Distribution Statement

Distribution A: Public Release.

UNIFORMED SERVICES UNIVERSITY OF THE HEALTH SCIENCES
AIR FORCE POSTGRADUATE DENTAL SCHOOL
2133 Pepperrell Street
Joint Base San Antonio- Lackland, Texas 78236-5345
www.usuhs.mil

THESIS APPROVAL PAGE FOR MASTER OF SCIENCE IN ORAL BIOLOGY

Title of Thesis: Targeted Endodontic Microsurgery: A dimensional analysis of projected osteotomy and resection pathways in mandibular molars

Name of Candidate: Paul T. Pryor
Master of Science Degree
May 26, 2023

THESIS/MANUSCRIPT APPROVED:

SEIBOLD.JELENA.CORINNE.1255912352 Digitally signed by SEIBOLD.JELENA.CORINNE.1255912352

Jelena C. Seibold, D.D.S., M.S.
Program Director, Air Force Postgraduate Dental School Endodontics Residency

CARLSON.TIMOTHY.A.1137630970 Digitally signed by CARLSON.TIMOTHY.A.1137630970 Date: 2023.06.29 11:43:34 -05'00'

Timothy A. Carlson, D.D.S., M.S.
Training Officer, Air Force Postgraduate Dental School Endodontics Residency

Targeted Endodontic Microsurgery: A Dimensional Analysis of Projected Osteotomy and Resection Pathways in Mandibular Molars

Paul T. Pryor, Jelena C. Seibold, Allen M. Pratt*

Abstract

Introduction: Targeted Endodontic Microsurgery (TEMS) utilizes trephine burs and 3D-printed guides to produce osteotomies with greater accuracy than that achieved by freehand surgery alone (1). This cone-beam computed tomography (CBCT)-based dimensional analysis study sought to determine the feasibility of performing TEMS on mandibular first and second molar roots.

Methods: Two board-certified endodontists analyzed 398 CBCT coronal slices of mandibular first and second molar roots for TEMS feasibility based on depth of osteotomy, anticipated trephine violation of lingual cortical plate, proximity to inferior alveolar canal, excessive bone loss from surgery, and unfavorable resection angle/length. Age and gender were analyzed for impact on TEMS feasibility. Chi-Square tests for categorical variables were conducted and t-test and analysis of variance (ANOVA) for continuous variables were conducted.

Results: TEMS-feasibility rates of mandibular first molar mesial and distal roots were found to be 85.71% and 75.24%, respectively, whereas that of mandibular second molar mesial and distal roots could be treated using TEMS at rates of 20.24% and 12.05%, respectively. Average osteotomy depth was significantly greater for TEMS non-feasible teeth (10.45mm) than for TEMS feasible teeth (7.64mm). Age and gender were not found to have significant impacts on TEMS feasibility.

Conclusions: Mandibular first molars are 6 times more likely to be treatable by TEMS than mandibular second molars. Although mandibular second molars pose more surgical and anatomical challenges, consideration should be given to TEMS as a treatment option for second molars that are favorably positioned.

SIGNIFICANCE

Mandibular second molar mesial and distal roots were considered TEMS-feasible at rates of 20.24% and 12.05%, respectively. Using coronal CBCT slices of mandibular molar roots is a valid screening mechanism to determine the feasibility of TEMS.

INTRODUCTION

Recent advancements in endodontic microsurgery (EMS) have allowed for precise evaluation and treatment planning of previously unpredictably surgically treatable apices like those of mandibular molars. Targeted Endodontic Microsurgery (TEMS) is one of these advancements and employs cylindrical trephine burs rotating in the sleeve of a 3D-printed guide to produce osteotomies and root resections with greater precision of positioning and angulation than is readily achievable with traditional freehand EMS (1). Mandibular molar teeth, especially second molars, present particularly challenging endodontic surgical scenarios. Thick cortical bone, difficult access due to soft tissue constraints, proximity of root apices to the inferior alveolar canal and mandibular buccal and lingual plates all pose special surgical and anatomical considerations (1-3).

In a CBCT study by Kim et al. it was found that the distance from the lateral surface of the buccal cortical bone to the root apices of the mandibular second molar is greater than any tooth in the mandibular arch with exception of the mandibular third molar. Additionally, they found that the total depth of the osteotomy, at 3mm coronal to the apex, would be 10.14 +/- 1.62mm for the mesial root and 10.75 +/- 2.03mm for the distal root (3). For comparison, the distance to the lingual aspect of the mesial root and distal root of the mandibular first molar is 7.95 +/- 1.25mm and 8.26 +/-1.5mm, respectively. This average additional depth in osteotomy of approximately 2mm can pose significant surgical challenges when osteotomy and resection for apical surgery are performed.

