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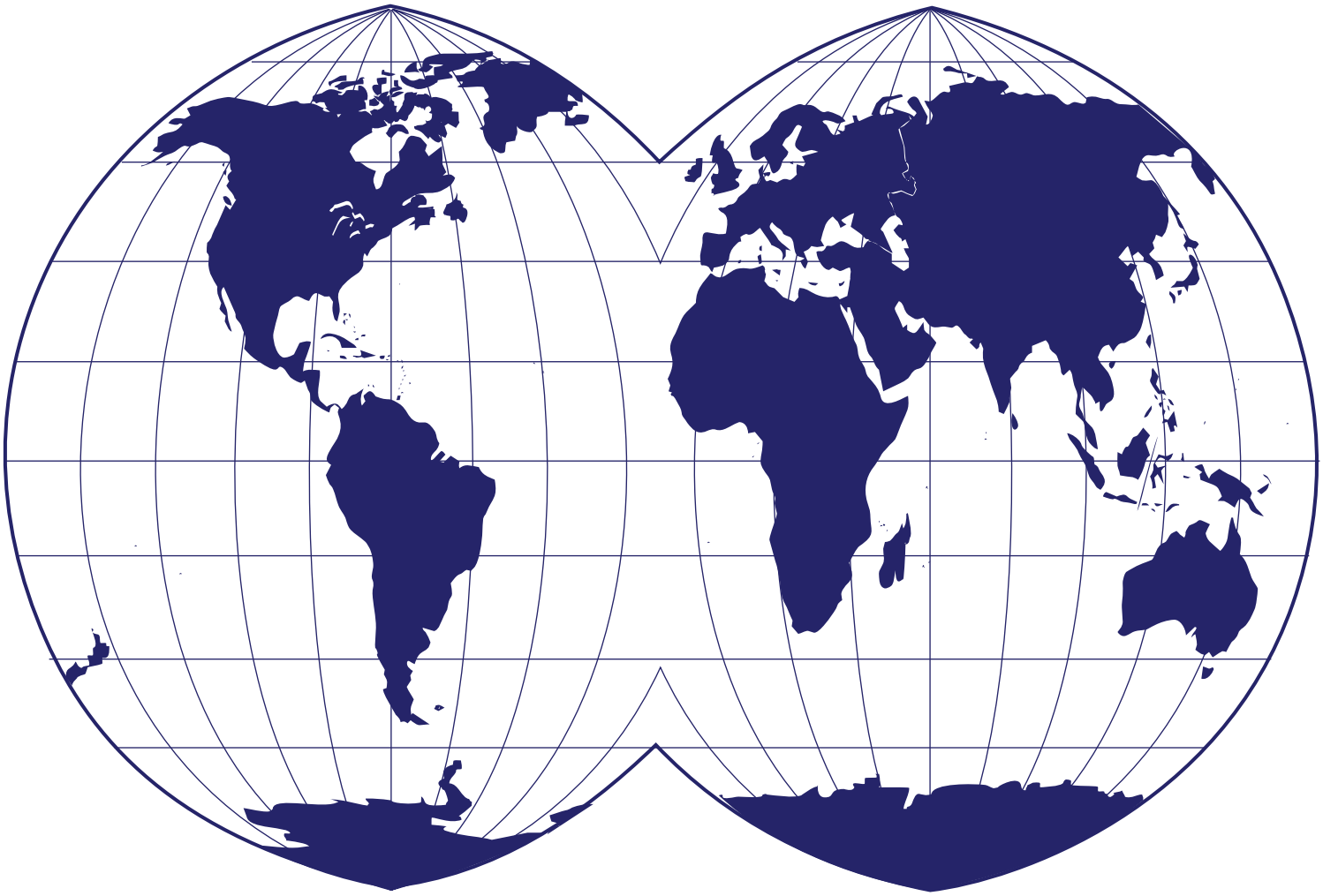

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# Journal of the International Academy of Periodontology

**Letter from President** 101

**Letter from Editor** 102

**Furcation Measurements: Realities and Limitations**
*Bangalore Varadhan Karthikeyan, Vasudevalu Sujatha and Munivenkatappa Lakshmaiah Venkatesh Prabhuji* 103

**Clinical and Radiographic Evaluation of the Periodontium with Biologic Width Invasion by Overextending Restoration Margins - A Pilot Study**
*Dhelfeson Willya Douglas de Oliveira, Marina Natássia Pacheco Maravilha, Thaís Nascimento dos Anjos, Patrícia Furtado Gonçalves, Olga Dumont Flecha and Prof. Karine Tavano* 116

**Systemic Chemotherapeutic Agents as Adjunctive Periodontal Therapy: A Narrative Review and Suggested Clinical Recommendations**
*Rachel A. Sheridan, Hom-Lay Wang, Robert Eber and Tae-Ju Oh* 123

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# Message from the President of the International Academy of Periodontology September 2015

My journey with the International Academy of Periodontology (IAP) started almost two decades ago when I was introduced to Dr. Thomas Van Dyke and immediately became a member of the association. I made my first visit to an IAP congress with a poster presentation in 1998 in Seoul, Korea. Since then, it has been a fascinating journey with the IAP. I look back and at times feel awed that today I have the honor of being president of this esteemed organization.

Last year we conducted the first ever IAP Conclave. It was an enriching and enlightening experience - three days spent with a large gathering of professionally acclaimed periodontists from around the world. All delegates who participated in the Conclave shared their significant expertise at various levels during the unique deliberation session. The Conclave resulted in some definitive statements endorsed by the more than 100 delegates present that will likely stimulate more research, new findings, and new therapies in the field of periodontology.

In my two-year term as president of the IAP, I would like to see our organization initiate fruitful partnerships and fresh initiatives in addition to the biennial congress that will take place in 2017. We have already begun a dialogue with the *Fédération Dentaire Internationale* (FDI, or World Dental Federation) to renew our partnership for the future. We have also begun a fruitful discussion with International Dental Exhibitions and Meetings (IDEM) Singapore for future collaboration. I thank our immediate past president, Dr. Mark Bartold, who initiated the idea of such collaboration. I personally will be at the FDI general assembly in 2015 to sign our partnership program, and will meet with group representatives to finalize the Academy's association with IDEM.

There has been strong discussion about collaborating and bringing together a scientific program focused on periodontal research, and I will strive towards creating this new initiative under the aegis of the IAP. I would like to invite and encourage more regional periodontal education programs supported by the IAP and am looking at the possibility of a strong regional program in India in 2016.

I thank all the IAP Board members and past presidents for all of their support when I was the secretary of the IAP and my presidential journey was just beginning. I have to again mention Dr. Tom Van Dyke, who has always been a guiding light for me in the IAP central office in Boston. I also wish to thank my mentor and guru, Dr. Klaus Lang, who has been an inspiration to me at all points in my professional career as a periodontist.

I wish the greatest of success and exponential growth to the IAP.

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# Message from the Editor of the Journal of the International Academy of Periodontology September 2015

This issue of the Journal of the International Academy of Periodontology marks the conclusion of the seventeenth year of publication of the Journal. I am pleased and honored to have served as the Editor of the Journal since 1999, when then IAP President Thomas Van Dyke conceived of expanding the IAP mission through publication and dissemination of periodontal research in an IAP journal.

Although during the first few years the Journal was faced with challenges, as all new journals are, we have developed a strong and dedicated Editorial Board and excellent reviewers with broad scientific expertise. In addition, utilizing the skills of a very experienced scientific editor, we have been able to offer assistance in editing of English grammar, vocabulary and syntax so that authors with limited abilities in English composition but papers of strong scientific merit have a venue for scientific publication. Thus the Journal of the International Academy of Periodontology helps fulfill the IAP mission of "promoting international exchange and communications between individuals of all nations…" especially for authors from developing countries.

To continue to expand the reach of IAP, the IAP Board met at the Fifteenth International Biennial Congress of IAP in Santiago, Chile in April 2015 to discuss the future of the Journal. The Board recommended that the Journal of the International Academy of Periodontology become an "on-line, open access" journal beginning in January 2016. Thus the October 2015 issue will be the last print issue of the Journal. It will be available to all without cost on the IAP website, http://perioiap.org/journals.aspx. The future quality of the Journal is mostly dependent on the merit of the papers submitted. I ask that the readers submit their best papers to the Journal and encourage their colleagues in the periodontal community to do the same. I look forward to continue to serve as Editor for the foreseeable future.

Mark R. Patters
Editor
Email: jiap@uthsc.edu

# Furcation Measurements: Realities and Limitations

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**Abstract**

Furcation involvement is a common sequela of severe chronic periodontal disease. Its effective management has a profound influence on the outcome of periodontal therapy. For the efficient clinical management of furcation defects, it is necessary to have a reliable diagnostic tool that can accurately measure and quantify the furcation defect. This article addresses the various diagnostic methods available and assesses their limitations. Further, it also highlights some new frontiers in the field of furcation diagnosis and measurements.

*Keywords: Furcation, measurement, periodontal disease, diagnosis, periodontal defect*

## Introduction

Reliable measurement of the degree of furcation in multi-rooted teeth offers a unique and challenging task, and remains an unresolved problem for the periodontist in clinical practice (Eickholz, 1995; Al-Shammari *et al.*, 2001). The furcation area creates situations in which routine periodontal procedures are limited and special procedures are generally required because of various confounding factors such as the size and shape of the tooth, roots and their alveolar housing, and the varied nature and patterns of periodontal destruction (Al-Shammari *et al.*, 2001; Lekovic *et al.*, 1998).

Since the early description and classification of furcation involvement by Glickman, it is a known fact that the measurement process has a profound influence on the detection and assessment of the furcation defect (Zappa *et al.*, 1993; Lindhe, 1983; Mealey *et al.*, 1994). It is believed that furcation measurements influence the prognosis of the involved tooth, which helps with the insurance claim, time and money spent to retain the tooth, and to determine the strategic importance of the tooth for the overall rehabilitation of the patient and allow development of a surgical treatment plan (Lindhe, 1983; Mealey *et al.*, 1994; Muller and Eger, 1999). Further, the decisions regarding treatment are vastly dependent on the severity of destruction, the strategic importance of the tooth, and the level of patient motivation, for which accurate diagnosis of the extent of involvement is a key factor. There are various traditional diagnostic tools to detect and evaluate the extent of the disease. However, inherent limitations exist in determining accurate measurements, especially in the horizontal direction, due to interference from the furcation anatomy, the need for the sound technical skills and compliance of the patient. Because of these factors there is always a quest for newer diagnostic tools and modern treatment modalities for accurate furcation diagnosis and treatment (Muller and Eger, 1999).

The objective of this review is to bring the reader up-to-date on the realities and limitations of the various traditional methods used for the diagnosis of furcation involvement and, in addition, the various advanced methods in furcation measurements are briefly discussed.

### *Call for accurate furcation measurement*

There exists a compelling need to accurately diagnose the extent of furcation involvement, as these defects represent a formidable problem in the treatment of periodontal disease, principally related to the complex and irregular anatomy of furcations (Marcaccini *et al.*, 2012; James *et al.,* 2013). One of the key points the clinician should keep in mind while measuring furcation involvement is that not much of an "inaccuracy" is acceptable because it may significantly alter the treatment plan (Mealey *et al.*, 1994). This highlights the great need for accurate furcation measurements, which can be summarized as follows:

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1. Furcation defects serve as risk factors for progressive loss of connective tissue attachment, alveolar bone resorption and tooth mobility (Bowers *et al.*, 2003).
2. After periodontal treatment, monitoring of the furcation lesion has to be done to ensure that there is no disease progression (Cortellini *et al.*, 1993).
3. Different therapeutic approaches are chosen based upon clinical determination of severity of involvement. Therefore, any discrepancy between pre- and intra-surgical findings may lead to an alteration in the surgical treatment (Mealey *et al.*, 1994; Muller and Eger, 1999).

### *Limitations in furcation measurements*
### *Influence of furcation anatomy*

Knowledge of the anatomy of multi-rooted teeth is essential in order to correctly identify the presence of furcation involvement. The furcation area can be divided into 3 parts; namely, the roof, the surface immediately coronal to the root separation (flute), and the area of root separation (Goldman and Cohen, 1988). There are some anatomical variations that are often encountered in the furcation area such as enamel pearls, bifurcation ridges, cervical enamel projections and fused roots, which limit the ability to manipulate the probe in negotiating the furcation to its vertical probing depth (VPD) and horizontal probing depth (HPD) (Shiloah and Kopczyk, 1979; Moskow and Canut, 1990; Hou and Tsai, 1997; Everett *et al.*, 1958; Bower, 1979). This is especially the case with distal furcations of maxillary molars that generally lie in a plane directly apical to the contact area, which is further exacerbated by the presence of a second or third molar distal to the tooth in question. In addition, this issue is worsened due to the lack of reliability of different diagnostic aids (Bower, 1979). With respect to the maxillary first premolars, bifurcation is generally present 40% of the time and the mean root trunk length is 8 mm on both mesial and distal aspects, a feature that further complicates access to the furcation involvement with respect to these teeth (Joseph, 1996). The variations in the normal anatomy with regard to furcations of different teeth are listed in *Table 1*.

### *Influence of investigator experience*

Investigator experience in various furcation measurements influences the accuracy and reproducibility of the diagnostic performance. Moriarty *et al.* (1988) investigated inter-examiner reliability of furcation measurements using a TPS (true pressure-sensitive) probe, and reported that the HPD measurements were not consistently recordable, and that the reproducibility of the facial and lingual furcation sites decreased with an increase in probing pocket depth and an increased degree of root separation. Greatz *et al.* (2014) showed that operator experience in interpretation of radiographs enhances the predictability of radiographic measurements and therefore the right diagnosis. Hence, to avoid investigator bias, the intra- and inter-examiner should be calibrated for the grade of agreement using the weighted kappa coefficient for open flap surgery, which is considered a gold standard for probing and radiographs.

### *Influence of diagnostic methods*

Furcation defects can be detected and measured using various clinical and radiographic techniques as discussed below:

## Clinical methods of furcation measurements
### *Furcation probing*

Traditionally, furcation defects have been measured with the help of probes like the straight periodontal probe (a variant of which is the TPS probe), automated probes, such as the Florida probe with disc attachment, and with certain other probes specially designed for furcations called furcation probes, such as the Nabers, ZA2, ZA3, HO2, NS2, NP2C and ACE probes (*Figure 1*). Using these probes, various classification systems have been proposed that help to arrive at a fairly accurate diagnosis (*Table 2*). However, there is no one classification system that is accepted and followed universally.

