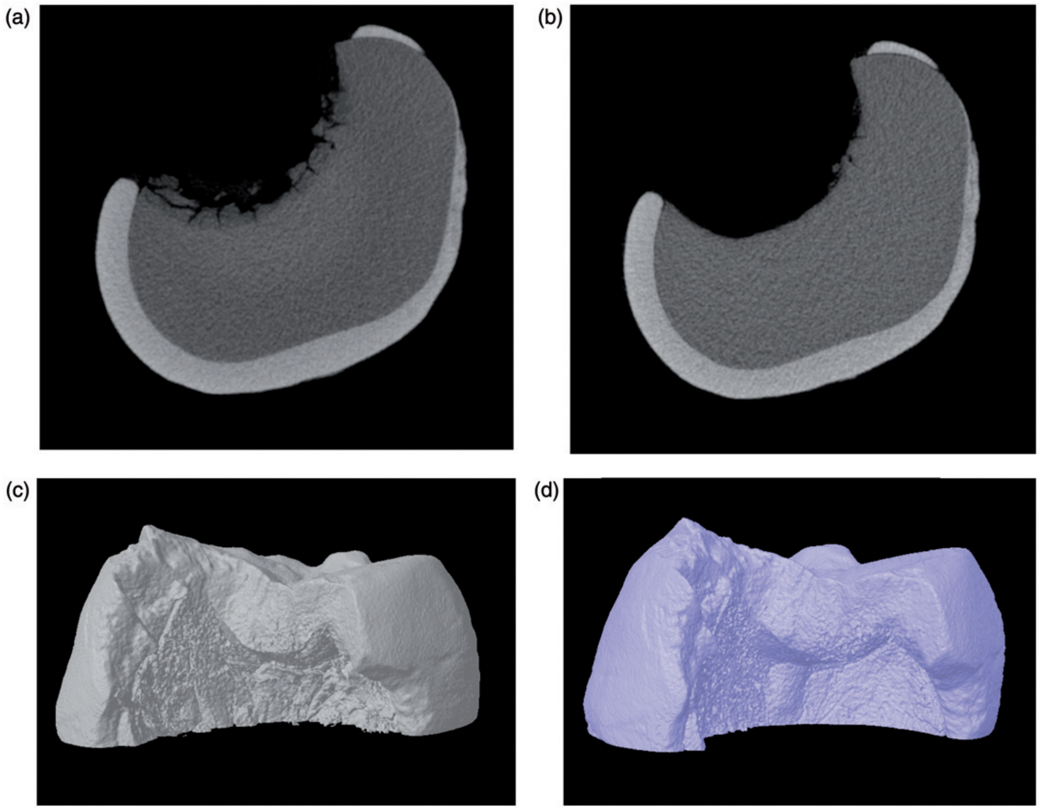


Figure 1. X-ray microtomography images of molars excavated with chemomechanical caries removal agents; two-dimensional image (a) before and (b) after excavation and three-dimensional image (c) before and (d) after excavation.

Table 1. Adjusted DMD in gm/cm$^3$ after caries excavation using Carisolv and Papacarie.

| | Carisolv | Papacarie |
|---|---|---|
| Adjusted mean (SD) | 1.39 (0.15) | 1.45 (0.17) |
| 95% CI | 1.08, 1.70 | 1.14, 1.76 |
| *p* value | .80 | |

Means were adjusted for baseline DMD.
SD: standard deviation; CI: confidence interval.

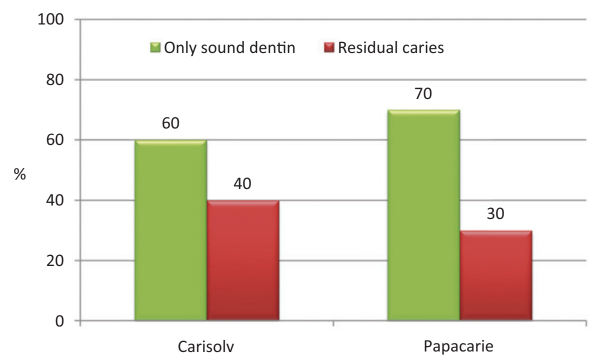


Figure 2. Cases with sound dentin only and residual caries after excavation by Carisolv and Papacarie.