Reports exist of mandibular second molar apical surgery creating a 20% lower lip sensory deficit rate and a 1% rate of permanent anesthesia with older techniques. In the same study, Wesson and Gale reported a threefold increase in permanent nerve damage when comparing mandibular second molar apical surgeries to mandibular first molar surgeries (5). One study reported direct communication with the mandibular canal in approximately 15% of mandibular second molar roots (4). According to Denio et al, 31% of mandibular canals followed an S-shaped curve and in a typical S-shaped curve, the mandibular canal was buccal to the distal root apex of the second molar and crossed to the lingual and inferior to the mesial root apex of the second molar. The average distances from the mesial root apex and distal root apex of the mandibular second molar were found to be 5.3 +/- 2.0mm and 5.2 +/- 2.3mm from the mandibular canal, respectively. Greater distances were observed for the mandibular first molars according to Denio, et al. (6) Knowing the path of and approximate distance from the mandibular canal is vital when considering treatment planning of apical surgery in the posterior mandible.

While inferior alveolar nerve violation is of high importance, the proximity of the mandibular molar roots to the lingual cortex and the proximity of the lingual nerve to the lingual cortical plate cannot be ignored. Using CBCT in 2018, Zahedi et al. found that the average distance between the external lingual cortex surface and the mandibular second molar root apices was between 2.9-3.2mm (7). A study of 14 cadavers shows that the lingual nerve in the area of the third molar tooth, in 5% of cases, may lie as close as 5.62mm or as far as 19.10mm from the crest of alveolar bone (8). Given this anatomic variability of position of the lingual nerve, violation of the mandibular lingual plate during endodontic apical surgery should be discouraged.

Three studies have shown that the distance between the second molar root apices and the mandibular canal is the shortest of any tooth (9-11). Therefore, a high degree of precision is required to mitigate intra-operative complications during second molar root end procedures. Pinsky et al proposed a technique in 2007 that combined CBCT planning and CAD/CAM surgical stents to produce guides for periapical osteotomy path determination. Importantly, it was found that surgical osteotomy accuracy and consistency were improved when using surgical guidance (12).

Following the work of Pinsky in 2007, Targeted Endodontic Microsurgery (TEMS), in 2017, combined a 3D printed surgical guide with implant trephine burs to perform osteotomy and root end resection together in a single step (13). TEMS allows endodontists to “complete osteotomy and root-end resection more efficiently with a more appropriate root-end resection volume and bevel angle”, according to Hawkins et al. (14) while Giacomino et al. concluded that TEMS “produced an osteotomy site with predictable angulations, diameter and depth” (1).

This study intended to use coronal CBCT slices of mandibular molar roots to: 1) determine the feasibility of performing TEMS on mandibular molars; 2) determine the location of the apices relative to the IAN; 3) determine whether CBCT alone is a satisfactory screening tool to determine the feasibility of TEMS for mandibular molars. The null hypothesis is that TEMS will not be feasible for any mandibular second molars due to apical root proximity to the inferior alveolar neurovascular bundle, risk of perforation of the lingual cortical plate, and/or the osteotomy pathway passing through adjacent tooth roots. The alternate hypothesis is that some cases are possible with TEMS depending on the skill and experience of the clinician.

MATERIALS AND METHODS

Image Selection

The 59th Medical Wing Institutional Review Board approved the design of this study. CBCT scans of a racially diverse patient pool seeking evaluation for dental treatment prior to December 2021 were acquired from a private network used to store CBCT images at the Air Force Postgraduate Dental School. CBCT images were included if they met the following criteria: the patient was ≥22 year old at time of scan, at least one mandibular first and/or second molar in each scan was visible without previous apical surgery, significant radiographic evidence of periodontal disease, or significant radiographic evidence of apical resorption. The included patient scans had fields of view of 40mm x 40mm, 60mm x 60mm, 80mm x 80mm with respective voxel sizes of 0.08, 0.125 and 0.160mm. All scans were acquired with a 3D Accuitomo 80 (J. Morita USA, Irvine, CA) at 5-7 mA, 65-90 kVp, and a 17.5 second exposure time.