**Table 1.** Significance of various anatomic variables of different teeth.

| Tooth | Cross-section of different roots | Incidence of different root trunk types | Incidence and depth of concavity | Root trunk length | Furcation entrance diameter |
|---|---|---|---|---|---|
| **Maxillary molars** | Mesio-buccal: ovoid, elongated in bucco-palatal direction<br>Disto-buccal: circular<br>Palatal: circular, wider in mesio-distal dimension | Type A: 34.9%<br>Type B: 61.8%<br>Type C: 3.3% | Mesio-buccal: 94% and 0.3 mm<br>Disto-buccal: 31% and 0.1 mm<br>Palatal: 17% and 0.1 mm | Mesial: 3mm<br>Distal: 3.5mm<br>Palatal: 5mm | Buccal: 0.5 to 1.5 mm<br>Mesial: 0.5 to 2 mm<br>Distal: 0.5 to 2 mm |
| **Mandibular molars** | Mesial: hour-glass, wider in bucco-lingual direction<br>Distal: circular | Type A: 62.5%<br>Type B: 37.5%<br>Type C: 0% | Mesial:100% and 0.7 mm<br>Distal: 99% and 0.5 mm | Buccal: >3 mm<br>Lingual: >4 mm | Buccal: <0.75 mm<br>Lingual: >0.75 mm |

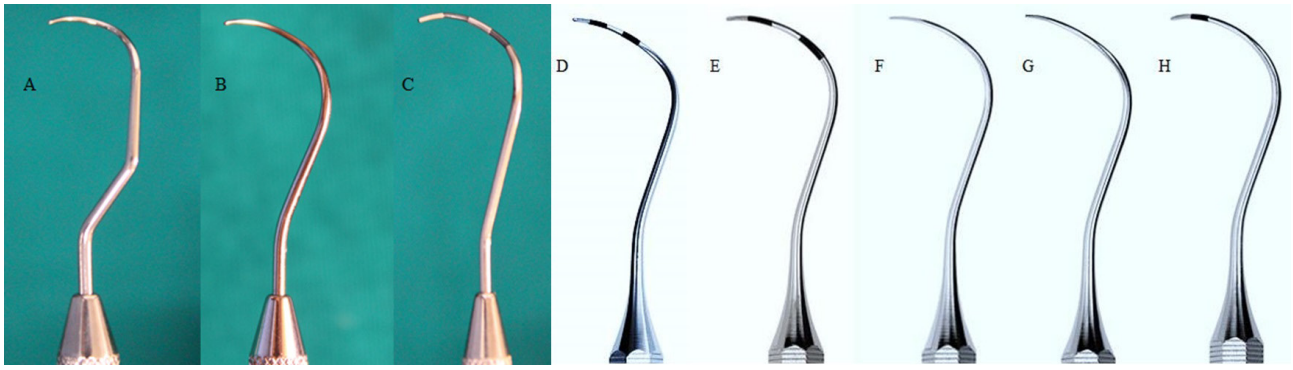


***Figure 1. Types of furcation probes: A) Nabers 1N, with smooth non-calibrated surface, and sharper, more defined curves/angles used for measuring mesial and distal furcations on maxillary molars; B) Nabers 2N, with smooth non-calibrated surface, has a shallower curve at the working end and accesses all buccal and lingual furcations; C) Nabers Q2N, color-coded variant of the 2N with color coding at 3, 6, 9 and 12 mm; D) ZA2 probe, with a diameter of 0.5 mm and graduations at 2, 4, 6 and 8 mm; E) ZA3 probe, with a diameter of 0.5 mm and graduations at 3, 6, 9 and 12 mm; F) HO2 probe is non-graduated and has a diameter of 0.4 mm; G) NS2 probe is non-graduated and has a diameter of 0.5 mm; H) NP2C probe has a diameter of 0.5mm and graduations at 3-5 mm.***

To measure the depth of furcation involvement, a straight probe, like the UNC-15 probe with 1 mm markings, is inserted into the periodontal pocket along the root surface to locate the initial fluting of the furcation. Once located, the distance from the gingival margin to the opening of the furcation is noted. The probe is then advanced apically until resistance is felt and the distance from the gingival margin to the vertical depth of probing is noted. The VPD of the furcation is recorded to the nearest millimeter as the difference between the two values. Similarly, the HPD of the furcation defect can be determined by measuring the horizontal extent of probe penetration into the furcation (Mealey *et al*., 1994). To detect furcation involvement with a furcation probe, the tip of the probe is moved towards the presumed location of the furcation and then curved into the furcation area. For the mesial surfaces of maxillary molars this is best done from a palatal direction, as the mesial furcation is located palatal to the midpoint of the mesial surface. The distal furcation of maxillary molars is located more towards the midline, and may be detected from a buccal or palatal approach (Lindhe *et al*., 2008).

The use of probes bears similarity to the difficulties encountered when the clinician measures the periodontal pocket, where probe penetration and probe tip position are affected by force, tip diameter, angulation, and tissue quality variability, especially while probing a furcation defect with inflammation (Freed *et al*., 1983; Durwin *et al*., 1985; Anderson *et al*., 1991). Further, reading error may result due to interference from calculus on the tooth/root surface, presence of an overhanging restoration or crown contours (Ramachandra *et al*., 2009). These limiting factors in turn affect the reliability and reproducibility of the measurements. The type of probe used is another factor affecting the recording of accurate values, as shown in a study comparing Nabers probes with the TPS probe, the results of which showed that the TPS probe underestimated furcation degrees significantly (Kim *et al*., 1996).

**Table 2.** Classifications proposed for furcation involvement.

| | |
|---|---|
| 1. Glickman classification (1953) | Grade I. Pocket formation into the furcation, but intact interradicular bone.<br>Grade II. Loss of interradicular bone and pocket formation but not extending through to the opposite side.<br>Grade III. Through-and-through lesion.<br>Grade IV. Through-and-through lesion with gingival recession, leading to a clearly visible furcation area. |
| 2. Goldman *et al.* classification (1958) | Grade I. Incipient.<br>Grade II. Cul-de-sac.<br>Grade III. Through-and-through. |
| 3. Staffileno's classification (1969) | Based on surface location, number of bony walls, degree of furcation exposure, as follows:<br>Class I. Furcations with a soft tissue lesion extending to furcal level but with minor degree of osseous destruction.<br>Class II. Furcations with a soft tissue lesion and variable degree of osseous destruction but not a through-and-through communication through the furca.<br>Class II F. Furcations with osseous destruction from facial aspect only.<br>Class II L. Furcations with osseous destruction from lingual aspect only.<br>Class II M. Furcations with osseous destruction from mesial aspect only.<br>Class II D. Furcations with osseous destruction from distal aspect only.<br>Class III. Furcations with osseous destruction that present with through-and-through communication from buccal to lingual aspect or mesial to distal aspect. |

Table 2 continued overleaf...

...Table 2 continued

| | |
|---|---|
| 4. Easley and Drennan (1969) | Class I. Incipient involvement, fluting coronal to furcation entrance is involved, but there is no horizontal component to the furca.<br>Class II. Divided further into Types 1 and 2<br>Type 1. A definite horizontal loss of attachment into the furcation, but pattern of bone loss remains horizontal.<br>Type 2. There is a buccal or lingual bony ledge and a definite vertical component to the furcation.<br>Class III. Through-and-through loss of attachment into the furcation, and the pattern is horizontal in Type 1 and vertical in Type 2. |
| 5. Hamp *et al.* (1975) | Degree I. Horizontal loss of periodontal tissue support not exceeding one third of the width of the tooth.<br>Degree II. Horizontal loss of periodontal support exceeding one third of the width of the tooth, but not encompassing the total width of the furcation area.<br>Degree III. Horizontal through-and-through destruction of the periodontal tissue in the furcation. |
| 6. Rosenberg (1978) | *Horizontal*<br>Degree I. When the result of probing is not greater than 4 mm.<br>Degree II. When probing shows a value greater than 4 mm (i.e., the bifurcation lesion has already passed the center of the trifurcation).<br>Degree III. Two or three furcations classified as degree II are found.<br>*Vertical*<br>Shallow. Slight lateral extension of an interradicular defect, from the center of the trifurcation in a horizontal direction, toward one or both adjacent furcations.<br>Deep. Internal furcation involvement denotes the greater lateral extension of the interradicular defect into but not penetrating the adjacent furcation. |
| 7. Ramfjord & Ash (1979) | Class I. Beginning involvement. Tissue destruction <2 mm (1/3 of tooth width) into the furcation.<br>Class II. Cul-de-sac, tissue destruction >2 mm (>1/3 of tooth width), but not through-and-through.<br>Class III. Through-and-through involvement. |
| 8. Goldman and Cohen (1980) | Degree I. Involves furcation entrance.<br>Degree II. Involvement extends under the roof of furcation but not through-and-through.<br>Degree III. Through-and-through involvement. |
| 9. Ricchetti (1982) | Class I. 1 mm of horizontal measurement; the root furrow.<br>Class Ia. 1–2 mm of horizontal invasion; earliest damage.<br>Class II. 2–4 mm of horizontal invasion.<br>Class IIa. 4–6 mm of horizontal invasion.<br>Class III. >6 mm of horizontal invasion. |
| 10. Tal and Lemmer (1982) | The degree of severity of the furcation defects affecting each molar is assigned to one of four groups designated 1, 2, 3 and 4, referred to as furcation involvement index (FII) scores.<br>Furcal rating 1. Depth of the furcation is 0 mm.<br>Furcal rating 2. Depth of the furcation is 1 to 2 mm.<br>Furcal rating 3. Depth of the furcation is 3 mm.<br>Furcal rating 4. Depth of the furcation is 4 mm or more. |
| 11. Tarnow & Fletcher (1984) | Each grade of furcation is further subdivided into three subgroups, based on the degree of vertical involvement.<br>Subclass A. 0–3 mm.<br>Subclass B. 4–6 mm.<br>Subclass C. >7 mm. |

Table 2 continued overleaf...

...Table 2 continued

| | |
|---|---|
| 12. Eskow and Kapin (1984) | Furcation involvement is classified as grade I subclasses A, B, and C. Sub-classification to classifications is based on the degree of vertical involvement and includes:<br>Subclass A. Vertical destruction up to one third of total interradicular height.<br>Subclass B. Vertical destruction reaching two-thirds of the interradicular height.<br>Subclass C. Vertical destruction beyond apical third of interradicular height. |
| 13. Fedi (1985) | Combined Glickman and Hamp classifications:<br>Grades are same as Glickman's grades I through IV, but grade II is subdivided into degrees I and II.<br>Degree I. The furcation bone loss possesses a vertical component of >1 but <3 mm<br>Degree II. The furcation bone loss possesses a vertical component of >3 mm, but still does not communicate through-and-through. |
| 14. Grant *et al.* (1988) | Class I. Involvement of the flute only.<br>Class II. Involvement partially under the roof or dome.<br>Class III. Through-and-through loss of furcation bone and attachment. |
| 15. Basaraba (1990) | Class I. Initial/incipient furcation involvement.<br>Class II. Partial/patent furcation involvement.<br>Class III. Patent furcation involvement that communicates with 2nd or 3rd furcation opening; *i.e.* communicating furcation involvement. |
| 16. Carnevale *et al.* (1997) | Modified Hamp *et al.* (1975) classification wherein the horizontal depth of furcation involvement is expressed in terms of 3 mm instead of thirds. |
| 17. Nevins and Capetta (1998) | Class I. Incipient or early loss of attachment.<br>Class II. A deeper invasion and loss of attachment that does not extend to a complete invasion.<br>Class III. Complete loss of periodontium extending from buccal surface to lingual surface.<br>Diagnosed radiographically and clinically. |
| 18. Hou *et al.* (1998) | Classification based on root trunk length and horizontal and vertical bone loss. Types of root trunk:<br>Type A. Furcation involving cervical third of root length.<br>Type B. Furcation involving cervical third and cervical two thirds of root length.<br>Type C. Furcation involving cervical two thirds of root length.<br>The different classes of furcation are:<br>Class I. Horizontal loss of periodontal tissue support <3 mm.<br>Class II. Horizontal loss of support >3 mm, but does not encompass the total width of the furcation area.<br>Class III. Horizontal " through-and-through" loss of periodontal tissue in the furcation.<br>Subclasses of furcation involvement relate to alveolar bone loss from the furcation roof apically to the root apex by radiographic assessment of the periapical view.<br>Sub-class 'a'. Suprabony defect.<br>Sub-class 'b'. Infrabony defect.<br>Classification of furcation:<br>AI, AII, AIII. Type A root trunks with class I, class II and class III furcations.<br>BI, BII, BIII. Type B root trunks with class I, class II and class III furcations.<br>CI, CII, CIII. Type C root trunks with class I, class II and class III furcations. |
| 19. Glossary of periodontal terms (2001) | Class I. Minimal but notable bone loss in furcation.<br>Class II. Variable degree of bone destruction but not extending completely through furcation.<br>Class III. Bone resorption extending completely through furcation. |
| 20. Walter *et al.* (2009) | Modification of the Hamp *et al.* classification, wherein degree II is divided into degrees II and II–III.<br>Degree II. Horizontal loss of support >3 mm, but no more than 6 mm.<br>Degree II–III. Horizontal loss of support >6 mm, but no detectable '' through-and-through'' destruction. |

