



## CLINICAL RESEARCH

# Oral Fine Motor Control of Teeth Treated with Endodontic Microsurgery: A Single-Blinded Case-control Study

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## SIGNIFICANCE

Endodontic microsurgery treatment does not perturb the sensory information of periodontal mechanoreceptors, thereby maintaining the force regulation properties and oral fine motor control, despite the loss of the root apex.

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## ABSTRACT

**Introduction:** Periodontal mechanoreceptors (PMRs) are refined neural receptors present in abundance at the root apex and have a pivotal role in oral fine motor control. This case-control study aimed to evaluate the oral fine motor control of teeth treated with endodontic microsurgery (EMS) in comparison with the control teeth using a standardized behavioral biting task. **Methods:** Fourteen eligible participants performed 5 trials of an oral fine motor control task that involved holding and splitting half of a peanut positioned on a force transducer with their EMS treated tooth and its contralateral control incisor tooth (28 teeth in total). The outcome variables were the mean food holding force, intra- and intertrial variability of the holding force, food splitting force, splitting duration, and the frequency of the stepwise splitting phase. The data were analyzed with parametric and nonparametric tests. **Results:** The results showed no statistically significant differences in the holding force, inter- and intratrial variability of the holding force, splitting force, or splitting duration between the teeth treated with EMS and the control ( $P > .05$ ). However, there was a significantly higher frequency of stepwise ramp increase during the splitting phase with EMS treated teeth compared with the control (48% and 37%, respectively;  $P < .05$ ). **Conclusions:** EMS treated teeth showed similar force regulation and oral fine motor control as the contralateral control. The findings of this study suggest that EMS treatment does not perturb the sensory information of PMRs and maintains the force regulation and oral fine motor control of the teeth. (*J Endod* 2021;47:226–233.)

## KEY WORDS

Force regulation; hold and split task; periodontal mechanoreceptors; root-end surgery; tooth function

Root-end surgery is considered a standard treatment for tooth preservation, typically if the primary endodontic treatment fails and nonsurgical root canal retreatment becomes impractical or unlikely to improve the prognosis of the treatment<sup>1,2</sup>. During the past 25 years, root-end surgery has experienced noticeable changes and emerged into endodontic microsurgery (EMS), which involves the use of magnification devices, technological advancement, microinstruments, and biocompatible filling materials<sup>3</sup>. With these developments, EMS treatment has emanated as a more successful and favorable clinical outcome over the traditional root-end surgery technique<sup>4</sup>.

Periodontal mechanoreceptors (PMRs) are highly refined neural receptors that convey sensory information to the brainstem and the trigeminal nuclei and are predominantly embraced in the activation and coordination of jaw movements<sup>5,6</sup>, force regulation, and other oral motor functions<sup>7</sup>. These receptors are situated in periodontal ligaments close to the alveolus portion of the socket and play an extraordinary role in detecting occlusal forces on the teeth<sup>8</sup>. Oral fine motor control entitles the capacity of the central nervous system in assimilating peripheral oral sensory information related to the motor (biting) task and integrating the learned sensory information to achieve a successful task-specific output<sup>9</sup>. However, it is suggested that the receptors closest to the apex of the tooth have their cell bodies in the mesencephalic nucleus, whereas those receptors located in the middle of the tooth root have their cell bodies in the trigeminal ganglion<sup>10</sup>. Therefore, it can be hypothesized that the functional roles between the 2 groups of afferents could be dissimilar because of their inputs to different regions of the brainstem.