## Results

Table 1 shows that the adjusted mean DMD in Carisolv cases (1.39 g/cm$^3$) was lower than in the Papacarie cases (1.45 g/cm$^3$), with no significant difference between the two groups ($p = .80$). Figure 2 shows that 60% of Carisolv cases had only sound dentin after excavation compared to 70% of Papacarie cases. This 10% difference in cases with only sound dentin in Papacarie compared to Carisolv was not statistically significant ($p = 1.00$).

Table 2 shows that at baseline, the volume of the tooth tissue in Carisolv cases (mean = 247.89 mm$^3$) was smaller than that in Papacarie cases (mean = 283.35 mm$^3$), $p = .05$. After excavation, the mean tooth tissue volume in the Carisolv group (225.22 mm$^3$) was significantly smaller than in the Papacarie group (262.62 mm$^3$), $p = .03$. A slightly larger volume of RT was observed in the Carisolv group (mean = 22.67 mm$^3$) than in the Papacarie group (mean = 20.74 mm$^3$), with no significant difference between groups ($p = .66$).

Table 3 shows that the percentage of RT to baseline in Carisolv cases (8.95%) was slightly higher than that in the Papacarie group (7.40%) with no significant difference between the two agents ($p = .31$). There was a larger percentage of RT in cavities that ended with sound dentin when Carisolv was used than when Papacarie was used although the difference was not statistically significant (9.15 versus 7.05%, $p = .21$). In cases with residual caries after excavation, there was more RT in the Carisolv than in the Papacarie group although the difference was not statistically significant (8.64 versus 8.21%, $p = .91$). In the Papacarie group, there was 22.95% less RT than in the Carisolv group to reach sound dentin.

## Discussion

In the present study, there were more cases with sound dentin after excavation using Papacarie with less tissue removed

**Table 2.** Comparison of volume of RT after Carisolv and Papacarie excavation.

| | Volume in $mm^3$, Mean (SD) [95% CI] | | | |
|---|---|---|---|---|
| | Carisolv | Papacarie | Difference | *p* value |
| Baseline | 247.89 (33.72) [222.84, 272.94] | 283.35 (41.31) [258.30, 308.40] | 35.46 (71.49) [0.03, 70.89] | .05 |
| After excavation | 225.22 (27.41) [201.60, 248.84] | 262.62 (42.16) [238.99, 286.24] | 37.40 (67.42) [3.99, 70.81] | .03[a] |
| RT | 22.67 (10.25) [16.16, 29.19] | 20.74 (9.35) [14.22, 27.25] | 1.94 (9.61) [−11.16, 7.28] | .66 |

SD: standard deviation; CI: confidence interval.
[a]Statistically significant at $p < .05$.

**Table 3.** Percentage of RT to baseline in Carisolv and Papacarie groups with sound dentin and residual caries after excavation.

| | Mean (SD) [95% CI] | | | | |
|---|---|---|---|---|---|
| | RT% | | | | |
| | Carisolv | Papacarie | Difference | RT% reduction (Papacarie to Carisolv) | *p* value |
| Cases with sound dentin only | 9.15 (3.50) [6.60, 11.70] | 7.05 (2.13) [4.69, 9.41] | 2.10 (2.82) [−1.38, 5.57] | 22.95 | .21 |
| Cases with residual caries | 8.64 (2.81) [2.74, 14.55] | 8.21 (6.40) [1.38, 15.03] | 0.44 (4.60) [−8.59, 9.46] | 4.98 | .91 |
| All cases | 8.95 (3.08) [6.74, 11.15] | 7.40 (3.53) [5.20, 9.60] | 1.55 (6.28) [−1.57, 4.66] | 17.23 | .31 |

SD: standard deviation; CI: confidence interval.

than when Carisolv was used although these differences were not statistically significant. Our results indicate a possible advantage of Papacarie over Carisolv as chemomechanical caries removal agent and this needs further confirmation in future studies.