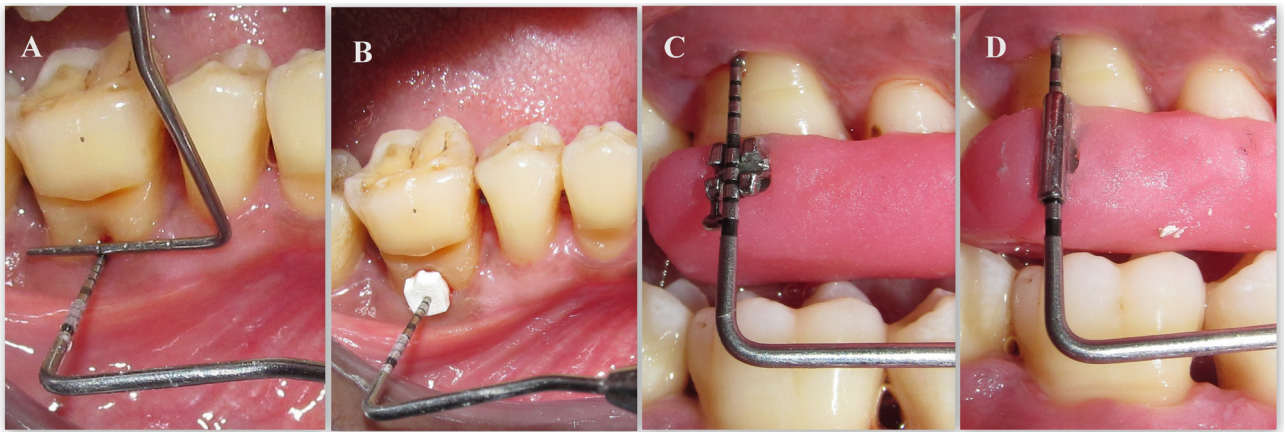


***Figure 2. Clinical furcation measurement techniques: A) Furcation measurement using intersection of two periodontal probes; B) Rubber stop placed on a periodontal probe acting as a reference point for depth of penetration; C) Stent with an orthodontic bracket acting as a reference point both for probe penetration and measurement of depth of furcation involvement; D) Stent with an orthodontic molar tube acting as a reference point both for probe penetration and measurement of depth of furcation involvement.***

To measure the depth of furcation involvement, a straight probe, like the UNC-15 probe with 1 mm markings, is inserted into the periodontal pocket along the root surface to locate the initial fluting of the furcation. Once located, the distance from the gingival margin to the opening of the furcation is noted. The probe is then advanced apically until resistance is felt and the distance from the gingival margin to the vertical depth of probing is noted. The VPD of the furcation is recorded to the nearest millimeter as the difference between the two values. Similarly, the HPD of the furcation defect can be determined by measuring the horizontal extent of probe penetration into the furcation (Mealey *et al.*, 1994). To detect furcation involvement with a furcation probe, the tip of the probe is moved towards the presumed location of the furcation and then curved into the furcation area. For the mesial surfaces of maxillary molars this is best done from a palatal direction, as the mesial furcation is located palatal to the midpoint of the mesial surface. The distal furcation of maxillary molars is located more towards the midline, and may be detected from a buccal or palatal approach (Lindhe *et al.*, 2008).

The use of probes bears similarity to the difficulties encountered when the clinician measures the periodontal pocket, where probe penetration and probe tip position are affected by force, tip diameter, angulation, and tissue quality variability, especially while probing a furcation defect with inflammation (Freed *et al.*, 1983; Durwin *et al.*, 1985; Anderson *et al.*, 1991). Further, reading error may result due to interference from calculus on the tooth/root surface, presence of an overhanging restoration or crown contours (Ramachandra *et al.*, 2009). These limiting factors in turn affect the reliability and reproducibility of the measurements. The type of probe used is another factor affecting the recording of accurate values, as shown in a study comparing Nabers probes with the TPS probe, the results of which showed that the TPS probe underestimated furcation degrees significantly (Kim *et al.*, 1996).

Various reference points have been routinely employed to measure the HPD of furcation defect using straight probes. One such approach uses two probes (*Figure 2A*), wherein the first periodontal probe is inserted into the furcation until its horizontal depth is reached, followed by placement of a second probe held against the furcation such that the point of intersection of the two probes indicates the depth of the horizontal component of the defect (Reddy and Jeffcoat, 2000). The disadvantage with this technique is that holding the reference probe at exactly the same point and the point of probe intersection is not easily reproducible, especially in the posterior regions of the mouth (Laxman *et al.*, 2009; Black *et al.*, 1994). Likewise, polyvinyl chloride (PVC) stops can provide fairly accurate defect depth values when positioned on the probe and inserted into the furcation in such a way that the stop would rest at the root surface concavity at the furcation entrance (*Figure 2B*). However, with this method the coronal position of the gingiva in some cases may obstruct the visual control (Zappa *et al.*, 1993). Further, the initial fluting of the furcation entrance can be used as a fixed reference point from which the VPD and HPD measurements can be made (Mealey *et al.*, 1994): while this can be done to standardize the reference point, the presence of the soft tissue covering the furcation fluting interferes with visualization and it is a subjective method, limiting its use (Zappa *et al.*, 1993; Mealey *et al.*, 1994). Also, an imaginary plane can be drawn tangential to the external root surface as a reference from which measurements can be taken (Pontoriero and Lindhe, 1995). This technique too has a lower reliability when used for measurements of distolingual furcations due to the impossibility of direct vision and difficulties probing this remote location (Pontoriero and Lindhe, 1995; Cortellini *et al.*, 1993; Eickholz and Staehle, 1994). Alternatively, custom stents can be used as fixed reference guides to measure the depth of probe penetration, which has been found to be a more promising method (Laxman *et al.*, 2009; Suh *et al.*, 2002).

Suh *et al.* (2002) fabricated stents that had vertical grooves made on the buccal and lingual extensions to the stent, which guided accurate probe placement. Similarly, Laxman *et al.* (2009) designed a stent that had a hole corresponding to the furcation entrance on the buccal plate of the stent which extended to the attached gingiva; the outer surface of the hole served as a reference point for measurements.

For vertical measurements, orthodontic brackets and molar tubes can be fixed to the acrylic stents such that the upper or lower margins serve as reference points for recordings. Further, such stents would permit consistently accurate and reproducible slots for placement of the probes, as shown in *Figure 2C* and *2D*.

These studies confirm that the various clinical methods of furcation evaluation by probing provide only an arbitrary clue to the severity of furcation involvement (Darby *et al.*, 2014), that the chances of misinterpreting the values remain high because of the inherent limitations of probes, and that specialized furcation probes have proved to be better than straight probes. With respect to the referencing system, custom stents have been shown to be fairly precise and reliable in monitoring the real time changes in the HPD of the furcation.

### *Furcation bone sounding*

This method is a trans-gingival probing technique that is used, under anesthesia, to plot the morphological outline of the furcation defect (Laxman *et al.*, 2009; Black *et al.*, 1994). Various studies have shown that furcation bone sounding measurements are very close to open bone measurements. The average difference between furcation bone sounding measurements and surgical measurements is 0.4 to 0.5 mm (Mealey *et al.*, 1994). Additionally, in another study, Suh *et al.* (2002) reported vertical and horizontal open bone levels to be 0.9 to 1.1 mm deeper than probing bone levels.

Because furcation bone sounding gives consistent measurements that are equivalent to open bone measurements, and in addition avoids a re-entry procedure, it can be considered as a good substitute for open bone measurements.

### *Surgical measurements*

Various methods have been proposed for direct measurements following surgical exposure of the furcation defect, which gives the most accurate values.

### *Open bone measurements with probes*

Following the reflection of the facial and lingual flaps, and the debridement of the defect area, measurements of the vertical attachment level (VAL) can be made to the nearest millimeter with a UNC-15 probe from the furcation fluting to the base of the defect. Similarly, horizontal attachment level (HAL) can be measured with a furcation probe from the furcation fluting to the horizontal extent of the defect. As the measurements of the defect are carried out directly, this method is considered to be the gold standard against which other methods are compared (Mealey *et al.*, 1994).

Comparison of clinical measurements using the Nabers probe, TPS probe and UNC-15 probe with intra-surgical measurements showed that for all probes, a statistically significantly smaller measurement error was observed in buccal and lingual sites than in mesial and distal furcations, and no significant differences were noted between pre- and intra-surgical HAL using the Nabers probe (Eickholz and Kim, 1998). Similarly, other studies have reported no significant difference between furcation degrees as assessed pre-surgically and intra-surgically with the Nabers probe and concluded that clinical furcation diagnosis provides reliable and valid information for prognosis and therapy of molars exhibiting furcation involvement (Eickholz, 1995; Eickholz and Staehle, 1994). However, controversial results have also been reported in others studies where clinical probing values varied significantly from surgical furcation measurements (Zappa *et al.*, 1993; Graetz *et al.*, 2014).

### *Impression method*

Furcation measurements can also be obtained by taking an impression of the furcation area, as reported by Zappa *et al.* (1993). In this method rubber base impression material is injected into the furcation defect with a syringe, following reflection of full thickness buccal and lingual flaps to expose the furcation area. The impression is then used to calculate the dimensions in terms of the volume of the furcation defect using a Leitz stereomicroscope. This equipment enables three-dimensional visualization of the sample and overlaps macrophotography for recording and examining solid samples with complex surface topography. Zappa *et al.* (1993) reported a mean absolute error for surgical probing measurements as 0.07 mm, and for the impression method as 0.02 mm. However, there are no subsequent studies to validate this. Further, this method is technically demanding, as it requires precisely injecting the impression material into narrow furcations, and limiting the flow of the material to within the furcation area. Also, the distortion caused while drawing out the set impression can be a challenge. Adding to this is the calculation of the volume of the impression material, for which the authors have suggested employing a stereomicroscope, the use of which requires prior training and sound knowledge of the technicalities, which further limits the feasibility of its practical application.

### *Mathematical algorithm*

Calculation of the volume of a furcation defect can also be carried out using a mathematical algorithm following the reflection of facial and lingual flaps and direct linear measurements of the defect morphology, as given by Bowers *et al.* (2003). The algorithm used was:

$$\frac{(\text{ROF-BOD})^2\,(\text{RDCB})\,(\text{HBOD-F})}{2(\text{ROF-COB})}$$

ROF-BOD denotes roof of furcation to base of defect, RDCB denotes root divergence at crest of bone, HBOD-F denotes horizontal extent (base) of defect at level of crest of bone, ROF-COB denotes roof of furcation to crest of bone at furcation entrance. Even though this method appears promising, there are no further studies to validate it.

From evidence in the literature, it can be concluded that the clinical method of bone sounding and clinical probing with furcation probes such as the Nabers probe can be simple, practical and reliable approaches for assessing the HAL and VAL dimensions of furcation involvement, without the need for surgical exposure of the furcation defect. When comparing furcation probing clinically and intra-surgically, it has been shown that clinical measurements underestimate the values compared to intra-surgical measurements because clinical probing assesses only horizontal tissue attachment, whereas intra-surgical probing assesses up to the bone level, which can be simulated with furcation bone sounding.

### *Radiographic diagnosis*

Traditionally, radiographic assessments in conjunction with clinical probing have been the chief diagnostic methods for detecting and characterizing furcation involvement. If radiographs are taken properly and processed, they can be used as a valuable supplementary tool in periodontal disease diagnosis to reveal the morphologic characteristics of alveolar bone (Gusmao *et al.*, 2014). Conventional radiographs are intra-oral peri-apical (IOPA) radiograph and orthopantomograms (OPG).

Conventional radiography is a 2-dimensional interpretation of a 3-dimensional object and is a mainstay in periodontal diagnosis because of its user-friendly image acquisition, cost effectiveness and ready accessibility. An OPG showing furcation involvement is shown in *Figure 3A*. Furcation involvement has been reported to be detected more frequently by conventional periapical radiographs compared to clinical measurements. The incidence of detection by IOPA was 22% in maxillary molars and 8% in mandibular molars, whereas for clinical examination it was 3% and 9% in maxillary and mandibular molars respectively (Ross and Thompson, 1980). Further, furcation involvement can be correctly identified with accuracy of 40.4% with panoramic radiographs, 43.7% in intra-oral dental radiographs and 54% with clinical probing alone (Topoll *et al.*, 1988).

The use of radiographs to diagnose proximal maxillary molar furcation involvement has always been a matter of debate. Hardekopf *et al.* (1987) proposed the term "furcation arrow" for a "subtle shadow" in the radiographs of maxillary first molars over the mesial root. The sensitivity of the furcation arrow image as a diagnostic marker was shown to be just 38.7% (Topoll *et al.*, 1988). It can be extrapolated that radiographs are more reliable in assessing furcation involvement in maxillary molars than by clinical examination, which is the opposite compared to the mandible. In addition, it can be inferred that the precision of conventional radiographs improves as the severity of the furcation involvement increases (Gusmao *et al.,* 2014). Thus, the shortcomings in traditional radiographs include an inability to detect initial alveolar bone changes, leading to variability in the perception of furcation involvement, distortions and variability in image quality due to processing errors, and overlapping of structures due to their 2-dimensional nature, further limiting the reliability in diagnosis (Jeffcoat, 1992; Furhmann *et al.*, 1997; Young *et al.*, 1996).

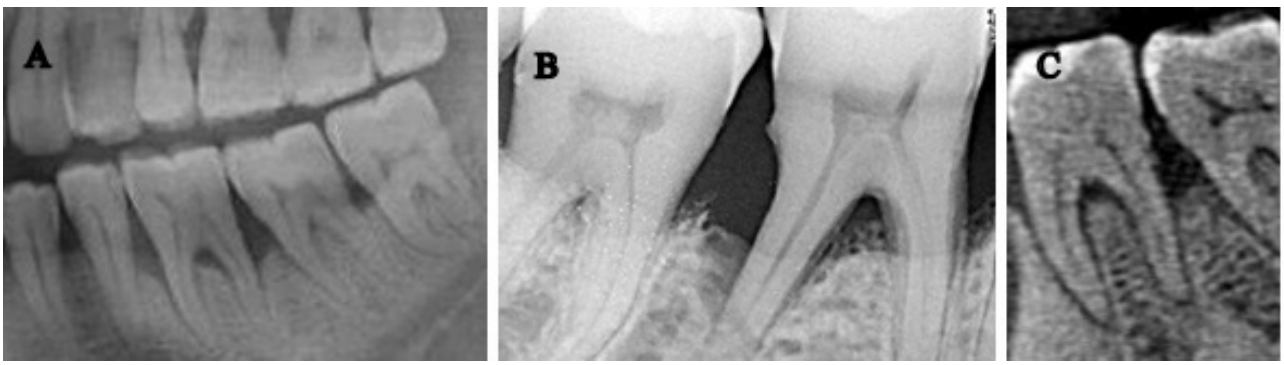


***Figure 3. Radiographic techniques of furcation measurement: A) A section of an orthopantomograms (OPG) showing furcation involvement with respect to a mandibular molar; B) A radiovisiograph (RVG) showing furcation involvement with respect to a mandibular molar; C) A cone beam computed tomograph (CBCT) of a mandibular molar with furcation involvement.***

### *Digital radiographs*

Radiovisiography (RVG) uses a digital detector to capture the radiographic image, which eliminates the chemical processing, reduces radiation exposure and offers tools for precise measurements (Mouyen and Benz, 1989; Bragger *et al*., 1988). An RVG showing furcation involvement is shown in *Figure 3B*. Radiographic evidence of interproximal bone loss can be considered as a fairly reliable indicator of possible initial interradicular bone loss. Grover, *et al.* (2014) reported a common association of early interradicular bone loss with an interproximal bone loss of around 4 mm. Comparison of images of digital intraoral radiographs (IOR) with cone beam computed tomography has shown that over- and underestimations of furcation defects are both 50% for the digital IOR, with a mean of 0.56 mm for the overestimations and 0.55 mm for the underestimations. Also, there is a 49% chance that a furcation defect may be left undetected in a digital IOR (Vandenberghe *et al*., 2008). Another study (Young *et al*., 1996), reported large underestimation of furcation lesions by 67% using RVG, showing that considerable variation may result in either underestimation or overestimation of bone loss.