The majority of the PMRs occupy the apical third of the periodontal ligament near the root apex<sup>11</sup>. During EMS, approximately 2–3 mm of the root apex is resected, and the pathologic tissue in the periapical area is removed<sup>3</sup>. Indeed, these procedures may reduce the number of PMRs and subsequently may disturb the sensory input of these receptors, resulting in perturbation in force regulation during biting. Few studies have assessed the occlusal forces of nonvital teeth or teeth treated by nonsurgical root canal therapy, with absolutely no consensus on their findings. In some studies, the occlusal forces of nonvital teeth were quite similar to the vital ones<sup>12–16</sup>. On the contrary, a higher level of occlusal forces had been reported in nonvital or endodontically treated teeth compared with vital teeth<sup>17–19</sup>. However, there is no contemporary evidence on oral fine motor control in terms of force regulation in teeth treated with EMS. We hypothesized that EMS treatment may perturb the sensory information of PMRs and consequently affect oral fine motor control. Therefore, this study aimed to evaluate oral fine motor control in teeth treated with EMS using a standardized behavioral biting task in comparison with contralateral control teeth.

## MATERIALS AND METHODS

### Ethical Considerations

The current study was approved by the regional ethical review board in Stockholm, Sweden (Dnr: 2018/726-31/2) in full accordance with the Declaration of Helsinki. The study was undertaken with the understanding and written consent of each participant following the previously mentioned principles.

### Study Participants

The effect size and sample size were calculated based on the data obtained from similar previous behavioral studies<sup>20,21</sup> using

G\*POWER software (version 3.1; Heinrich Heine University Dusseldorf, Dusseldorf, Germany). Accordingly, a sample of 10 teeth per group with an effect size of 0.58 would have 80% power for determining the differences in force regulation between the EMS-treated teeth and their controls at a 5% level of significance.

Participants for this case-control study were identified from the dental records among the patients treated with EMS on their upper incisors between January 2013 and December 2018 at Endodontic Specialist Clinics, Department of Dental Medicine, Karolinska Institute, Stockholm, Sweden. The inclusion and exclusion criteria of the study participants are presented in Table 1. Seventeen patients met the inclusion criteria, and 14 of them consented to participate in the study.

### EMS Treatment Protocol

EMS treatment in all of the teeth was performed following the contemporary EMS treatment protocol with the aid of a dental operating microscope<sup>3</sup>. Briefly, the treatment comprised the administration of a local anesthetic agent (2% xylocaine with epinephrine 1:80,000; Dentsply Sirona, Charlotte, NC), incision with a 15c surgical blade, a triangular full mucoperiosteal flap with 1 vertical incision, small-size osteotomy with a high-speed bur, curettage of soft tissues neighboring the root, root-end resection of 2–3 mm with minimal or no bevel using a high-speed bur, retrograde cavity preparation using ultrasonic tips to at least a 3-mm depth, surgical hemostasis with small-size gauze with epinephrine, retrograde filling with gray mineral trioxide aggregate (Gray MTA; Angelus, Londrina, PR, Brazil), flap reapproximation, and sutures.

### Force Measurement Device

A custom-made force transducer device (DC 200 Hz; Department of Integrative Medical Biology, Umeå University, Umeå, Sweden) was