Image Measurements and Inferior Alveolar Canal (IAC) Position Categorization

The 397 accepted CBCT images were analyzed using iDixel software (J. Morita USA, Irvine, CA). Images were oriented so that coronal slices bisected the long axis of each mandibular molar root as close to perpendicular to a simulated 0 degree bevel from a sagittal aspect at approximately 3mm from the radiographic apex as possible. The following measurements were then made in sequential order: 1) 3mm from the radiographic apex advancing coronally (ideal level of root resection) 2) distance from buccal cortical plate to lingual aspect of root perpendicular to measurement #1 3) distance from radiographic apex to the closest cortication of the inferior alveolar canal (Fig. 1). All measurements, root and tooth type (1- mandibular first molar mesial root, 2-mandibular first molar distal root, 3-mandibular second molar mesial root, 4-mandibular second molar distal root, 5-mandibular second molar fused roots), patient age and sex (male or female) were recorded.

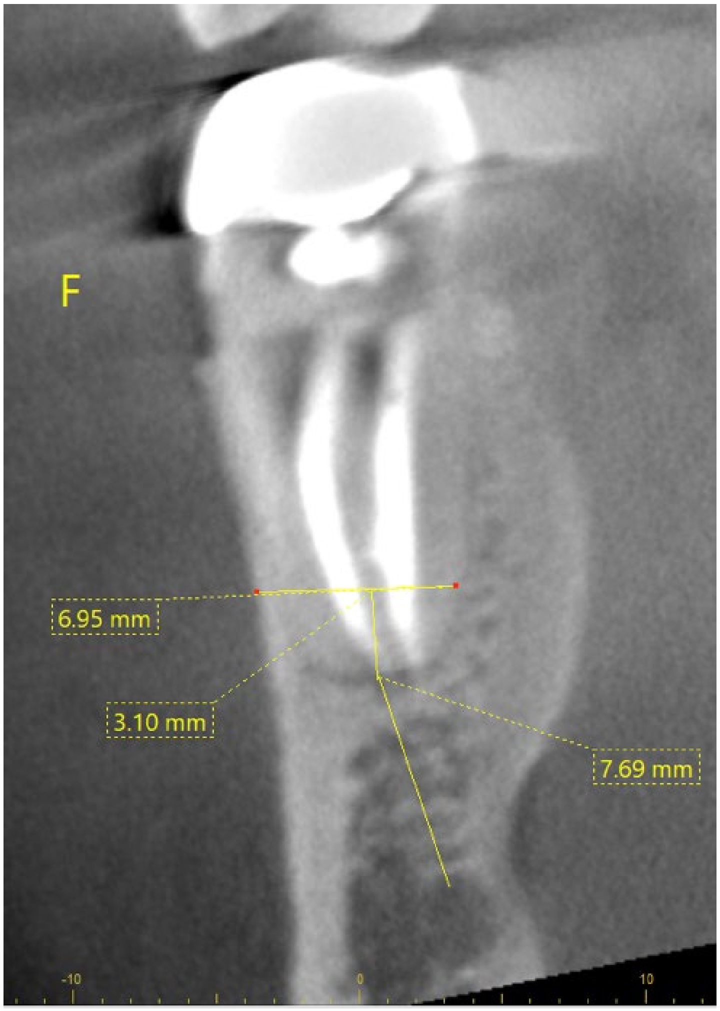

Figure 1: Coronal slice of mandibular molar with 3 measurements. 3.10mm is simulated proposed amount of root resection and is oriented in long axis of the root. 6.95mm is distance from buccal surface of buccal cortical plate to lingual aspect of root perpendicular to long axis of root. 7.69mm is distance from radiographic apex to IAC.

The position of the inferior alveolar canal was categorized as: 1) Facial 2) Apical 3) Lingual, by using the same coronal slices and orienting a circle divided by two lines projecting from the center that equally divided the circle into quarters centered around the radiographic apex (Figure 2). Positioning of IAC was recorded.