### *Subtraction radiography*

This technique permits visualization of change in image densities at different time intervals and allows detection of mineral changes as little as 5%. Subtracted images of furcation lesions, when compared to physical measurements of the area and volume of interest, showed an overall 67% underestimation of the bone loss; however, in deeper lesions, the underestimation was only about 4%, which could be due to structured noise of the image produced by inadequate alignment of the radiographs (Young *et al*., 1996). At present, this imaging system is not sufficiently accurate to determine furcation bone loss, and it involves time and effort, which could limit its usefulness as a diagnostic tool (Young *et al*., 1996). However, computer-assisted densitometric image analysis (CADIA), has shown favorable results over digital subtraction radiography when used to study alveolar bone density changes in furcations (Bragger *et al*., 1988; Bragger *et al*., 1989).

### *Digital image ratio*

This method is based on computation of the mass ratio of digitalized radiographs. It directly shows changes in alveolar bone mass, and thus avoids some of the drawbacks of quantitative digital subtraction radiography. Further, it takes the advantage of low X-ray machine voltage [50 kilovolts (Kv)] at short exposure times, making it possible to study several sites on the same patient with a low radiation dose (Jean *et al*., 1996a; 1996b). However, there are no subsequent studies to further substantiate this method as being effective for accurate measurements of furcation involvement.

### *Computed tomography (CT)*

Computed tomography is a sophisticated X-ray procedure used to view cross-sectional images of the furcation without superimpositions. It uses X-rays emitted from a fan-shaped X-ray source to produce sectional images of the area of interest that are captured by crystal or gas detectors, then the intensity of the X-ray beam emerging from the patient is measured and converted into digital data, which are further converted into a gray scale representing different tissue densities, allowing three dimensional visual images to be generated. It has been reported that CT can identify 100% of HAL and VAL furcation involvement (Furhmann *et al*., 1997). Further, another study (Mengel *et al*., 2005), showed the possibility of measurements of all furcations in three planes and a clear-cut differentiation between Class I, II, and III furcations; these measurements of the radiographic images, when compared to histologic sections, have a mean deviation of $0.16 \pm 0.10$ mm.

Similarly, a recent study (Laky *et al*., 2013) compared clinical probing using a Nabers probe with CT scans, and reported that the degree of furcation involvement on clinical findings was confirmed by CT in 56% of the sites, whereas clinically 21% were overestimated and 23% underestimated. Only 32% of Class III furcations detected by CT scan were detected clinically. However, despite the attractive features, it also has certain drawbacks: firstly, it has a high radiation dose, high cost, unfavorable cost-benefit ratio, and low resolution (Schuller *et al*., 1992; Vandenberghe *et al*., 2007), and secondly, CT scans can be degraded in patients with apically extended fixed restorations and metallic fillings, limiting the CT image quality (Vandenberghe *et al*., 2007).

### *Cone beam CT (CBCT)*

CBCT is also known as digital volume tomography (DVT). The working principle of CBCT is similar to CT, except that it employs a cone-shaped X-ray beam instead of the flat fan-shaped beam used in CT, which helps to record the patient volume in a single rotation, thereby lowering the radiation dose and saving on cost. A CBCT image showing a Class III furcation involvement is shown in *Figure 3C*. Various authors (Mengel *et al*., 2005; Vandenberghe *et al*., 2007) have reported that furcation involvement can be differentiated into Class I, II and III furcations clearly with both CT and CBCT. However, in terms of image quality the CBCT scans were superior to the CT scans, with the periodontal ligament space in particular being represented exactly in all three planes, and that CBCT resolution can be as small as 0.2 mm, as compared to 0.5-1 mm for CT. In comparison with intraoral radiographs, studies have shown a significant advantage of CBCT owing to its high resolution and three dimensional capabilities to assess buccal and lingual surfaces, which makes it a very reliable tool for detecting incipient furcation involvement (Umetsubo *et al.,* 2014; de Faria Vasconcelos *et al.,* 2012; Misch *et al.,* 2006).

When clinical probing measurements versus CBCT were compared to diagnose furcation involvement, it was shown that clinical probing either over- or underestimated the actual extent of furcation involvement. This was especially so in the case of Class I furcation involvement, where it was commonly overestimated (Darby *et al.,* 2014). Similarly, surgical and CBCT measurements have been shown to be equivalent about 82-84% of the time, and very rarely over- and underestimated, which makes CBCT measurements a reliable alternative to surgical measurements (Qiao *et al.*, 2014; Walter *et al.*, 2009; Umetsubo *et al.,* 2012).

With the advent of digital technology, the diagnostic efficacy of radiographs are improved. Even though, CBCT is more accurate compared to other techniques in diagnosing furcation involvement, the evidence is not compelling enough to recommend a CBCT scan to diagnose furcation involvement in view of its high radiation levels.

We should understand the strengths and weaknesses of diagnostic imaging, and weigh the costs and benefits, with due consideration to the amount of radiation exposure, before prescribing it (Darby *et al.,* 2014; Walter *et al.,* 2012). It has also been emphasized that radiographs are not superior to clinical findings and are only ancillary tools to diagnosis (Payot *et al.,* 1987; Waerhaug, 1980). These points imply that clinical diagnosis should be combined with radiographic findings for improving the precision in diagnosis (Gusmao et al., 2014).

## *New frontiers*

The quest for accurate and reliable diagnosis of furcation defects has led to the evolution of newer diagnostic tools, which can improve our ability to diagnose more precisely and accurately.

## *Natural frequency analysis*

Natural frequency is the dynamic response of a vibrating object related to the material properties and boundary conditions of the structure. This method requires the placement of an electronic transducer on the area of interest, and the passing of a low-voltage current through the transducer. The resistance to the vibration of the transducer in the surrounding bone is digitally registered. Originally, it was used for evaluating stability of natural teeth and implants. It has recently been shown to have higher identification rate of furcation involvement than traditional diagnostic methods, and it has been suggested that it be combined with traditional methods to overcome inaccuracies in measurements (Wang *et al.*, 2009). Similar to the digital image ratio study, there have been no subsequent studies carried out to validate its usefulness in measurement of furcation involvement.

## *Ultrasonography*

Ultrasonography is a non-invasive investigation technique that uses a very high frequency (7.5-20 MHz) pulsed ultrasound beam to produce high-resolution images of structures. As the ultrasound waves travel through the tissues, some of them are reflected back by tissue interfaces to produce echoes that are picked up and converted into electrical signals, which in turn are converted into black, white and grey images and are displayed on a computer screen. Using ultrasound in furcation diagnosis, a study by Chandrashekhar *et al.* (2014) showed that it was 76% accurate as compared to surgical measurements (clinical measurements showed 70% accuracy). Further studies, however, are required to substantiate its effectiveness in furcation measurements.

## *Optical coherence tomography (OCT)*

The optical coherence tomography system uses a white light that is able to penetrate into the tissues without biologically harmful effects. Differences in the reflection of the light are used to generate a signal that corresponds to the morphology and composition of the underlying tissues. It has been reported to be a new diagnostic tool and as a sensitive method for detecting periodontal defects (Otis *et al.*, 2000). Colston *et al.* (2000) reported that OCT can be used for precise measurement of both volumes and distances, and used to interpret both soft and hard tissues. This system is alleged to be able to provide both 2- and 3-dimensioal intraoral images with good lateral and axial optical resolution and good microstructural detail. Also, using this new technology, visual recordings of periodontal tissue contour, sulcular depth and connective tissue attachment are possible. However, presently there are no studies conducted to assess the efficacy of OCT in furcation measurements.

## *Fiberscopes*

Fiberscopes are based on fiberoptic endoscopy technology, and they are minimally invasive miniature periodontal endoscopes with which a magnification of 24-48X can be achieved. Fiberscopes, when applied clinically as reported by Ozawa *et al.* (1999), allowed visualization of the fields involved in periodontal disease. When inserted through a fistula, the extent of bone loss, the soft tissues and root surfaces involved in periodontal lesions could be differentiated. It can also be applied to furcation diagnosis; however, to date there are no studies conducted to assess the efficacy of fiberscopes in furcation measurements.

## *Conclusion*

In spite of the availability of an array of diagnostic aids, accurate measurement of the degree of furcation involvement in periodontal disease still remains a potential challenge to the practitioner. Clinical probing provides a fairly accurate picture of the extent of destruction within the furcation; it is simple, practical and the least expensive compared to all other methods. Bone sounding and advanced radiography seem to provide values that are closest to the actual existing bone levels. Modern digital radiography

like CBCT have been shown to be very reliable and promising gauges; however, the high cost and lack of availability limits it primarily to use as a research tool, and its large scale clinical usage is still far from a reality in diagnosing furcation involvement. In addition, other parameters, such as the diagnostic experience of the examiner, tooth anatomy and the type of diagnostic aid, adds to the complexity in diagnosing furcation involvement. Hence, it can be concluded at this time that the present furcation diagnostic techniques do not have sufficient long-term controlled documentation to substantiate the diagnostic advantage of one technique over the other, and that no single method is totally accurate and reliable. A combined assessment with one or more techniques may prove to be a better guide.

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# Clinical and Radiographic Evaluation of the Periodontium with Biologic Width Invasion by Overextending Restoration Margins - A Pilot Study

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**Abstract**

**Aim:** The aim of this study was to correlate radiographic examination with the clinical periodontal condition in cases of biologic width invasion by overextending restoration margins in restored premolars and molars.

**Materials and methods:** The present pilot study involved nine people (mean age 32 years) with biologic width invasion by 21 surfaces overextending restoration margins in restored premolars and molars. Radiographs were made in a standardized unit using the interproximal technique and were evaluated by a single calibrated investigator. The clinical periodontal parameters were analyzed with the use of a computerized periodontal probe. Exploratory analysis and Spearman's correlation were used to perform statistical analyses (SPSS, $p < 0.05$).

**Results:** The most prevalent teeth with biologic width invasion were second premolars and first molars. Mean plaque index was 30.76%, and bleeding on probing was 27.0%. The mesial surface was invaded in 47.6% of cases and the distal surface in 52.4%. The 21 sites with biologic width invasion were found in patients with the following periodontal status: periodontal health (11 sites), gingivitis (2 sites), mild periodontitis (7 sites) and moderate periodontitis (1 site). There was a correlation between plaque index and bleeding on probing with the horizontal component of the bone level.

**Conclusions:** There was correlation between the radiographic parameters of biologic width invasion and clinical conditions. The measure of the bone crest level correlated with the gingival recession. The horizontal component of bone defect correlated with plaque index and bleeding on probing.

*Key words: Biologic width invasion, radiography, pilot study*

## Introduction

The periodontal biologic width is defined as the dimension of the soft tissue that is attached to the portion of the tooth coronal to the crest of the alveolar bone (Tomar *et al.,* 2013; Rosenberg *et al.,* 1999). The dimension of biologic width is not constant; it depends on the location of the tooth in the alveolus, varies from tooth to tooth and from surface to surface of a specific tooth. A clinically average dimension is 3 mm from the alveolar bone crest up to the cementoenamel junction (CEJ) in healthy conditions, or up to the margins of the restoration in restored teeth. The average sulcal depth is 0.69 mm, the average length of epithelial attachment is 0.97 mm, and the average length of connective tissue attachment is 1.07 mm (Khuller and Sharma, 2009; Gargiulo *et al.*, 1961).

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These distances allow the appropriate biologic width even when the restoration margins are placed 0.5 mm within the gingival sulcus (Nugala *et al.,* 2012; Oh, 2010).

The existence of the biologic width is fundamental to the insertion of the junctional epithelium and the connective tissue fibers to teeth, and these periodontal structures should be respected during restorative procedures in order to preserve periodontal health (Jorgic-Srdjak *et al.,* 2000; Makigusa, 2009). The placement of a restoration margin seems to be of importance for periodontal health (Amiri-Jezeh *et al.,* 2006). In addition to the influence of several risk factors, the position of the restoration margin may affect the initiation and progression of periodontal diseases (Kosyfaki *et al.*, 2010).

When the restoration margin levels are being evaluated with a periodontal probe and the patient feels discomfort in the gingiva close to a restoration, it may be suggestive that the margin extends into the attachment and that a biologic width invasion has occurred (Galgali and Gontiya, 2011). The signs of invasion of the biologic width are chronic progressive gingival inflammation around the restoration, bleeding on probing, localized gingival hyperplasia, gingival recession, pocket formation, gingivitis and clinical attachment loss (Felippe *et al.,* 2003). Gingival recession is more often found in thin periodontium and periodontal pockets are commonly formed in thicker periodontium (Felippe *et al.,* 2003).

Interproximal radiographic examination can identify interproximal biologic width invasion, and bitewing radiographies are considered the ideal technique for a more accurate assessment (Shobha *et al.,* 2010). Biologic width violations can be corrected by either surgically removing bone proximal to the restoration margin or orthodontically extruding the tooth and thus moving the margin away from the bone (Felippe *et al.,* 2003; Khuller and Sharma, 2009). In such cases, the clinical crown increases and the biologic width is re-established. Then, biological dimensions for connective tissue attachment, epithelial attachment and gingival sulcus are properly sized and arranged around the tooth in order to physiologically keep the supracrestal distance [average 3 mm (Robbins, 2007; Pontoriero and Carnevale, 2001)].