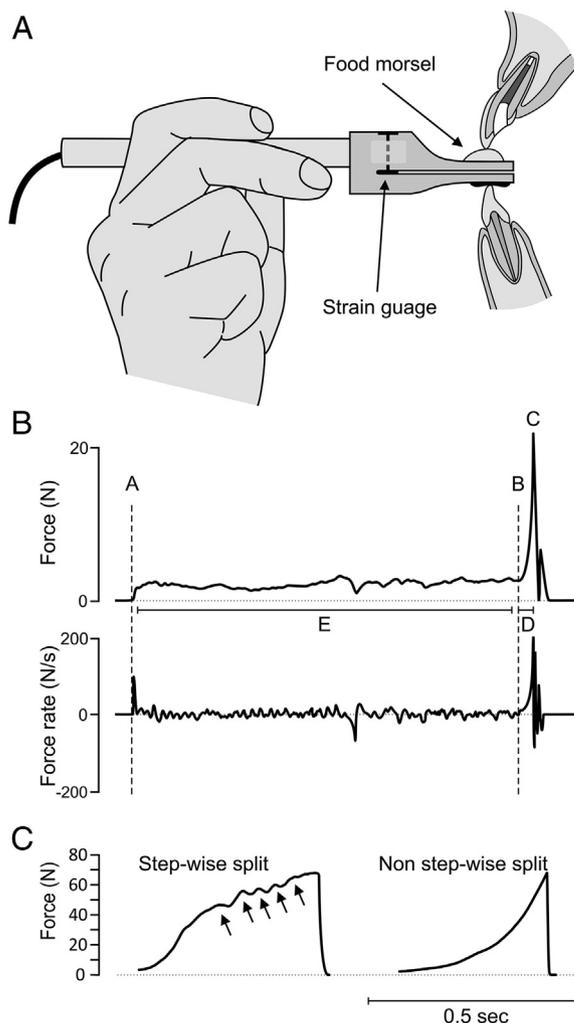
used to perform the standardized behavioral “hold-and-split” task. This device consists of a 10-cm aluminum tube connected to 2 duralumin blocks (total weight = 28 g; stiffness between the plates = 50 N/mm). The 2 duralumin blocks were terminated into 2 parallel and thin plates where the test food morsel was resting on the upper plate (Fig. 1A). To facilitate the placement of the force transducer into patients’ lower incisors, grooved plexiglass was glued on the lower plate (4-mm thick). The distance between the edge of the upper plate and the notch of the plexiglass at the lower plate was 8 mm<sup>24</sup>. The force transducer was designed to ensure an equal force recording regardless of the location of the force application. The forces applied on the upper plate were continuously monitored and stored off-line for analysis.

### Behavioral Task

The study was conducted in a well-lit, quiet room where the participants sat on a comfortable office chair with arm support. The behavioral task was to “hold and split” half of a roasted and salted peanut (Estrella AB, Angered, Sweden) placed on the force transducer in accordance with the previous studies<sup>24–30</sup>. The participants were asked to perform the task with their upper incisor teeth treated with EMS and the contralateral control teeth. To reduce any potential bias, an independent “blinded” trained examiner (N.A.) introduced and performed the hold-and-split task for the participants. The participants were instructed to hold the force transducer with their arms resting on the table to ensure a horizontal relationship of the anterior teeth to the upper transducer’s plate. The participants were asked to gently hold the food morsel (half of a peanut) between 2 antagonist teeth and avoid applying any unnecessary force than needed to control the food morsel. Subsequently, the participants held the food morsel between their teeth for approximately 4–5 seconds before they were asked to split it.

**TABLE 1** - The Inclusion and Exclusion Criteria Implemented in the Recruitment of the Study Participants

Inclusion	Exclusion
<ul style="list-style-type: none"> <li>• Presence of complete periapical healing in the recall periapical radiograph with a minimum of a 1-year follow-up<sup>22,23</sup></li> <li>• Presence of adequate coronal restoration with intact margins</li> <li>• The tooth is not an abutment or part of a fixed partial prosthesis.</li> <li>• The root to the crown ratio is <math>\geq 1:1</math>.</li> <li>• Presence of contralateral tooth with healthy periapical tissue and devoid from any previous history of root-end surgery to act as a control</li> </ul>	<ul style="list-style-type: none"> <li>• Presence of any systemic, neurologic, or infectious diseases</li> <li>• Current use of analgesics, antibiotic therapy, or allergy to peanuts</li> <li>• Presence of any orofacial pain, malfunction, or temporomandibular disorder</li> <li>• Previous history of orthodontic treatment</li> <li>• Presence of periodontal diseases, mobility, and gross malocclusion</li> <li>• Abnormal clinical findings during tooth percussion and/or palpation</li> <li>• Absence of antagonist lower incisors teeth</li> </ul>