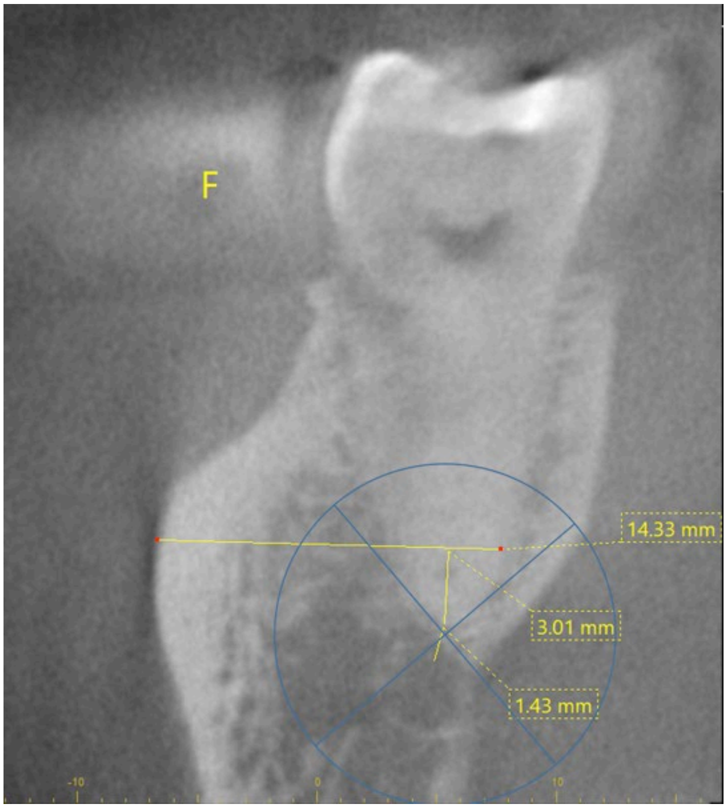

Figure 2: Coronal images used to categorize position of IAC

Calibration

Prior to viewing study slices, two board certified endodontists, one with clinical TEMS experience and one without, viewed a presentation of the literature relating the anatomical challenges of mandibular second molar apical surgery including details of the depth of osteotomy, course of the IAC, lingual plate proximity, and importance of avoiding the lingual nerve space (2, 5, 6).

Assessment by Evaluators

Evaluators jointly assessed all 397 coronal root images and categorized each as either TEMS-feasible or TEMS-unfeasible. Reasons for TEMS-unfeasible included: 1) excessive depth of osteotomy (negative impact on visualization of root-end) 2) violation of lingual cortical plate (potential for violation of lingual nerve) 3) proximity to IAC (potential for encroachment within 2mm of neurovascular bundle) 4) excessive bone loss from surgery (unfavorable soft tissue healing) 5) unfavorable resection length/angle (potential for excessive root removal or too steep of angle) 6) other (evaluator specified reason). Evaluators later repeated joint assessments of 104 coronal slices for interrater and intrarater reliability metrics. Evaluators discussed reasoning for rejecting a case, but were not required to agree on whether or not TEMS was feasible or their reasons for rejection. All TEMS-feasible, TEMS-unfeasible and reasons for rejection were recorded.

CBCT data of TEMS-feasible mandibular second molar roots were imported into Blue Sky Bio software. A surgical pathway for each root was planned in Blue Sky Bio software to attempt to simulate the orientation of a guide tube within a 3D-printed guide that would facilitate root end resection of each TEMS-feasible root. If an acceptable pathway could be established then a "YES" was recorded, but if no acceptable pathway could be established then a "No" was recorded.

Statistical Analyses

Statistical analyses were performed using SAS version 9.4 (Statistical Analysis Software, Cary, NC). Chi-Square Test for categorical variables, t-test and Analysis of Variance (ANOVA) for continuous variables were conducted. Pairwise comparisons using post-hoc tests with Bonferroni Adjustment were made amongst the 5 different root types analyzed. Reasons for rejection of TEMS-feasibility were collected and are presented as raw data, no associations were sought. Evaluator agreement was measured using Kohen's kappa for inter-rater reliability and intra-rater reliability.

RESULTS

A total of 105 mandibular first molars (210 roots) and 104 mandibular second molars (187 roots, 20 analyzed roots were considered fused and one root was excluded from analysis) were collected from CBCT scans. Statistical analysis included 216 roots (54.4%) from female patients and 181 roots (45.6%) from male patients. The average patient age was 42.63 years (range 22-87).

TEMS feasibility

Total number of roots per group deemed TEMS-feasible: first molar mesial roots) 90 (85.71%) first molar distal roots) 79 (75.24%) second molar mesial roots) 17 (20.24%) second molar distal roots) 10 (12.05%) second molar fused roots) 0 (0%). Total number of roots per group deemed TEMS-unfeasible: 1) 15 (14.29%) 2) 26 (24.76%) 3) 67 (79.76%) 4) 73 (87.95%) 5) 20 (100%), results are presented in Table 1.