The suggested physiological function of the biologic width is that of a protective barrier for the subjacent periodontal ligament and the supporting alveolar bone from the attack of a pathogenic biofilm present in the oral cavity (Bosshardt and Lang, 2005). Evidence from a recent review suggests that a breach of the biologic width may have an impact on periodontal health by affecting the homeostasis of the periodontal tissues (Schmidt *et al.,* 2013).

However, several views and/or data exist concerning the ideal dimensions of the biologic width, leading to difficulties with respect to the development of clinical recommendations (Schmidt *et al.,* 2013). The aim of this study was to correlate the radiographic examination with the clinical periodontal condition in cases of periodontium with biologic width invasion by overextending restoration margins in restored premolars and molars.

## Materials and methods

This study was approved by the Research Ethics Committee of the Federal University of Jequitinhonha and Mucuri Valleys (UFVJM; protocol #026/12). The study was conducted in accordance with the Declaration of Helsinki, 1975, revised in 2013.

The participants were diagnosed as periodontally healthy or not in accordance with the American Academy of Periodontology classification system for periodontal diseases and conditions (Armitage, 1999). They were informed about the purpose of the study, as well as benefits and risks of participating in the research. Afterward, they received and signed an informed consent form.

The inclusion criteria of this study were patients aged 18 years or more, in good general health, presenting restored posterior teeth with biologic width invasion in the mesial or distal surface, diagnosed clinically and radiographically. According to this criteria, 21 cases with biologic width invasion were selected. The participants were of both genders, with dental records in the UFVJM dental clinic.

Interproximal x-rays were used for the radiographic analysis. The radiographs were made in a single appliance with a standardized time of 0.63 ms by the technique of parallelism and with the use of a holder aid. All patients were dressed according to the standard of biosecurity. The film processing was performed with the time/temperature method (Lannucci and Jansen, 2011). This procedure was carried out by one trained researcher (TNA). The x-rays were assessed by another properly calibrated single researcher (MNPM). To improve image-viewing conditions, black masking was used in order to act as an overlay on the areas outside of the collimated exposure field.

Before the study began, the investigator (MNPM) in charge of radiographic assessments was trained and calibrated for intraexaminer repeatability. The examiner measured a set of randomly chosen radiographic sites twice, with an interval of 7 days between the measurements. The intraclass correlation coefficient was 0.98.

Because there is no consensus in the literature for biologic width invasion determination, the diagnostic method of this condition was based on a systematic review (Schmidt *et al.*, 2013). Briefly, the attachment level was measured by periodontal probing, and the evaluation of the restoration margin and alveolar bone level was made by X-rays. The cut-point to determine biologic width invasion was a distance ≤ 3 mm between the bone crest and the restoration margin (*Figure 1*).

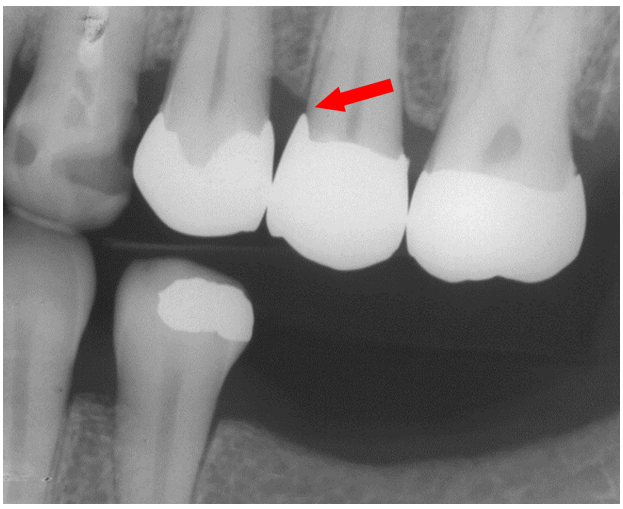

***Figure 1. Interproximal radiography of biologic width invasion by overextending margin restoration.***

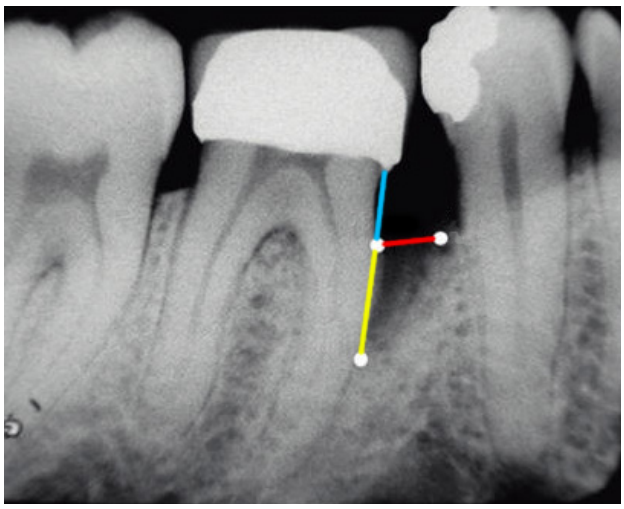

***Figure 2 (Adapted from Parashis et al., 2012). Radiographic parameters evaluated: intrabony component (yellow line), bone crest level (blue line), bone defect level (yellow + blue lines), horizontal component (red line).***

The clinical parameters analyzed were:

1. plaque index (PI; Loe, 1967)
2. bleeding on probing (BP; Mühlemann and Son, 1972)
3. probing depth (PD), determined by the distance from the gingival margin to the base of the gingival sulcus clinically detectable and measured with a computerized periodontal probe (Florida Probe®, Gainesville, FL, USA)
4. height of the gingival recession (HGR), which is the distance from the CEJ to the apical extension of the gingival margin. In cases of biologic width invasion, the more apical extension of the restoration was used as a reference
5. clinical attachment level (CAL), given by the sum of the PD with the HRG;
6. width of the gingival recession (WGR), given by the distance between the mesial and distal gingival margins of the tooth with gingival recession (on a horizontal line tangential to the CEJ)
7. keratinized tissue height (KTH), which is the distance from the gingival margin to the mucogiengival line
8. keratinized tissue thickness (KTT), measured using a digital endodontic spreader (Dentsply, Rio de Janeiro, RJ, Brazil) perpendicular to a midpoint between the gingival margin and mucogingival junction and through the soft tissue with light pressure until a hard surface was felt.

The HGR, WGR, KTH and KTT were determined with manual probes and measured in millimeters on the buccal surface. The PI and BP parameters were analyzed throughout the oral cavity and were measured with a computerized periodontal probe at six gingival sites: mesio-buccal, mid-buccal, disto-buccal, mesio-lingual, mid-lingual, and disto-lingual. The other variables were collected only in regions that had invasion of the biologic width.

In cases of intrabony defects, the following radiographic parameters were evaluated (Parashis *et al.*, 2012):

1. bone defect level (BDL), vertical distance from the CEJ to the base of the bone defect at which the periodontal ligament space appeared normal (*Figure 2,* yellow + blue lines)
2. bone crest level (BCL), vertical distance between the CEJ and the bone crest (*Figure 2,* blue line)
3. intrabony component (INTRA), defined by subtracting BDL-BCL, *i.e.*, the vertical distance from the bone crest to the base of the defect (*Figure 2,* yellow line)
4. horizontal component (HC), horizontal distance from the bone crest to the root surface in a perpendicular line to the axis of the tooth with biologic width invasion (*Figure 2,* red line).

As the present study used teeth with overextending restorations, the more apical extension of the restoration was used as a reference instead the CEJ. These measures were taken with a drypoint compass and measured in millimeters with the aid of a caliper to two decimal places, for greater precision and reliability. These measures (*Figure 2,* adapted from Parashis *et al.*, 2012) were obtained by a single researcher (MNPM), properly calibrated and trained.

The statistical analyses were conducted using the statistical package SPSS® (Statistical Package for the Social Sciences Inc, IBM, Armonk, NY, USA) version 22.0. Exploratory analysis of the data provided frequencies, averages and standard deviations. The 95% confidence interval and 5% significance level were used. The evaluation of normality of the data was checked by the Shapiro-Wilk test. Spearman's rank correlation coefficient was used to verify the association between clinical and radiographic findings.

## Results

The sample consisted of 8 women (88.8%) and 1 man (11.2%), with an average age of 32.10 ± 1.65 years (range 29 to 34 years). The teeth with higher prevalence of biologic width invasion were second premolars and first molars, followed by first premolars, and the teeth with lower prevalence were second molars (*Table 1*). The average plaque index was 30.76 ± 8.01%, and the bleeding on probing was 27.0 ± 7.0%.

In the teeth that showed biologic width invasion, the mesial surface was involved in 47.6% (n=10) and the distal surface in 52.4% (n=11) of the cases (*Table 1*). The radiographic findings are presented in *Table 2*.

The 21 sites with biologic width invasion were found in patients with the following periodontal status: periodontal health (11 sites), gingivitis (2 sites), mild periodontitis (7 sites) and moderate periodontitis (1 site). Two teeth presented with mobility class I, corresponding to 9.5% of the teeth with biologic width invasion. No teeth with biologic width invasion presented with furcation defects.

The correlation between the clinical and radiographic findings is shown in *Table 3*. There was a significant positive correlation between the plaque index and bleeding on probing with the horizontal component, as well as the height and width of the gingival recession with the bone crest level.

**Table 1.** Prevalence of biologic width invasion by tooth type and dental surface.

| Parameter | Total | |
|---|---|---|
| | N | % |
| Tooth | | |
| First pre-molar | 3 | 14.3 |
| Second pre-molar | 8 | 38.1 |
| First molar | 8 | 38.1 |
| Second molar | 2 | 9.5 |
| Surface | | |
| Mesial | 10 | 47.6 |
| Distal | 11 | 52.4 |

**Table 2.** Average of the parameters related to the sites probed (n = 21).

| Parameters related to the sites probed | Mean ± SD (mm) |
|---|---|
| Probing depth | 2.23 ± 0.18 |
| Clinical attachment level | 2.23 ± 0.18 |
| Height of gingival recession | 0.50 ± 0.18 |
| Width of gingival recession | 1.38 ± 0.52 |
| Keratinized tissue height | 4.85 ± 0.30 |
| Keratinized tissue thickness | 1.40 ± 0.16 |
| Level of bone defect | 2.81 ± 0.13 |
| Bone crest level | 1.98 ± 0.08 |
| Intrabony component | 0.83 ± 0.10 |
| Horizontal component | 1.05 ± 0.15 |

**Table 3.** Spearman rank correlation coefficient ($r_s$) of clinical and radiographic findings.

| Clinical parameters | Radiographic parameters | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | Level of bone defect | | Bone crest level | | Intrabony component | | Horizontal component | |
| | $r_s$ | *p* | $r_s$ | *p* | $r_s$ | *p* | $r_s$ | *p* |
| Tooth | 0.289 | 0.102 | -0.078 | 0.369 | 0.289 | 0.102 | -0.240 | 0.148 |
| Site | -0.182 | 0.215 | 0.103 | 0.329 | -0.333 | 0.070 | -0.356 | 0.057 |
| Plaque index | 0,150 | 0.258 | -0.065 | 0.390 | 0.267 | 0.121 | 0.555 | 0.004* |
| Bleeding on probing | 0.058 | 0.401 | 0.005 | 0.492 | 0.189 | 0.206 | 0.558 | 0.004* |
| Probing depth | 0.261 | 0.127 | 0.096 | 0.339 | 0.100 | 0.333 | 0.291 | 0.101 |
| Clinical attachment level | 0.217 | 0.172 | 0.033 | 0.444 | 0.050 | 0.414 | 0.259 | 0.128 |
| Height of gingival recession | 0.198 | 0.195 | 0.393 | 0.039* | 0.134 | 0.281 | -0.272 | 0.117 |
| Width of gingival revession | 0.134 | 0.281 | 0.426 | 0.027* | 0.032 | 0.445 | -0.327 | 0.074 |
| Keratinized tissue height | 0.166 | 0.237 | -0.096 | 0.339 | 0.336 | 0.068 | 0.176 | 0.223 |
| Keratinized tissue thickness | 0.151 | 0.257 | -0.195 | 0.198 | 0.258 | 0.130 | -0.097 | 0.337 |
| Diagnosis | -0.085 | 0.357 | 0.068 | 0.385 | 0.103 | 0.328 | 0.247 | 0.140 |

*Statistically significant correlation

## Discussion

In daily practice, overextending margins of dental restorations are a problem frequently observed (Schätzle *et al.,* 2001). Periodontal health is preserved by the correct insertion of the junctional epithelium and the connective tissue fibers to the tooth along the biologic width. There are several studies focused on the relationship between periodontal tissues (clinically assessed) and overhanging prosthetic restorations; however, there is a lack of knowledge about the relationship of clinical periodontal parameters with radiographic findings in biological width invasion in posterior tooth sites. The present research showed a correlation between the radiographic parameters of biologic width invasion and the clinical conditions, mainly the plaque index and bleeding on probing.

When the periodontium is disturbed by clinical procedures and techniques such as cavity fillings, definitive restorations, provisional restorations and dental impressions, tissues can respond with an inflammatory process, eventually followed by apical migration of junctional epithelium and formation of pockets, if other factors favor biofilm formation. Excessive inflammation of the periodontium usually leads to gingival recession in free facial and interproximal surfaces (Sanavi *et al.,* 1998). Gingival recession and inflammation were notably observed in this study. The increase in the width and height components of gingival recession is correlated with increased bone crest level.

Measurements on the buccal surface were performed because all periodontal tissues of the neighboring tooth may also be affected in cases of biologic width invasion in the proximal surfaces (Albandar, 2002; Albandar *et al.*, 1995). The inflammatory process in the mesial/distal surfaces probably spreads throughout surrounding tissues. Thus, signs of periodontal damage, such as gingival inflammation and gingival recession, occur at the free surfaces.