**FIGURE 1** – A schematic illustration of the hold-and-split apparatus. (A) The apparatus consists of a handheld force transducer that terminates into 2 thin rectangular plates where the test food morsel (ie, half of a peanut) was placed on the terminal end of the upper plate. The participants were asked to gently hold the food morsel between 2 antagonist teeth and avoid applying any unnecessary force than needed to control the food morsel. Subsequently, the participants held the peanut between their teeth for approximately 4–5 seconds before they were asked to split it. (B) The typical force profile obtained from an individual hold-and-split trial of the tooth with EMS treatment. The upper trace represents the magnitude of holding force measured in newtons, and the lower trace represents the force rate measured in newtons per second. Several time points were identified: (A) the initial contact with the food morsel, (B) onset of the splitting phase at which the force rate exceeded 5 N/s, (C) the peak of the splitting force, (D) the duration of the splitting phase in seconds, and (E) the holding phase interval beginning 0.2 seconds after the initial contact with the food morsel and ending 0.2 seconds before the onset of the splitting phase. (C) A close-up view of the splitting phase example comparing the stepwise splitting profile with the non-stepwise splitting. The *black arrows* indicate the force decay and the compensatory force increase in the stepwise splitting profile.

After receiving the instructions, each participant completed at least 5 practice trials before starting the task. After the familiarization session, the participants performed 10 trials of the hold-and-split task for every tooth with EMS and the control. The data of the last 5 successful trials for both teeth in each participant were extracted for analysis.

### Data Analysis

The force signals were sampled at 1000 Hz (low-pass filtered 250 Hz) and analyzed with a

personal computer-based computer system (WinSC/WinZoom; Department of Integrative Medical Biology, Umeå University, Umeå, Sweden). The rate of variation in the force was attained by symmetrical, numerical time differentiation ( $\pm 10$  points) of the force signal. In each trial, 2 distinguishable phases were recognized from the temporal force profile: the holding phase and the splitting phase. Numerous force measurements were calculated from individual trials (Fig. 1B). The average holding force was determined as the

mean value of the force during the interval, beginning 0.2 seconds after the initial tooth contact with the peanut (A) and ending 0.2 seconds before the onset (B) of the splitting phase (Fig. 1B). The splitting phase began when the force rate exceeded 5 N/s and was characterized by a distinct rapid ramp increase of force, which eventually led to splitting the peanut (C). These phases were consistently detected by the computer system and manually checked for accuracy. The standard deviation of the holding force represented the force variability within individual trials (intra-trial variability) and between the 5 trials performed by the same participant (inter-trial variability). The splitting force (C) was measured as the maximum force recorded during the splitting phase followed by a rapid force decline, which indicates the end of the splitting phase. The splitting duration (D) was determined as the time taken in seconds from the onset of the splitting phase until reaching the splitting force. The pattern of the force ramp increase during the splitting phase was visually assessed to determine the frequency of the stepwise ramp force increase (Fig. 1C). To specify whether an individual trial has a stepwise ramp force increase, the force profile should demonstrate bi- or multiphasic force decay followed by a compensatory force increase, which leads to peanut splitting.

### Statistical Analysis

The outcome variables of the holding and splitting phases were presented as means ( $\pm$  standard deviation). The normality of the data was determined by the Shapiro-Wilk test, histograms, and normal Q-Q plots. The Wilcoxon signed rank test was applied for variables deviated from the normal distribution (ie, holding force, intra- and inter-trial variabilities, splitting duration, and stepwise frequency), whereas the normally distributed variable (splitting force) was analyzed by a dependent, “paired” sample *t* test. The sum of the trials displaying the stepwise ramp increase of force was calculated in both the EMS and control teeth. Furthermore, the data pertaining to the stepwise ramp increase of force is presented as the frequency (%) of occurrence from the total trials for the EMS and control teeth. Statistical analysis was performed using the SPSS Version version 24.0 (IBM Corp, Armonk, NY). The results were considered statistically significant when the *P* value was  $<.05$ .