Root type	TEMS-feasibility	N	TEMS Rate (%)	BlueSkyBio Analysis N (%)
1st molar M root	**YES**	**90**	**85.71**	N/A
	NO	15	14.29	N/A
1st molar D root	**YES**	**79**	**75.24**	N/A
	NO	26	24.76	N/A
2nd molar M root	**YES**	**17**	**20.24**	15 (88.2%)
	NO	67	79.76	2 (11.8%)
2nd molar D root	**YES**	**10**	**12.05**	12 (100%)
	NO	73	87.95	0
2nd molar fused root	**YES**	**0**	**0**	N/A
	NO	20	100	N/A

Table 1: TEMS feasibility results for each root type.

Groups 1 and 2 were considered to be statistically significantly more likely to be TEMS-feasible than groups 3, 4, and 5. Group 3 was considered to be statistically significantly more likely to be TEMS-feasible than group 5. The pairwise comparisons are presented in Table 2.

Root Type Groups	1	2	3	4	5
1st molar M root	*				
1st molar D root	0.06	*			
2nd molar M root	**<.0001**	**<.0001**	*		
2nd molar D root	**<.0001**	**<.0001**	0.15	*	
2nd molar fused root	**<.0001**	**<.0001**	**0.004**	0.10	*

Table 2: Pairwise comparisons of 5 root type groups. *: annotates comparisons of groups to themselves. P<0.005 considered significant due to Bonferroni adjustment following post-hoc pairwise comparisons.

Among the roots studied from female patients 102 were considered TEMS-feasible and 94 of the roots studied from male patients were considered TEMS-feasible. No statistically significant difference was found between men and women for TEMS-feasibility rates (p-value=0.35). These results are presented in Table 3.

Sex	TEMS-feasibility	N	% of Total	p-value
F	**YES**	102	52.04%	**0.35**
	NO	114	56.72	
M	**YES**	94	47.96	
	NO	87	43.28	

Table 3: Totals of female and male TEMS-feasibility data.

The frequencies of the location of the IAC were as follows: 22 IAC facial to radiographic apex, 364 IAC apical to radiographic apex, 8 IAC lingual to radiographic apex. TEMS-feasible rates of the 3 locations of the IAC were as follows: facial, 5%, apical 52%, lingual 50%. Apical and lingual IAC locations were found to be significantly more likely to be TEMS-feasible than if the IAC was located facially [$\chi^2(2)$ =18.85, p <.0001]. 4 IAC were not visible on the coronal images during the evaluation by the primary author and were excluded from analysis. The average recorded distance from the radiographic apex to the closest cortication of the IAC was 4.86mm with a range of 0-12.01mm. These results are presented in Table 4.

Location of IAC	**TEMS**		
	YES (relative percentage of total, %)	**NO (relative percentage of total, %)**	**Total**
Facial	1 (4.55)	21 (95.45)	22
Apical	190 (52.2)	174 (47.8)	364
Lingual	4 (50)	4 (50)	8
Total	195	199	394
Frequency Missing = 4			

Table 4: Total number of TEMS-feasible and TEMS-unfeasible roots and cumulative percentages.

Role of Depth of Osteotomy

The average depth of osteotomy for the TEMS-feasible groups were: first molar mesial root: 7.39 ± 1.02mm first molar distal root: 7.58 ± 1.25mm, second molar mesial root: 8.59 ± 1.1mm second molar distal root: 8.8 ± 0.8mm second molar fused root: No roots were found to be TEMS-feasible. The average depth of osteotomy for the TEMS-unfeasible groups were: first molar mesial root: 8.04 ± 1.47mm first molar distal root: 8.53 ± 1.55mm, second molar mesial root: 10.6 ± 1.51mm, second molar distal root: 11.17 ± 1.53mm, second molar fused root: 11.63 ± 1.47mm. T-test results indicated that the depths of osteotomy of TEMS Yes were significantly smaller than ones of TEMS No for mandibular first molar distal roots, mandibular second molar mesial and distal roots, but not for the second molar fused group. No comparison could be made for group 5 because no fused roots were found to be feasible with TEMS. Average depth of osteotomies are presented in Table 5.