It has been accepted that overextending restorations promote gingivitis by promoting local accumulation of bacterial biofilm rather than resulting in mechanical irritation (Schätzle *et al.,* 2001). In the present study, the high plaque index may be due to the plaque-retaining properties of the rough surface areas brought into the gingival sulcus when indirect restorations were cemented. This condition could potentially lead to more severe gingival inflammation followed by periodontal destruction with increased pocket depth, loss of attachment and gingival recession (Schmidt *et al.*, 2013; Kosyfaki *et al.*, 2010), increasing the vertical bone resorption and then raising the horizontal component. It was not possible to correlate the findings of this study with the literature, as the literature reported studies using anterior teeth (Sadan and Adar, 1998).

Moreover, the placement of slightly overextending restoration margins was shown to result in a change of the subgingival microbiota adjacent to the subgingival restoration, favoring the colonization of Gram-negative, strictly anaerobic rods (Schmidt *et al.*, 2013). It is suggested that the shift of the composition of the subgingival microbiota towards an increased proportion of periodontopathic microorganisms will eventually lead to loss of periodontal support (Schätzle *et al.,* 2001).

Other possible parameters relating to adverse effects of dental restorations on the supportive tissue have also been identified in the literature (Valderhauge *et al.*, 1993), such as the contour (Grosso *et al.*, 1984), the surface roughness of the crown or the cement (Sorensen, 1989), and the time of restoration existence since its insertion (Schätzle *et al.,* 2001). To what extent these factors have influenced the present results is unpredictable.

Many studies describe the importance of radiographic examination for diagnosis of biologic width violation. However, a standard technique for such evaluation has not been established. In this study, the interproximal technique was used because there is less distortion when compared to other techniques, and it allows a greater approximation of reality when probe measurements are compared (Pimentel *et al.,* 2006). The clinical examination of dental restorations should be done in addition to radiographic examination in order to raise the validity of the diagnostic of biologic width invasion.

Studies in this area are important to the establishment of the diagnosis of biologic width invasion when there is a need for restoration procedures in posterior teeth. Some factors are requisites for the success of tooth restorations, including soft tissue integrity and non-violation of the biologic width. Therefore, an understanding of the anatomy and physiology of gingival tissue regarding the teeth and margins of restorations is necessary to achieve satisfactory mastication, aesthetics, and a healthy interface between the restoration and the surrounding soft tissues (Sanavi *et al.,* 1998; Sadan and Adar, 1998).

The present results show that gingival inflammation and bone crest resorption are common findings in cases of restored posterior teeth with biologic width invasion. Considering the natural history and etiopathogenesis of periodontal disease (Tatakis and Kumar, 2005), it might suggest that in cases of posterior restored teeth the presence of intense bleeding and plaque accumulation lead to bone resorption and may cause interproximal bone defects. The present study has corroborated the long-held concept that restorations placed below the gingival margin are detrimental to gingival health (Schätzle *et al.,* 2001). Clinicians should pay attention in these clinical conditions in order to prevent the evolution of bone loss.

Clinical observations show that the gingiva supporting prosthodontically treated teeth often are inflamed and that pocket formation and recession of gingiva may occur (Valderhaug *et al.*, 1993). These characteristics are also observed in periodontitis and gingivitis, and a differential diagnosis has to be done. In cases of periodontium with biologic width invasion, the clinical signs of periodontal reaction are more restricted to the restored tooth. Moreover, bitewing radiographs should be taken in order to evaluate the restoration margins and the bone crest level. The combination of both clinical and radiographic exams is suitable to diagnose biological width invasion. It is important to note that biologic width invasion is closely associated with local periodontal disease and should be classified as acquired deformities and conditions (Armitage, 1999).

The clinical signs observed in the periodontium with biologic width invasion are also frequent in patients with gingivitis and periodontitis. In this study, patients presented with different periodontal health conditions, and this may be one of the limitations of the study. The importance of including only patients who have an exclusive diagnosis of general periodontal health in future studies was noted. Similarly, the absence of a control group may be considered another limitation of the present study, as a control group gives reliable data with which to compare results.

Clinical studies with a greater sample size are needed to corroborate or refute the findings of this study. Also suggested are new longitudinal studies to investigate more relevant periodontal correlations, and the use of regression analysis in order to determine the behavior and causality between the variables.

## Conclusions

It was concluded that the distance from the more apical extension of the restoration to the bone crest positively correlated with the height and width of the gingival recession. The horizontal component of bone defect positively correlated with the plaque index and bleeding on probing. Thus, there was a positive correlation between the radiographic parameters of biologic width invasion and the clinical conditions.

Clinicians should use interproximal radiography and clinical evaluation to diagnose cases of biologic width invasion. The presence of bone resorption associated with plaque accumulation, bleeding on probing and gingival recession in restored posterior teeth with overextending restorations may be considered as biologic width invasion.

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# Systemic Chemotherapeutic Agents as Adjunctive Periodontal Therapy: A Narrative Review and Suggested Clinical Recommendations

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**Abstract**

Periodontitis is an inflammatory condition of the periodontium that leads to destruction of the supporting structures of the tooth, including loss of attachment and alveolar bone. A clinician's first line of treatment for periodontitis is traditionally mechanical periodontal therapy, including oral hygiene instructions together with scaling and root planing. However, it has been shown that mechanical therapy may not always be effective in halting disease. Adjunctive chemotherapeutics, such as systemic antibiotics or host-modulating agents, may improve the treatment outcome of periodontitis. Using relevant terms such as "adjunctive antibiotics" and "systemic chemotherapeutics" in a manual search of the PubMed database, the authors have prepared a narrative review of the chemotherapeutics currently used in the field. Results of the search and review show that adjunctive antibiotics may be useful in cases of aggressive periodontitis, refractory periodontitis, and in some patients who are immunocompromised, such as heavy smokers or poorly controlled diabetics. Host-modulating agents are generally recommended only as the last resort and are limited to the use of submicrobial dose doxycycline. Microbial testing may be indicated, particularly in aggressive periodontitis cases or refractory cases. Using these results, a decision tree is provided for clinicians to determine when adjunctive chemotherapeutics may be indicated.

*Key words: Antibiotics, anti-bacterial agents, host-modulation, periodontitis, chemotherapeutic*

## Introduction

Periodontitis is an inflammatory condition of the periodontium that leads to destruction of the supporting structures of the tooth, including loss of attachment and alveolar bone (American Academy of Periodontology, 2001). This can result in periodontal pocket formation, gingival recession, bone loss, tooth mobility, and, eventually, tooth loss. An estimated 47% of Americans suffer from periodontitis (Eke *et al*., 2012), which has both chronic and aggressive presentations. Chronic periodontitis, the more common form, is often associated with local factors, such as plaque (the microbial biofilm) and calculus. Aggressive periodontitis, however, is characterized by rapid loss of attachment that is not matched by severe local factors (Armitage, 1999). The etiology of periodontitis is bacterial plaque and its byproducts in a susceptible host. While Theilade (1986) proposed that total microbial load, rather than specific species were responsible for periodontal disease (also known as the "non-specific plaque hypothesis"), Loesche disagreed. Loesche (1976) described the "specific plaque hypothesis," in which he theorized that periodontitis was caused by the presence of select, putative pathogens. Socransky and Haffajee (1998) later classified bacterial species associated with chronic periodontitis, including the red complex bacteria: *Porphyromonas gingivalis* (*Pg*), *Treponema denticola* (*Td*), and *Tannerella forsythia* (*Tf*) (*Loesche and Grossman*, 2001). Additional species have also been implicated in chronic periodontitis, including *Prevotella intermedia* (*Pi*) and *Fusobacterium nucleatum* (*Fn*) (*Loesche* and *Grossman*, 2001). In addition to the red complex species, a multitude of pathogens have been linked to periodontitis.

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For example, *Aggregatibacter actinomycetemcomitans* (*Aa*) has been shown to be associated with periodontitis, particularly aggressive periodontitis (Slots, 1979).

A clinician's first line of treatment for periodontitis is the hygienic phase of the treatment plan. Traditionally, this includes mechanical periodontal therapy, including oral hygiene instructions together with scaling and root planing (SRP). After completion of the hygiene phase of the treatment plan, the clinician moves to the next stage of treatment, the corrective phase. In periodontal treatment, this includes mechanical therapy performed through periodontal flap surgery (FS). However, it has been shown that mechanical therapy may not always be effective in halting disease (Slots and Rosling, 1983; Kornman and Robertson, 1985). SRP and FS have failed to suppress *Aa* in patients with aggressive periodontitis (Slots and Rosling, 1983; Kornman and Robertson, 1985; Mombelli *et al.,* 2000; Doungudomdacha *et al*., 2001). Several possible reasons for this exist: 1) tooth-related and general anatomical factors may limit access for instrumentation (Bower, 1979; Stambaugh *et al*., 1981); 2) compromised host defense mechanisms (Slots, 2004); and 3) the inability to eliminate the pathogens that invade periodontal tissues (Saglie *et al*., 1982). Therefore, in some cases, treatment must also include adjunctive therapies. Adjunctive therapy describes the use of supplemental treatments used in addition to traditional periodontal therapy. Examples include occlusal therapy, restorative care, lasers and chemotherapy. Chemotherapeutics are chemical agents used to prevent, treat or adjunctively manage periodontal disease (American Academy of Periodontology, 2001). Current periodontal treatments are aimed toward more conservative methods in order to preserve surrounding tissues and to minimize tissue trauma and patient discomfort while eliminating associated bacterial pathogens. Adjunctive chemotherapy may fulfill the above goals. The aims of periodontal chemotherapy are to inhibit bacterial growth, kill putative periodontal pathogens, and to inhibit tissue destruction through host modulation. Adjunctive chemotherapeutics target two primary pathways: 1) therapies to inhibit or kill specific bacterial species, and 2) host-modulation therapies to prevent tissue destruction and bone loss (*Figure 1*). Thus, adjunctive, systemic chemotherapeutic options include antibiotics and host-modulating agents. The purposes of this paper are to update the aims of systemic, adjunctive chemotherapy, to discuss currently used chemotherapeutics in the field, and to provide a decision tree for clinicians to determine when adjunctive chemotherapeutics may be indicated.

A literature search was completed using the PubMed database to create a narrative review that updates the aims of systemic, adjunctive chemotherapy, and discusses currently used chemotherapeutics in the field. Additionally, information from the literature was used to provide a decision tree for clinicians to determine when adjunctive chemotherapeutics may be indicated. Two reviewers (R.S. and T.J.O.) searched the PubMed database manually using several search terms and pairs of search terms, including, but not limited to, the words "adjunctive antibiotics," "adjunctive therapy," "systemic antibiotics," "adjunctive chemotherapeutics," "chemotherapeutics," "host-modulation," "periodontitis," and "periodontal disease." In addition, a manual search of the following journals was conducted: *International Journal of Periodontics and Restorative Dentistry, Journal of Periodontology,* and *Journal of Clinical Periodontology.* Relevant articles from January 1970 to the present were considered under the condition that they were published in the English language. The final date of the literature search was completed on September 26, 2015.

### *Systemic antibiotics*

Systemic antibiotics are the most commonly used systemic chemotherapeutic option (*Table 1*). Inhibiting or killing bacterial species prevents the release of virulence factors, such as lipopolysaccharide (LPS), that can damage the periodontal tissues (*Figure 1*). A systematic review by Herrera *et al.* (2002) showed that systemic antibiotic therapy, in combination with SRP, has significant benefits regarding attachment level (CAL) gain and pocket depth (PD) reduction when compared to SRP alone. In a meta-analysis by Haffajee *et al.* (2003), similar results were found regarding mean CAL gain (0.45 mm). In both papers, the largest benefits were shown for deep pockets (≥ 6 mm) in patients with aggressive periodontitis.

Bactericidal antibiotics kill microorganisms by inhibiting key processes for their survival. Examples used in periodontics include metronidazole, which inhibits DNA synthesis, and penicillins, a class of antibiotics that inhibit cell wall synthesis. Metronidazole is particularly effective against species involved in various forms of periodontitis, such as red complex bacteria and *Pi.* Loesche *et al.* (1992) found that SRP in conjunction with metronidazole reduces the need for periodontal surgery. In 2012, Soares *et al.* found that patients with chronic periodontitis given adjunctive metronidazole with SRP had a lower amount of periodontal pathogens after therapy than patients treated with SRP alone. Results from a systematic review by Rabelo *et al.* (2015) show that SRP in conjunction with metronidazole is also more beneficial to aggressive periodontitis patients than SRP alone.

This implies that adjunctive antibiotic therapy may produce improved clinical outcomes; however, it does not imply that adjunctive antibiotics should be used in lieu of traditional periodontal therapy. Contraindications for the use of metronidazole include hepatic disease and the use of alcohol; metronidazole combined with alcohol may cause effects similar to disulfiram, including severe headaches, nausea and vomiting. A commonly prescribed penicillin for orodental infection is amoxicillin. Amoxicillin targets both Gram-positive and Gram-negative bacterial species.

**Table 1.** Systemic antibiotics commonly used adjunctively in periodontal disease

| Antibiotic | Microbes targeted | Common Adult Dosage |
|---|---|---|
| Doxycycline | Non-specific | 250 milligrams once daily for 21 days |
| Metronidazole | *Porphyromonas gingivalis, Tannerella forsythia, Treponema spp.* | 500 milligrams three times daily for 8 days |
| Azithromycin | *Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans* | 500 milligrams once daily for 4-7 days |
| Clindamycin | Gram-negative anaerobes | 300 milligrams three times daily for eight days |
| Metronidazole + Amoxicillin | *Aggregatibacter actinomycetemcomitans* or *Porphyromonas gingivalis* with high numbers of Gram-positive pathogens | 250 milligrams of metronidazole and 375 milligrams of amoxicillin, each three times daily for 8 days |
| Metronidazole + Ciprofloxacin | *Aggregatibacter actinomycetemcomitans* or presence of susceptible enteric microorganisms | 500 milligrams of each taken four times daily for 8 days |

Footnote: Table references Slots (2004) and van Winkelhoff and Winkel (2005).