### RESULTS

Table 2 illustrates the demographic data of the included participants. In the hold-and-split task, both the teeth with EMS treatment and

**TABLE 2** - Demographic Data of the Participating Patients in the Study (N = 14)

Patient no.	Sex	Age	Control			EMS		
			Tooth no.	Coronal restoration	Pulpal diagnosis	Tooth no.	Coronal restoration	Recall time (mo)
1	F	53	21	None	Normal pulp	11	Crown + post	14
2	M	46	21	Composite	Previously treated	11	Crown + post	27
3	M	60	12	None	Normal pulp	22	Composite	37
4	M	72	22	None	Normal pulp	12	Crown + post	21
5	F	73	12	None	Normal pulp	22	Composite	50
6	M	25	21	None	Normal pulp	11	Composite	60
7	F	55	22	None	Normal pulp	12	Composite	44
8	F	47	11	None	Normal pulp	21	Crown + post	60
9	F	66	12	None	Normal pulp	22	Crown + post	63
10	M	61	11	None	Normal pulp	21	Crown + post	43
11	M	35	21	None	Normal pulp	11	Composite	45
12	M	29	11	None	Normal pulp	21	Composite	32
13	F	77	11	Crown + post	Previously treated	21	Crown + post	14
14	F	32	11	Composite	Normal pulp	21	Crown	14

EMS, endodontic microsurgery; F, female; M, male.

Each participant had a tooth with EMS treatment and a contralateral control tooth. Pulpal diagnosis of the control teeth was made using standardized diagnostic terms recommended by the American Association of Endodontics.

the control teeth showed a relatively low steady force during the holding phase that lasted for a few seconds followed by a rapid increase of force that led to splitting the food morsel. The statistical analysis of the outcome variables obtained during the holding and splitting phases are presented later.

### Holding Phase

The mean holding force levels were similar for both the EMS and control teeth with no statistical significance differences ( $1.21 \pm 0.65$  N and  $1.27 \pm 0.58$  N, respectively;  $P > .05$ ; Fig. 2A). Similarly, there were no statistically significant differences in intratrial variability

between the EMS-treated teeth and their controls ( $P > .05$ , Fig. 2B). Likewise, the intertrial variability did not change significantly between the EMS-treated teeth and the control ( $P > .05$ ; Fig. 2C;  $0.44 \pm 0.38$  N in EMS-treated teeth and  $0.38 \pm 0.20$  N in the control teeth).

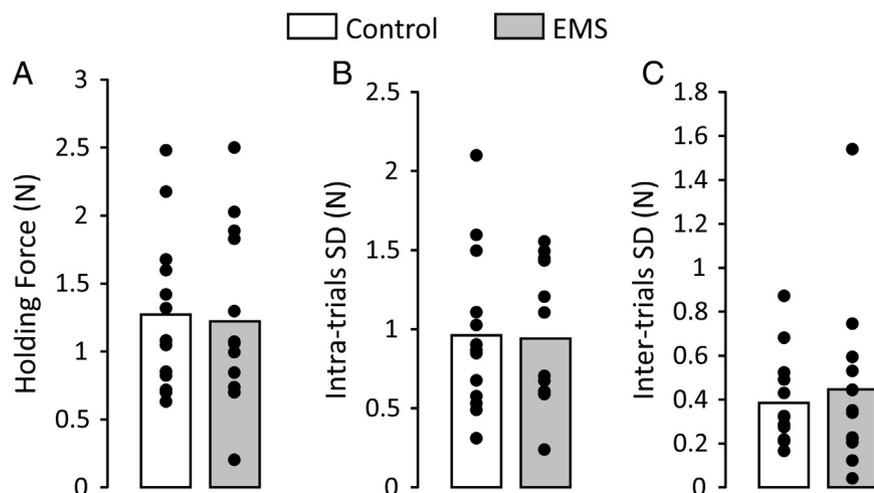
### Splitting Phase

The splitting force of the food morsel did not differ significantly in the EMS-treated teeth or the control teeth ( $P > .05$ ; Fig. 3A;  $60.89 \pm 14.13$  N in EMS-treated teeth and  $65.00 \pm 11.13$  N in the control teeth). Similarly, no significant difference was noted in the duration