Root type	TEMS-feasibility	N	Mean	Standard Deviation	Range	P-value
1st molar M root	**YES**	90	**7.39**	**1.02**	4.86 - 10.67	0.11
	NO	15	8.04	1.47	5.93 - 10.72	
1st molar D root	**YES**	79	**7.58**	**1.25**	3.05 - 9.86	**0.002**
	NO	26	8.53	1.55	5.71 - 12.9	
2nd molar M root	**YES**	17	**8.59**	**1.1**	7.08 - 11.09	**<.0001**
	NO	67	10.6	1.51	7.21 - 14.62	
2nd molar D root	**YES**	10	**8.8**	**0.8**	7.56 - 10.04	**<.0001**
	NO	73	11.17	1.53	7.15 - 15.21	
2nd molar fused root	YES	0	-	-	-	NS
	NO	20	11.63	1.47	9.45 - 14.91	

Table 5: Distances from buccal surface of buccal cortical plate to lingual aspect of root measured on a line perpendicular to long axis of root, in millimeters, for TEMS-feasible and TEMS-unfeasible groups for each root type.

Reasons cited in roots deemed TEMS-unfeasible

201 (50.6%) of the roots studied were deemed TEMS-unfeasible. Evaluators were instructed to indicate their reasons for rejection. Reasons for TEMS-unfeasible were excessive depth of osteotomy (59.20%), violation of lingual cortical plate (21.39%), proximity to IAC (45.27%), excessive bone loss from surgery (20.39%), unfavorable resection length/angle (14.90%), other (5.90%). Reasons in the other category included proximity to the mental foramen and possible vascular anomaly. Results are presented in Table 6 and examples of each reason for case rejection are presented in Figure 3.