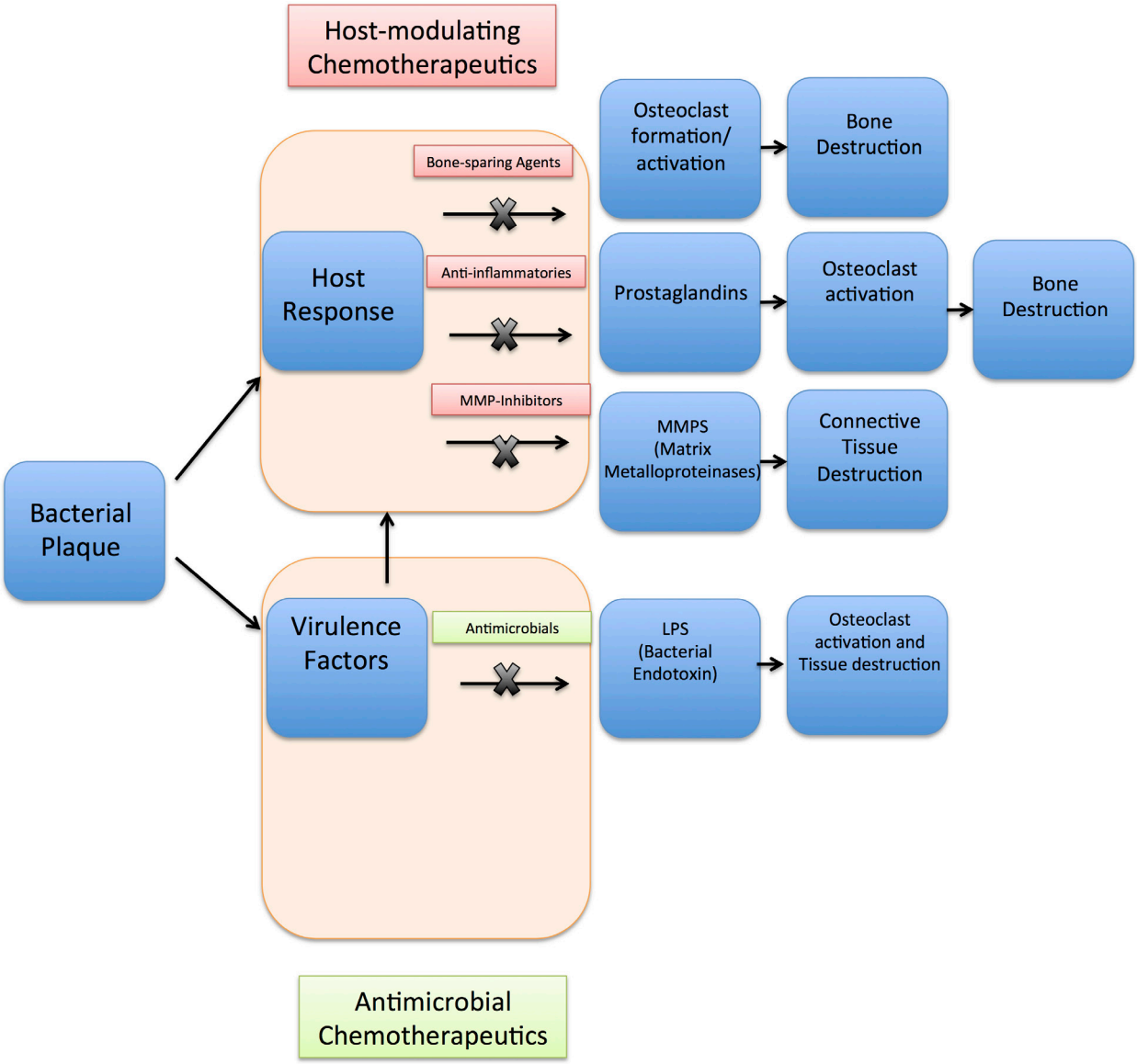


***Figure 1. Adjunctive systemic chemotherapeutic therapy targets***

Feres *et al.* (2012) showed that amoxicillin, in combination with SRP, reduced red-complex and orange-complex bacterial species. This included a 71% reduction of *Pg* one year after treatment (Feres *et al.*, 2012). However, it has been shown that amoxicillin alone is ineffective in treating chronic and aggressive periodontitis, but is effective when used in combination with metronidazole (Soares *et al.*, 2012; Rabelo *et al.,* 2015). Two considerations for the prescription of amoxicillin include common allergy to penicillin drugs and its inhibition by the beta-lactamase enzyme. Due to this inhibition, the use of augmentin (amoxicillin + clavulanic acid) is often prescribed in lieu of amoxicillin.

Bacteriostatic antibiotics inhibit bacterial growth without killing. In periodontics, the bacteriostatic drugs used are tetracyclines, azithromycin, and clindamycin. They inhibit protein synthesis by binding to the 30s (tetracycline) or 50s (azithromycin and clindamycin) subunits.

Tetracyclines include tetracycline and the semi-synthetics, minocycline and doxycycline. They are used as an adjunctive chemotherapeutic in chronic periodontitis, aggressive and refractory periodontitis cases (Seymour and Heasman, 1995). In one study, more gain in clinical attachment was seen following systemic tetracycline use in combination with non-surgical therapy compared to non-surgical therapy alone (Ramberg *et al.*, 2001). However, these results lasted only short-term (one year.) Several studies show that tetracycline as an adjunct to SRP leads to decreased pocket depths, including moderate and deep pockets (Herrera *et al.,* 2002), and slight increases in clinical attachment (Herrera *et al.*, 2002; Haffajee *et al.*, 2003). In a classic study by Kornman and Robertson (1985) SRP alone was unable to resolve any cases of localized juvenile periodontitis (now referred to as localized aggressive periodontitis, or LAP). However, SRP combined with adjunctive tetracycline administration was effective for some patients. Specifically, the SRP and adjunctive tetracycline was effective for patients who did not test positive for *Bacteroides* species; neither SRP nor SRP with adjunctive tetracycline was effective for patients who did test positive for *Bacteroides* species. These results stress the importance of microbial testing prior to the use of systemic chemotherapy. For example, if microbial testing results show that a patient tests positive for *Bacteroides* species, a clinician would not assume that SRP or SRP with adjunctive tetracycline would be an effective way to treat periodontitis.

Semi-synthetic tetracyclines have increased in popularity due to their less frequent administration rate, longer excretion rate, longer serum half-life, fewer renal effects, and less interaction with dairy products than tetracycline (Goodson, 1994; Slots, 2004). Doxycycline has the highest protein binding capacity and longest half-life of the tetracyclines (Slots, 2004).

Minocycline has the best absorption and tissue penetration, and is more effective than tetracycline in inhibiting Gram-negative, facultative anaerobes (Goodson, 1994; Slots, 2004). There are important interactions of the tetracyclines with the drug warfarin and with food, especially magnesium and calcium. For this reason, they should be taken one hour prior to or two hours after eating. Initially, it was theorized that minocycline could provide beneficial clinical results for deep probing depths because they could decrease levels of salivary proteases (Atilla *et al.*, 1996). To date, minocycline has not shown beneficial clinical results when used as a systemic, adjunctive antibiotic (Herrera *et al.,* 2002).

Azithromycin, a macrolide, is effective against a wide variety of oral bacteria (Blandizzi *et al.*, 1999; Slots, 2004), particularly the red complex species (Mascarenhas *et al.*, 2005). The impact of adjunctive, systematic azithromycin treatment used in conjunction with periodontal therapy has yielded mixed results. Buset *et al.* (2015) wrote a systematic review of randomized control trials (RCTs) utilizing azithromycin as an adjunct to SRP that showed conflicting results for both chronic and aggressive periodontitis patients. Five of seven RCTs with chronic periodontitis patients showed beneficial effects in patients using azithromycin. For example, greater probing depth reductions were shown after 6 months in one study, and smaller mean probing depths at 6 months were observed in another study. The other two RCTs, however, showed no beneficial effects. Regarding aggressive periodontitis, only two RCTs were found; one reporting a positive effect of adjunctive azithromycin on a percentage of teeth with probing depth reductions of 2 mm or more, and one that found no significant difference in probing depth measures between groups utilizing adjunctive azithromycin versus SRP alone.

Although clindamycin works very effectively against Gram-negative anaerobic bacteria (Goodson, 1994), it is infrequently prescribed because of its association with pseudomembranous colitis (a life-threatening condition caused by an overgrowth of *Clostridium dificile).* One study showed that systemic clindamycin used adjunctively with SRP could decrease pocket depths, increase CAL gain, and decrease sulcular bleeding index compared to SRP alone in rapidly progressing periodontitis patients (Sigusch *et al.,* 2001). Despite this finding, systematic reviews show a lack of clinical evidence exists to show that clindamycin is a good selection as an adjunctive, systemic therapy for patients with any form of periodontitis (Herrera *et al.*, 2002; Haffajee *et al.* 2003).

Combination therapy refers to the simultaneous use of antibiotics from different drug classes. Using combination therapy allows for the targeting of a wider range of bacterial species. A synergy between the antibiotic drugs also occurs (Slots, 2004). When using combination therapy it is important that bacteriostatic and bactericidal drugs are not used together. Bactericidal antibiotics require active bacterial growth in order to be effective and are thus ineffective when combined with a bacteriostatic drug that inhibits growth.

Perhaps the most common antibiotic combination therapy used adjunctively with periodontal treatment is metronidazole and amoxicillin. Both drugs are bactericidal. Due to extensive study by van Winkelhoff *et al.* (1989) this combination is coined the "van Winkelhoff cocktail." This combination is particularly effective against *Aa*, eliminating the species in 96.6% (114 of 118) of patients with aggressive, chronic, and refractory periodontitis (van Winkelhoff *et al.*, 1992). Significant reductions were also found in *Pg* and *Pi* (although not as dramatically as the reduction of *Aa*). Patients administered the combination therapy also had lower mean PDs and higher gains in CAL.

Several systematic reviews and meta-analyses have shown promising results for the combination of metronidazole and amoxicillin. Herrera *et al.* (2002) revealed that adjunctive to SRP, the combination leads to the largest change in CAL in deep pockets when compared to other antibiotics. Sgolastra *et al.* (2013) showed that as an adjunct to SRP in chronic periodontitis patients, this combination leads to decreased PD and increased CAL gain compared to SRP alone. However, it failed to show significant differences in bleeding upon probing, suppuration, or the reduction of microbial pathogens. In both chronic and aggressive periodontitis, Zandbergen *et al.* (2013) found the mean reduction in PD was 3.72 mm and mean gain in CAL was 2.66 mm in pockets ≥ 7 mm. In patients with sensitivities to penicillins, a combination therapy of metronidazole and ciprofloxacin, a bactericidal drug that inhibits nucleic acid synthesis, also targets *Aa* (van Winkelhoff and Winkel, 2005). A recent meta-analysis by Keestra *et al.* (2015) showed that, in general, no antibiotic was superior to another as an adjunct to SRP. That said, initial clinical effects on mean probing depths were capable of being sustained for one year only with the combination of metronidazole and amoxicillin, and effects did not last as long with other antibiotics.

The use of systemic antibiotics adjunctive to SRP can provide clinical benefits for patients with both chronic and aggressive forms of periodontitis (Haffajee *et al.* 2003.) The difference in clinical parameters appears remarkable for patients with aggressive periodontitis (Slots and Ting, 2002) and is much more notable than the impact on chronic periodontitis (Haffajee *et al.* 2003).

### *Host-modulating agents*

Destruction of periodontal connective tissue and alveolar bone occurs primarily through the host response to bacterial plaque and its byproducts. The presence of pathogens may lead to the release of pro-inflammatory cytokines, proteases, and other mediators that can cause extracellular matrix destruction and bone resorption (Oringer, 2002). The concept of host-modulation is based upon modulating the host response to the bacterial insult to limit tissue destruction. The three primary treatment modalities for host-modulating chemotherapeutics include 1) enzyme inhibitors (including matrix metalloproteinase (MMP) inhibitors), 2) inhibitors of pro-inflammatory mediators (e.g., prostaglandins ($PGE_2$), and 3) osteoclast inhibitors (*Table 1, Figure 1*).

It is hypothesized that in response to bacterial invasion, the host produces MMPs of the collagenase family (Caton *et al.*, 2000; Oringer, 2002). MMPs are proteolytic enzymes involved in connective tissue destruction. Therefore, one host-modulating chemotherapeutic modality used in periodontal therapy is MMP inhibitors. The use of host-modulating chemotherapeutics was pioneered in periodontitis by Golub *et al.* (1984), who discovered that tetracyclines possess host-modulating ability by inhibiting tissue collagenase activity in addition to their antimicrobial properties. At low dosage, too low to produce antimicrobial effects, doxycycline is called "sub-antimicrobial dose doxycycline (SDD)." This dosage is often prescribed for long periods of time, ranging from 3-12 months. In a series of studies, Caton *et al.* (2000) found that 1) long-term SDD did not lead to an overgrowth of doxycycline-resistant organisms or changes in the microbial normal flora, 2) SDD had more effectiveness in sites with higher disease severity, and 3) SDD reduced the overall percentage of spirochetes, but did not alter the percentages of other cellular morphotypes. Statistically significant gains were made in CAL and reductions in PD in the treatment groups after 3, 6, and 9 months of treatment. A follow-up study revealed that PD and CAL reductions remained significantly reduced 3 months after discontinuing use of the SDD (Caton *et al.*, 2001). It was hypothesized that SDD may be a beneficial treatment option for patients with periodontitis who smoke; however, smokers with SRP alone had comparable clinical outcomes and biomarker levels to smokers with SRP and adjunctive SDD (Needleman *et al.*, 2007). Anti-inflammatory medications target prostaglandins, inhibiting them from activating osteoclasts. In patients with progressing periodontal disease, prostaglandin ($PGE_2$) is significantly elevated compared to periodontally stable patients (Oringer, 2002). Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the cyclooxygenase (COX) pathway and $PGE_2$ synthesis. However, effects appear to be minimal (Williams *et al.*, 1989; Oringer, 2002) and concerns of long-term side effects have limited the use of this modality. Bone-sparing agents, such as bisphosphonates, directly target osteoclasts, thereby decreasing bone destruction. Alendronate has been shown to limit progressive bone loss [Oringer, 2002; however, its use as an adjunctive therapy is not recommended because of concerns of drug side effects including medication-related osteonecrosis of the jaw, MRONJ Fernandez Ayora *et al.*, 2015, Mawardi *et al.* 2011, Braun and Iacono, 2006, Hellstein *et al.*, 2011]. While other host-modulating therapies are under investigation, long-term data regarding their safety and side effects is imperative prior to their introduction into clinic (Oringer, 2002). At this time, bisphosphonate use is not recommended for adjunctive periodontal therapy.