of the splitting phase between the EMS-treated teeth and their controls ( $P > .05$ , Fig. 3B). Occasionally, the rapid ramp increase of force during the splitting phase showed bi- or multiphasic force decay followed by a compensatory force, which led to the splitting of the food morsel (ie, stepwise splitting phase). The frequency of the stepwise ramp increase of force during the splitting phase was significantly higher in the EMS-treated teeth (48%) than the control teeth (37%) ( $P = .046$ , Fig. 3C).

## DISCUSSION

The current study evaluated oral fine motor control of incisors treated with EMS compared with their contralateral control teeth. Oral fine motor control was assessed by a standardized hold-and-split behavioral task in accordance with previous studies<sup>24-30</sup>. The behavioral task simulates the natural situation of positing and holding a food morsel between the teeth and applying the optimum force required to break the food morsel before the rhythmic act of chewing. The results of the present study showed that the participants with EMS-treated teeth exhibited similar holding forces and force variability during the holding phase compared with the control teeth. Furthermore, the participants also exhibited similar splitting forces with EMS-treated teeth compared with their contralateral control teeth. However, the frequency of the "compensatory" stepwise ramp increase of force was significantly higher in teeth with EMS treatment than the controls. Overall, the findings of the current study indicate that oral fine motor control is not compromised in teeth treated with EMS despite the removal of the root end. To the



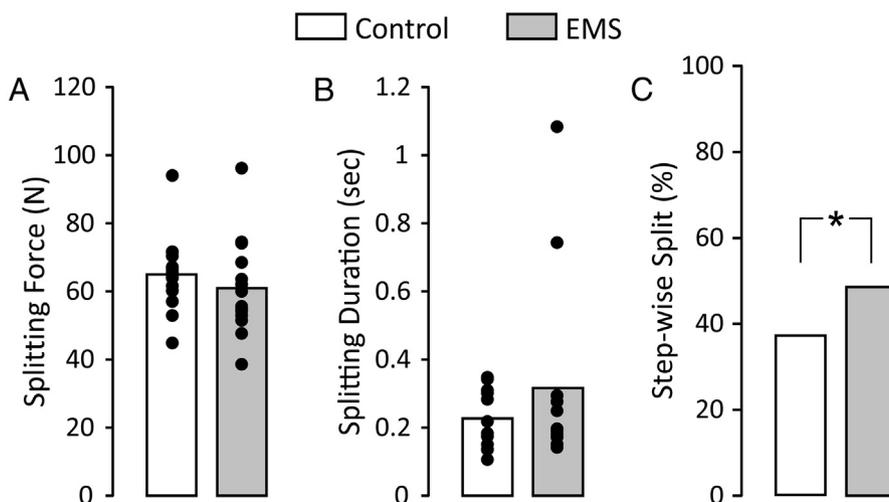
**FIGURE 2** – The outcome variables of the participating patients obtained during the holding phase for teeth with EMS treatment and the control teeth. (A–C) Bar histograms demonstrating (A) the mean holding force measured in newtons and its (B) intra- and (C) intertrial variability. The black dots in each bar histogram represent the mean value of trials obtained from individual participants.

best of our knowledge, this is the first study that explored oral fine motor control in teeth treated with EMS.