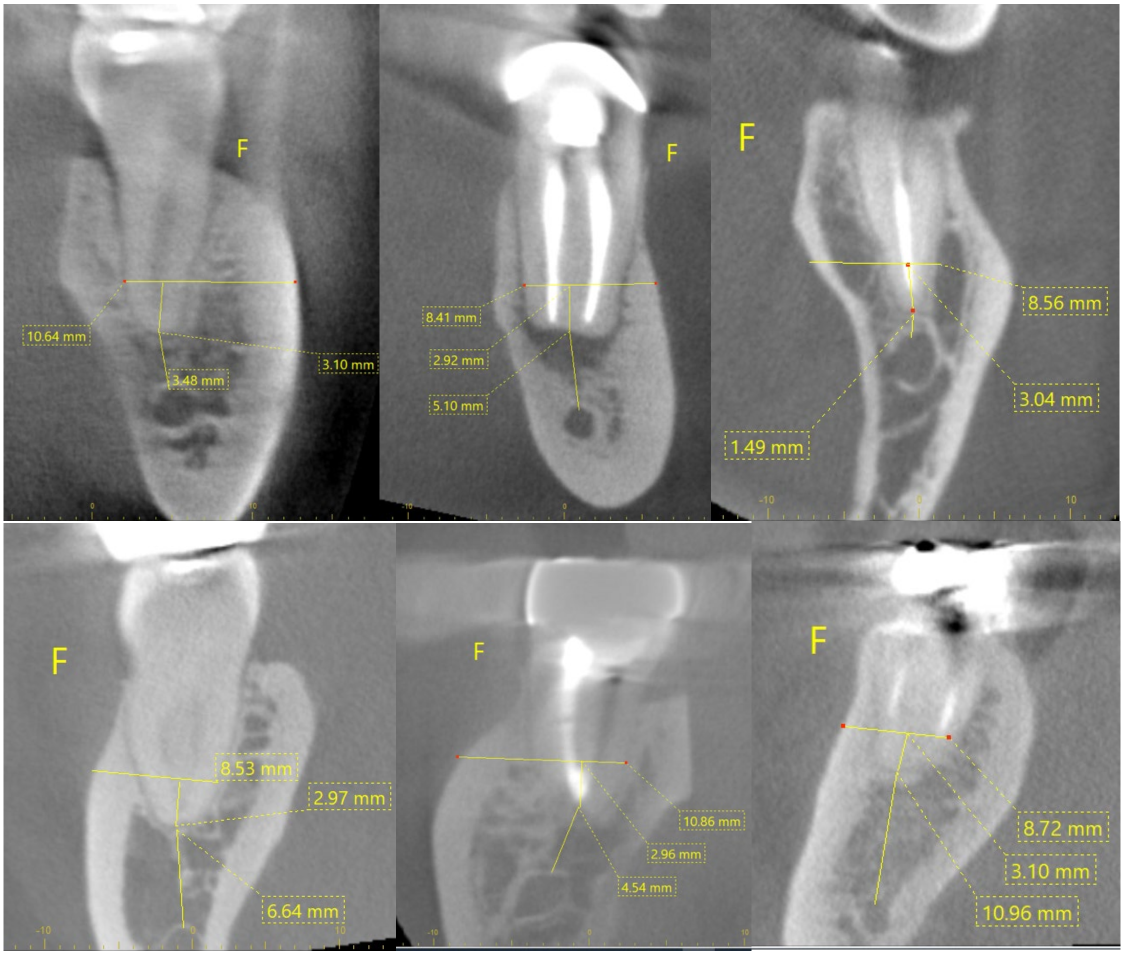

Figure 3: In order from top left to bottom right. Reasons for TEMS-unfeasible were excessive depth of osteotomy, violation of lingual cortical plate, proximity to IAC, excessive bone loss from surgery, unfavorable resection length/angle, other. Reasons in category 6 included proximity to the mental foramen and possible vascular anomaly.

Reason	Frequency	Unfeasible (%)
Excessive depth of osteotomy	119	59.20%
Violation of lingual plate	42	21.39%
Proximity to IAC	91	45.27%
Excessive bone loss from surgery	41	20.39%
Unfavorable resection length/angle	30	14.90%
Other	12	5.90%

Table 6: Frequency and percentage of total TEMS-unfeasible roots. Reasons: 1) excessive depth of osteotomy (negative impact on visualization of root-end) 2) violation of lingual cortical plate (potential for violation of lingual nerve) 3) proximity to IAC (potential for encroachment within 2mm of neurovascular bundle) 4) excessive bone loss from surgery (unfavorable soft tissue healing) 5) unfavorable resection length/angle (potential for excessive root removal or too steep of an angle) 6) other (evaluator specified reason)

BlueSky Bio Analysis

17 mandibular second molar mesial roots and 12 second molar distal roots were deemed TEMS-feasible and analyzed using BlueSky Bio software. 2 second molar mesial roots (11.8%) were deemed TEMS-unfeasible following surgical planning in BlueSky Bio. The remaining 27 second molar roots (93.1%) were deemed TEMS-feasible following surgical planning in BlueSky Bio. These results are reported in Table 1.

Inter and Intra-rater Agreement

Inter-rater agreement was “moderate” for TEMS-feasibility data (kappa for observer 1 = 0.65 and observer 2 = 0.67). Inter-rater reliability was “almost perfect” for TEMS-feasibility data (kappa = 0.94)

DISCUSSION

The null hypothesis that TEMS will not be feasible for any mandibular second molar roots can be rejected and the alternative hypothesis can be accepted based on presented data. Location of the IAC was determined to be apical to the radiographic apex in 92.4% of the studied samples and measured distance from radiographic apex to the closest cortication of the IAC was 4.86 with a range of 0-12.01mm. These data largely agree with Denio et al that found that the distances from the mesial and distal root apices of mandibular second molar teeth were 5.3 $\pm$ 2.0 mm and 5.2 $\pm$ 2.3 mm, respectively. The final aim of the study was to determine if CBCT coronal slices would be a satisfactory screening tool to determine the feasibility of performing TEMS on mandibular molars. All mandibular second molars that were deemed TEMS-feasible by the evaluators were analyzed using Bluesky Bio software and 92.5% of those roots were determined to have a surgically acceptable TEMS pathway. This finding validates the use of the coronal CBCT images as a potential screening tool for mandibular molar TEMS surgery.

The significant difference of the average depth of TEMS-feasible groups 2, 3, and 4 show that depth of osteotomy played a large role during evaluation. It is possible that, as clinicians, the evaluators understood that, though TEMS would be possible at increased depth, the retropreparation and retrofilling of the root end would be technically extremely challenging. Depth of osteotomy was listed as the most common reason for a root to be deemed TEMS-unfeasible and was indicated in 60% of TEMS-unfeasible roots.

A major limitation of this study is a complete lack of consideration for soft tissue constraints. Providers considering TEMS as a treatment option for mandibular second molar surgery should be acutely aware of the required retraction of the soft tissue to accommodate the surgical guide and trephine at the designed osteotomy angle. Surgical treatment planning should be made with a maximally mesially angulated surgical path to alleviate, as much as possible, the soft tissue retraction that would be required for surgical access while maintaining safe working distances from adjacent anatomic structure such as neighboring tooth roots. A second limitation of the present study is that using one coronal CBCT image that bisected each root allowed for efficiency and enable the primary author to evaluate a large volume of potential TEMS surgeries. However, clinicians with CBCT will be able to definitely locate all relevant anatomical structures including IAC, lingual plate, adjacent tooth roots, and appropriate angulation and positioning of all roots and teeth involved in surgical treatment planning. Obviously, one coronal CBCT does not provide sufficient information to definitively determine whether TEMS is possible, but it seems as though it can provide enough information to definitively determine that TEMS is *not* possible. Future research, including case reports and series, on TEMS feasibility of anatomically challenging clinical situations such as the mandibular second molars are warranted.