### *Treatment considerations and decision tree*

The American Academy of Periodontology recommends the use of adjunctive chemotherapeutics for patients with aggressive, refractory, or recurrent periodontitis, patients with immunosuppression, or patients who do not respond to mechanical therapy (Slots, 2004). Their primary purpose is to be used as a supplement, not replacement for, mechanical debridement. Their use will not provide additional benefits for patients with gingival inflammation or gingivitis (Slots and Rams, 1990), as these conditions are reversible with the use of mechanical therapy alone. There is a great heterogeneity and variability in the studies of antibiotic therapy, including the antibiotic selected, timing of administration, dosage, and duration of use. While no specific recommendation exists regarding timing of administration, Herrera *et al.* (2008) suggest beginning adjunctive antibiotic use at the conclusion of mechanical debridement.

*Figure 2* represents the authors' suggestions regarding the adjunctive use of chemotherapeutics in practice based on the literature described in this paper. If a patient presents with chronic periodontitis but is systemically healthy, adjunctive antibiotics are not recommended unless the patient fails to respond to mechanical therapy. Mechanical therapy such as SRP should be completed (Herrera *et al.*, 2008), followed by periodontal surgery in cases that require further treatment. However, if the patient does not respond to surgical therapy, the use of adjunctive antibiotics may be indicated. It is recommended that patients with aggressive periodontitis have adjunctive antibiotic therapy used during their initial, non-surgical treatment. Adjunctive antibiotic use during initial therapy has been shown to result in greater pocket depth reduction than adjunctive antibiotic use in re-treatment (Griffiths *et al.,* 2011.) If a patient presents with a health condition that places them into the immunocompromised category, adjunctive antibiotics may be considered during initial therapy. Conditions in this category include human immunodeficiency virus (HIV), poorly controlled diabetes, heavy use of tobacco products (for example, more than two packs per day), or other conditions affecting the ability to fight infection or host response to inflammatory factors.

Miranda *et al.* studied the impact of adjunctive antibiotics in type 2 diabetics with a randomized control trial in 2014. The control group received SRP alone, while the test group was given adjunctive metronidazole and amoxicillin after SRP. Analysis of the subgingival biofilm showed a decrease in red complex bacterial species (*Tf, Td,* and *Pg*) and *Pi* at 3 months and 12 months in the adjunctive antibiotic group. Additionally, better clinical results were seen, such as a higher mean pocket depth reduction, and higher gains in clinical attachment level. These results were sustained at 12 months. The adjunctive antibiotic group showed a significantly lower amount of residual pocket depths greater than 5 mm compared to controls (4 sites versus 14.9 sites.) This study suggests that adjunctive antibiotics may lead to better results than SRP alone in diabetic patients; however, the clinician should still exercise clinical judgment when deciding if a diabetic patient is considered immunocompromised or if the diabetes is well-controlled.

Compared to non-smokers, smokers have decreased gingival blood flow, decreased gingival crevicular fluid (Morozumi *et al.*, 2004) and a different subgingival microflora (van Winkelhoff, 2001). For example, van Winkelhoff (2001) showed that smokers had higher subgingival levels of *Bacteriodes forsythus* (now referred to as *Tannerella forsythia*), *Peptostreptococcus micros*, *Fusobacterium nucleatum*, and *Campylobacter rectus* when *Aa* and *Pg* are not present. Smokers also have lower neutrophil levels compared to non-smokers, and reduced neutrophil and phagocytosis function (Fredricksson *et al.,* 1999, Pauletto *et al.,* 2000). This cumulative information implies that smokers may have commensal bacteria leading to periodontal infection even when putative pathogens such as *Aa* and *Pg* are not present (van Winkelhoff, 2001), and that smokers have a reduced capacity to fight infection.

Several adjunctive antibiotic regimens have been studied in smokers. In 1999, Palmer *et al.* examined the effect of metronidazole as adjunctive therapy to SRP in smokers and non-smokers and found that it did not have a significant impact on smokers or non-smokers when compared to SRP alone. Smokers had poorer clinical results when compared to non-smokers, though. Winkel *et al.* (2001) combined metronidazole with amoxicillin as an adjunct to SRP and found a better clinical response in smokers compared to those receiving a placebo drug. For example, smokers had decreases in bleeding index, probing pocket depth, and increases in CAL gain when they received the adjunctive antibiotic compared to the placebo. Thus, the authors concluded that smoking may be an important factor in the decision to prescribe adjunctive antibiotics.

**Table 2.** Host-modulating agents used adjunctively in treating periodontal disease

| Host-modulating Agent | Mechanism of Action |
|---|---|
| Subantimicrobial dose doxycyline (Periostat®) | Matrix metalloproteinase inhibition |
| Ibuprofen | Non-steroidal anti-inflammatory drug inhibiting prostaglandin synthesis |
| Flurbiprofen | Non-steroidal anti-inflammatory drug inhibiting prostaglandin synthesis |
| Bisphosphonate (alendronate; trade name: Fosamax) | Osteoclast inhibition |


***Figure 2. Adjunctive Systemic Chemotherapy Flow Chart***

Additionally, smokers' clinical response was comparable to that of non-smokers. Matarazzo *et al.* (2008) also saw clinical benefits in smokers who had SRP performed with adjunctive antibiotics when compared to SRP alone; this was true for adjunctive therapy with metronidazole alone, but more so for a combination of metronidazole and amoxicillin. Patients with the adjunctive combination therapy had improvements in mean probing depths and clinical attachment levels. Additionally, microbial testing showed that smokers with the adjunctive combination therapy had fewer pathogenic bacteria harbored subgingivally than controls (Matarazzo et al., 2008).

Adjunctive azithromycin use in smokers has been studied by several groups. In smokers with chronic periodontitis, Mascarenhas *et al.* (2005) found that SRP combined with azithromycin compared to SRP alone resulted in a greater PD reduction and CAL gain for moderate-deep pockets (Sgolastra *et al.*, 2013). Dastoor *et al.* (2007) found more rapid healing and decreased gingival inflammation with azithromycin combined with surgery; however, they did not find significant differences in PD or CAL. While some clinicians favor the use of adjunctive azithromycin in smokers, an Angaji *et al.* (2010) systematic review found that no definitive clinical recommendation could be determined. As previously mentioned, the use of SDD adjunctive to SRP did not have significant clinical benefits or changes to biomarkers in smokers when compared to smokers who had SRP alone (Needleman *et al.*, 2007).

It should be kept in mind that smokers might require a prolonged exposure to systemic antibiotics (van Winkelhoff and Winkel, 2005) because smoking decreases gingival blood flow, thus decreasing the amount of antibiotic reaching the periodontal pocket (Morozumi *et al.* 2004).

Prior to prescribing an antibiotic, it is important to consider this decision using sound clinical judgment and evidence. Adverse effects of using antibiotics include possible drug allergy, arbitrary prescription, and the development of antibiotic resistance. The over-prescription of antibiotics and antibiotic resistance are a major, national health concern. Thus, adjunctive antibiotics should only be used as indicated here, in refractory periodontitis cases. While not all patients who are immunocompromised need to immediately be prescribed adjunctive antibiotics with the completion of SRP, it may be a consideration for the clinician. This requires clinical judgment on behalf of the practitioner and possible collaboration with the primary care physician. For example, while the Winkel *et al.* 2001 study discussed previously showed better clinical results for smokers with the use of adjunctive antibiotics, the authors recommended this treatment option be considered in smokers with refractory periodontitis.

According to Slots (2004), the use of microbial testing in conjunction with systemic antibiotic use is highly recommended. Shaddox and Walker, in a 2009 review, stated that microbial testing is useful if it positively affects disease diagnosis, treatment planning, and/or outcome. In this review, they mentioned several studies that showed a positive impact on one or more of these factors after the use of microbial testing. Levy *et al.* (1993) compared the treatment plans of patients with microbial testing involved in the diagnosis versus clinical diagnosis alone and found that patients with microbial testing had less future periodontal surgery performed.

Advantages of using microbial testing include avoiding arbitrary antibiotic prescription, thus, a possible decrease in antibiotic resistance (Suchett-Kaye *et al.*, 2001). In addition, microbial testing can lead to the discovery of bacterial strains resistant to antibiotic therapy (Shaddox and Walker, 2009). Disadvantages include problems with sample collection and/or transport, lack of controlled studies that show real benefit, and the fact that the presence of a species does not indicate its involvement in disease activity (Shaddox and Walker, 2009). Additionally, it is unclear whether or not the sites sampled are representative of the entire mouth (Loomer, 2004; Suchett-Kaye *et al.*, 2001). Samples should be taken from multiple sites of the mouth: when using DNA probes to identify species, the false negative rate was approximately 68% (Haffajee and Socransky, 1992).

Microbial tests should be used to identify specific microorganisms as desired targets for antibiotic therapy; without identifying a target organism, multiple, arbitrary antibiotic prescriptions could be given to the patient (Shaddox and Walker, 2009). Fine (1994) reported cases of refractory periodontitis that were unsuccessfully treated with arbitrary antibiotic therapy that, after microbial testing, were succesfully treated. Performing microbial testing to evaluate pathogens and prescribe an antibiotic according to target pathogens follows the model used in the medical field (Loomer, 2004). The prescription of antibiotics does not necessarily result in better clinical outcomes or the resolution of periodontitis. Mombelli *et al.* (2013) did not see a difference in clinical outcomes when a *Aa*-positive patients had SRP with antibiotics (an amoxicillin and metronidazole combination) versus SRP alone. However, Guerrero *et al.* (2014) found greater improvements in patients who were *Aa*-positive at baseline than those who were not with the use of the same antibiotic combination. Microbial testing may be most valuable in refractory and aggressive cases of periodontitis (Shaddox and Walker, 2009; Loomer, 2004; D'Ercole *et al.,* 2008). While it is arguably most valuable for these patients, microbial testing cannot be used to differentitate between chronic and aggressive forms of periodontitis (Mombelli, 2002).

Microbial testing options include: culture and sensitivity tests, DNA probe (hybridization) (Shaddox and Walker, 2009) or benzoyl-DL-arginine-napthylamide (BANA) testing for red complex bacterial species (Listgarten, 1992). Microbial testing should be completed initially to determine which species are present and the most effective antibiotic for targeting them (Shaddox and Walker, 2009; Fine, 1994). Re-testing is recommended to ensure that the antibiotic is successful; although there is no clinical standard for timing between re-testing, Shaddox and Walker (2009) suggest re-testing at 3 months. Additionally, it may be of benefit to see a negative microbiological finding, which has been associated with periodontal health during maintenance (Loomer, 2004).

If a patient fails to respond to mechanical therapy, surgical therapy, and the use of antibiotics, host-modulating agents may be used in conjunction with a compromised maintenance recall schedule (2 to 3 months recall). At this time, the only host-modulating agent recommended would be the use of submicrobial dose doxycyline.

The *Journal of the American Dental Association* recently published clinical guidelines for the use of adjunctive therapy in periodontics. A task force found that there was favorable evidence to support the use of SDD, because antimicrobial resistance was not of concern and because the benefits of SDD, while small, outweighed potential for harm (Smiley *et al.*, 2015). Weak evidence was found to support adjunctive therapy using systemtic antibiotics, as the moderate benefits were outweighed by potential risks, including allergy, microbial resistance, or other adverse effects. For this reason the authors do not suggest the use of adjunctive antibiotics in every case of periodontitis and reserve the use of adjunctive antibiotics for aggressive periodontitis, immunocompromised patients, or refractory periodontitis cases.

Antibiotic selection should be based on the type of periodontitis, as aggressive and chronic periodontitis are associated with different species of bacteria. Patient factors should be of consideration too, such as allergies to any particular antibiotic class or risk of adverse effects related to that drug class. Regarding chronic periodontitis, Keestra *et al.* (2015) did not find any antibiotic superior to another, statistically. This meta-analysis did not come to a firm conclusion that any antibiotic should be selected over another in treating chronic periodontitis patients. Some microbial testing companies provide recommendations for antibiotic regimens based upon the identified bacterial species present in the patient sample. Additionally, the Shaddox and Walker (2009) report makes recommendations for targeting specific bacterial species. Most bacterial species are susceptible to multiple drugs; however, it is unlikely to be able to target all bacterial species with one antibiotic. Selecting an antibiotic that targets bacterial species capable of invasion (*Aa, Pg, Pi*) may be of value (Shaddox and Walker, 2009). Amoxicillin, azithromycin, ciprofloxacin, and the combination of amoxicillin with metronidazole (Walker and Karpinia, 2002) are good antibiotic selections for targeting *Aa*. Red complex species should not be targeted with amoxicillin alone because beta-lactamases often inhibit this antibiotic. Thus, Shaddox and Walker recommend clindamycin, doxycycline, minocycline, metronidazole, or the combination of amoxicillin with metronidazole.

Regarding aggressive periodontitis, Rabelo *et al.* (2015) showed that metronidazole, metronidazole in combination with amoxicillin, and azithromycin provided clinical benefits in the treatment of aggressive periodontitis when compared to SRP alone. The authors performed two meta-analyses: a standard analysis and a Bayesian network analysis. The standard meta-analysis showed that the use of metronidazole and metronidazole with amoxicillin lead to better PD and CAL results, and azithromycin leads to more CAL gain when compared to SRP alone. The Bayesian network meta-analysis performed additionally showed limited results with doxycycline. Thus, at this time, present evidence suggests that metronidazole or metronidazole with amoxicillin may provide the best results for aggressive periodontitis cases. As previously mentioned, this may be altered by results of microbial testing or patient factors.

## Conclusion

In order to responsibly prescribe adjunctive therapy, the clinician must consider the indications for adjunctive chemotherapy use, risk:benefit ratios, as well as statistical and clinical significance of the selected treatment modality. Consideration of these factors on a case-by-case basis can lead to improved outcomes, decreased side effects, and higher overall patient satisfaction. Thus, adjunctive chemotherapeutics can provide an effective way to treat periodontitis when used correctly and responsibly. As always, the principles of evidence-based dentistry should be considered when providing the patient with treatment options.

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