The PMRs innervating the anterior (incisor) teeth are recognized as nonsaturated receptors and characterized by a higher sensitivity to the changes in the applied occlusal forces, whereas the PMRs supplying the posterior "multirrooted" teeth are more saturated and less sensitive to the changes in the occlusal forces<sup>8</sup>. Therefore, the participants with incisors treated with EMS were selected as the study subjects for the current experimental study. Previous studies have shown that participants with an intact periodontium typically use low holding forces to control the food morsel, which reflects a higher sensitivity of PMRs to low forces (around 1 N)<sup>20,30</sup>. The holding forces generated by teeth with EMS treatment and their control in the present study were comparable with the previous studies on participants with a healthy periodontium<sup>20,21,24,29-31</sup>. On the other hand, patients with reduced periodontal support or dental implants and people subjected to local anesthesia displayed impairment in the oral fine motor control reflected in higher and more variable holding forces<sup>21,29-31</sup>. These findings from the previous studies strongly indicate that the oral fine motor control during behavioral biting tasks could be impaired significantly when the sensory information of the PMRs is altered. However, in the current study, it was evident that there was no difference in the holding forces between the EMS-treated teeth and their contralateral control, suggesting that the EMS-treated teeth perhaps physiologically function similar to the control in terms of force regulation.

During the splitting phase, both EMS-treated teeth and the control teeth showed a rapid increase in force, which led to the crushing of the food morsel and a subsequent drastic rapid decline in force. The splitting force and splitting duration for teeth treated with EMS were comparable with the control teeth. In agreement with previous studies<sup>20,21,26,29,30</sup>, the current findings suggest that the PMRs did not play any crucial role in the regulation of the splitting forces. Furthermore, the splitting forces are governed by different factors such as mechanical characteristics of the tested food morsels and the cutting efficacy of the incisors' edges<sup>29</sup>. However, when the food morsel was not crushed by the first force ramp, a compensatory increase in force appeared. The frequency of these compensatory "stepwise force increases" was more prominent in the EMS-treated teeth compared with their controls. Indeed, some of the PMRs (20%) are not saturated receptors and can express the force profile during the splitting phase<sup>32</sup>. Furthermore, the generated signals by these receptors may have a role in yielding positive feedback (ie, moment to moment control) during the transition from the hold to the splitting phase, which could clarify the higher tendency of compensatory increases in force in teeth with EMS treatment<sup>29</sup>. However, because there were no noteworthy differences in the splitting duration between the EMS-treated teeth and the control teeth, no clear clinical interpretation could be inferred from the higher frequency of "stepwise force increase" in teeth with EMS treatment, and further clinical and experimental studies are needed.

Few studies in endodontics have investigated the occlusal forces of nonvital or endodontically treated teeth in comparison with vital teeth<sup>12-19</sup>. In agreement with our results, some of the previous studies have shown no significant differences in the occlusal forces between vital and nonvital teeth<sup>12-16</sup>. Specifically, Woodmansey et al<sup>16</sup> evaluated the occlusal bite force of 25 patients with endodontically treated teeth in the mandibular molar region. They observed that endodontically treated teeth had the same occlusal forces compared with vital teeth. Contradictory to these studies, others have reported that the occlusal forces of nonvital teeth were higher than those of vital teeth<sup>17-19</sup>. The dissimilarities in the occlusal forces between vital and nonvital/endodontically treated teeth in previous studies were attributed to either the significant contribution of the low threshold interdental mechanoreceptive receptors in the vital teeth or the impairment of PMRs because of the presence of a periapical lesion and/or overinstrumentation during root canal treatment in the nonvital teeth<sup>12,17</sup>. However, all of the control teeth in the current study had normal periapical tissue, and 85% of them were sensible to thermal tests (ie, diagnosed as vital teeth), ruling out the potential effect of pulpal mechanoreceptors in the regulation of occlusal forces and oral fine motor control of the teeth<sup>13,16</sup>. It is also noteworthy to mention that 2 of the control teeth in the current study were diagnosed with previous root canal treatment and normal periapical tissue. As a matter of fact, the set inclusion criteria for the



**FIGURE 3** – The outcome variables of the participating patients obtained during the splitting phase for teeth with EMS treatment and the control teeth. (A–C) Bar histograms demonstrating (A) the mean splitting force measured in newtons, (B) the splitting duration as measured in seconds, and (C) the pooled frequency (%) of the stepwise ramp force increase during the splitting phase. The black dots in each bar histogram represent the mean value of trials obtained from individual participants. \*A statistically significant difference ( $P < .05$ ).

control teeth were focused on a contralateral tooth with a complete root apex and devoid of any history of EMS treatment or periapical pathosis, irrespective of the pulpal condition of the tooth. Further studies could be designed to study the specific effect of pulpal mechanoreceptors in oral fine motor control.