In the present study, the Papacarie group had higher DMD and more cases with sound dentin after excavation. This agrees with Clementino-Luedemann et al. [19] who used X-ray microtomography to compare Carisolv and an experimental enzyme-based caries removal agent (SFC-V) in primary teeth. They reported a slightly higher DMD of the enzyme-based agent compared to Carisolv (0.90 $g/cm^3$ and 0.85 $g/cm^3$), $p = .05$. Their DMD values, however, were lower than the values in our study of the two groups and the cut point for sound dentin. This can be explained by their using a different X-ray microtomography scanning protocol with different cut points for sound dentin (0.59 $g/cm^3$). They also reported less thickness of residual caries layer (0.27 mm versus 0.32 mm). Our results disagree with Neves et al. [21] who reported that there were 30% residual caries after excavation using Carisolv and 65% after enzyme-based experimental agents (SFC-III and V) with a plastic instrument. When they used metallic excavator with the enzyme-based agents, there were 20% with residual caries so that their enzyme-based agent had better caries removal effect similar to our study.

In the present study, there were cases with lower DMD than sound dentin cut-point in the two groups. Neves et al. [24] attributed a similar finding in their study to the partial volume effects (PVE). This occurs between the cavity edge and background where a single voxel contains a mixture of background and material value [25]. Teeth with larger cavities—such as those used in our study—have a higher chance of suffering from PVE than teeth with smaller cavities. Our results also agree with previous studies using Carisolv [26] or Papacarie [22,24] and reporting low DMD after excavation. The identification of cases as with sound dentin or with residual caries depends on the selection of cut point (1.11 $g/cm^3$ in our study) and whether the classification is dichotomous (sound versus carious like in our study) or includes more categories. For example, Djomehri et al. [27] identified two types of diseased dentin with different DMD; lower DMD (0.4–0.6 $g/cm^3$) and low DMD (0.6–1 $g/cm^3$). The DMD values of residual caries cases in our study were within that low DMD range described by Djomehri et al. [27] This remaining layer of dentin with DMD less than that of sound dentin but higher than that of infected dentin was reported by Hamama et al. [10] to be the main difference between both Carisolv or Papacarie and rotary instruments. They identified this layer as the affected dentin that can be left without jeopardizing the success of the restoration. Clementino-Luedemann et al. [19] also reported that as minerals deposit into this residual layer of dentin left after chemomechanical caries removal, caries arrest occurs and there is no further progression of the lesion. The segmentation of Micro CT slices into different tissues is an image analysis issue that needs to be addressed in further studies using computer-generated algorithms.

In the present study, there was less RT after Papacarie excavation. Our results disagree with the only study where the amount of RT by Carisolv and Papacarie was directly compared [11]. The authors reported that the volume of RT after Papacarie (mean = 135.99 $mm^3$) was greater than that removed by Carisolv (126.33 $mm^3$) but not significantly so ($p > .05$). This, however, was a clinical study and therefore, not directly comparable to ours. Our result agrees with Clementino-Luedemann et al. [19] who compared the RT after excavation with Carisolv and an enzyme-based caries removal agent (SFC-V) in primary teeth using X-ray microtomography and reported non-statistically significant differences between both groups ($p = .96$).

The volume of the initial cavities in the present study agrees with the baseline enamel volume of 213.08 $mm^3$ reported by Neves et al. [24] after enzyme-based caries removal and so does the volume of RT in our study which agrees with the excavated enamel material they reported (22.57 $mm^3$). These similarities maybe attributed to their use of similar X-ray microtomography scanning and tooth preparation methods where they scanned the whole tooth. The volumes in our study, however, disagree with their later study [22] where they reported much smaller initial volumes

(0.62–5.20 $mm^3$) and RT (0.2–7.8 $mm^3$). The differences between their and our study may be attributed to how they prepared the teeth in this case where they removed the upper portion of the occlusal surface flat-cutting it to allow better visualization.

Our study fills a gap in knowledge about chemomechanical caries removal where the effect of the two commercially available agents, Carisolv and Papacarie, was directly compared in the same study regarding both RT and DMD thus building on previous studies that focused on only one agent or parameter. We used X-ray microtomography with a scanning and visualization method that was different from that used by others [19,21,22,24] and obtained comparable results. Although not proven statistically, Papacarie excavation was associated with 17% increase in cases with sound dentin and 23% reduction in RT showing its potential advantage over Carisolv. This needs further confirmation in future studies including cavities with various sizes in addition to quantifying the volume of remaining carious tissue after excavation as well as the amount of sound dentin removed so that better decisions can be made about which agent to select.

## Disclosure statement

No potential conflict of interest was reported by the authors.

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