CONCLUSIONS

Mandibular first molars are 6 times more likely to be treatable by TEMS than mandibular second molars. Although mandibular second molars pose more surgical and anatomical challenges, consideration should be given to TEMS as a treatment option for second molars that are favorably positioned.

AUTHORS

Maj Paul T. Pryor, DMD, Resident, Air Force Postgraduate Dental School and Uniformed Services University of the Health Sciences Postgraduate Dental College.

Lt Col Jelena C. Seibold, DDS, M.S. Endodontics Residency Training Officer, Air Force Postgraduate Dental School and Uniformed Services University of the Health Sciences Postgraduate Dental College.

Lt Col Allen M. Pratt, DMD, Endodontics Residency Program Director, Air Force Postgraduate Dental School and Uniformed Services University of the Health Sciences Postgraduate Dental College.

The views expressed are those of the authors and do not reflect the official views or policy of the Department of Defense or its Components or the Uniformed Services University of the Health Sciences.

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

Acknowledgements
Special acknowledgements to Mr. James Pizzini who assisted with all digital planning within BlueSky Bio software and Dr. Jisuk Park for statistical support.

Bibliography

1. Giacomino CM, Ray JJ, Wealleans JA. Targeted Endodontic Microsurgery: A Novel Approach to Anatomically Challenging Scenarios Using 3-dimensional-printed Guides and Trephine Burs-A Report of 3 Cases. J Endod 2018;44(4):671-677.
2. Porto OCL, Silva BSF, Silva JA, Estrela CRA, Alencar AHG, Bueno MDR, et al. CBCT assessment of bone thickness in maxillary and mandibular teeth: an anatomic study. J Appl Oral Sci 2020;28:e20190148.
3. Kim D, Ha JH, Jin MU, Kim YK, Kim SK. Proximity of the mandibular molar root apex from the buccal bone surface: a cone-beam computed tomographic study. Restor Dent Endod 2016;41(3):182-188.
4. Bürklein S, Grund C, Schäfer E. Relationship between Root Apices and the Mandibular Canal: A Cone-beam Computed Tomographic Analysis in a German Population. J Endod 2015;41(10):1696-1700.
5. Wesson CM, Gale TM. Molar apicectomy with amalgam root-end filling: results of a prospective study in two district general hospitals. Br Dent J 2003;195(12):707-714; discussion 698.
6. Denio D, Torabinejad M, Bakland LK. Anatomical relationship of the mandibular canal to its surrounding structures in mature mandibles. J Endod 1992;18(4):161-165.

7. Zahedi S, Mostafavi M, Lotfirikan N. Anatomic Study of Mandibular Posterior Teeth Using Cone-beam Computed Tomography for Endodontic Surgery. J Endod 2018;44(5):738-743.
8. Al-Amery SM, Nambiar P, Naidu M, Ngeow WC. Variation in Lingual Nerve Course: A Human Cadaveric Study. PLoS One 2016;11(9):e0162773.
9. Nair UP, Yazdi MH, Nayar GM, Parry H, Katkar RA, Nair MK. Configuration of the inferior alveolar canal as detected by cone beam computed tomography. J Conserv Dent 2013;16(6):518-521.
10. Kovisto T, Ahmad M, Bowles WR. Proximity of the mandibular canal to the tooth apex. J Endod 2011;37(3):311-315.
11. Lvovsky A, Bachrach S, Kim HC, Pawar A, Levinzon O, Ben Itzhak J, et al. Relationship between Root Apices and the Mandibular Canal: A Cone-beam Computed Tomographic Comparison of 3 Populations. J Endod 2018;44(4):555-558.
12. Pinsky HM, Champleboux G, Sarment DP. Periapical surgery using CAD/CAM guidance: preclinical results. J Endod 2007;33(2):148-151.
13. Ray JJ. Targeted Endodontic Microsurgery. 2019.
14. Hawkins TK, Wealleans JA, Pratt AM, Ray JJ. Targeted endodontic microsurgery and endodontic microsurgery: a surgical simulation comparison. Int Endod J 2020;53(5):715-722.