Different speculations could explain the similarity in the oral fine motor control in teeth treated with EMS compared with their control. Certainly, EMS treatment is a minimally invasive procedure that aims to preserve the teeth roots and the surrounding structures<sup>3</sup>. In addition, the typical protocol of EMS treatment necessitates the use of biocompatible retrograde filling material such as mineral trioxide aggregate. A series of histologic studies have shown that mineral trioxide aggregate can regenerate the periapical tissue including periodontal ligaments and cementogenesis around the root end<sup>33,34</sup>. Therefore, we could speculate that the regenerated periapical tissue could be associated with the repopulation of the PMRs over the resected root-end area and could have resulted in restoring oral fine motor control. Moreover, the nerve fibers supplying the PMRs around the root apex have their cell bodies in the trigeminal mesencephalic nucleus, whereas the nerve fibers supplying the midroot PMRs have their cell bodies in the trigeminal ganglion<sup>10</sup>. Therefore, PMR signals in EMS teeth could be generated by the scattered receptors situated in the midroot area independently from the apically located one, rendering equivalent sensorial information to the control teeth. However, the results of the present study are limited to the behavioral and clinical assessments rather than histologic analysis of PMRs in teeth treated with EMS. Histologic investigation of PMRs in teeth treated with EMS will afford a better understanding of their mechanoreceptive behavior and force regulation.

In contrast to our study, previous occlusal bite force studies on endodontically treated teeth did not address the impact of the follow-up time and treatment outcome on their study results<sup>16,19</sup>. Although these inclusion criteria have a pivotal role in the behavioral assessment of the teeth, they also have a negative influence on the total sample size<sup>35</sup>. Even though the sample size of the present study fulfills the a priori-estimated effect size required for the hold-and-split behavioral task study, the exact prerequisite effect size for detecting the significant differences between the EMS-treated teeth and their control could potentially differ from the previous behavioral studies<sup>20,21</sup>. Therefore, future studies could be designed with a relatively larger sample size. The present study also involved a wide age range of the participants for the standardized hold-and-split behavioral task. It could be hypothesized that the age of the participants may affect the oral fine motor control of the teeth. However, no previous study has explored the impact of age on oral fine motor control during the behavioral biting task. Nonetheless, in the current study, the contralateral tooth was used as an internal inherent control. This parried design is 1 of the positive attributes of the current study and may enhance the validity of the results by eliminating the interindividual variability.

## CONCLUSIONS

The current study showed similar force regulation between EMS-treated teeth and their contralateral control teeth. These findings indicate that EMS treatment does not perturb the sensory information of PMRs and maintains the force regulation and oral fine motor control during the behavioral biting task. Based on the study results, it could be implied that EMS treatment has a pivotal role in the preservation of oral function in teeth with

posttreatment apical periodontitis. Further investigations on the influence of the periapical infection and healing process on the PMRs will elucidate more details about their function.

## CREDIT AUTHORSHIP CONTRIBUTION STATEMENT

**Khaled Al-Manei:** Conceptualization, Methodology, Software, Formal analysis, Data curation, Writing - original draft, Visualization.

**Nabeel Almotairy:** Conceptualization, Methodology, Software, Data curation, Validation, Visualization. **Kholod Khalil Al-Manei:** Conceptualization, Methodology, Writing - review & editing, Visualization.

**Abhishek Kumar:** Conceptualization, Methodology, Formal analysis, Writing - review & editing, Visualization, Supervision.

**Anastasios Grigoriadis:** Conceptualization, Methodology, Writing - review & editing, Supervision, Project administration.

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*The authors deny any conflicts of interest related to this study.*

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