Adrian Kasaj
Alexandra Chiriachide
Brita Willershausen

The adjunctive use of a controlled-release chlorhexidine chip following treatment with a new ultrasonic device in supportive periodontal therapy: a prospective, controlled clinical study

Authors' affiliations:
Adrian Kasaj, *Alexandra Chiriachide*, *Brita Willershausen*, Department of Operative Dentistry, Johannes Gutenberg-University, Mainz, Germany

Correspondence to:
Adrian Kasaj
Department of Operative Dentistry
Johannes Gutenberg-University Mainz,
Augustusplatz 2 55131 Mainz
Germany
Tel.: +49 6131 177246
Fax: +49 6131 173406
E-mail: Kasaj@gmx.de

Dates:
Accepted 12 April 2007

To cite this article:
Int J Dent Hygiene **5**, 2007; 225–231
Kasaj A, Chiriachide A, Willershausen B. The adjunctive use of a controlled-release chlorhexidine chip following treatment with a new ultrasonic device in supportive periodontal therapy: a prospective, controlled clinical study.

Abstract: *Objective:* The aim of this randomised, split-mouth, controlled clinical trial was to evaluate the effectiveness of a controlled-release chlorhexidine chip (CHX chip) as an adjunctive therapy to scaling and root planing (SRP) with a newly developed ultrasonic device in supportive periodontal therapy (SPT). *Materials and methods:* Twenty patients with moderate-to-severe chronic periodontitis, displaying at least four sites with probing depth (PD) ≥5 mm and persistent bleeding on probing (BOP), were recruited for the study. The target sites were randomly treated with either a newly developed piezo-driven ultrasonic device Vector™- or ultrasonic system (VUS) + CHX chip or VUS alone without adjunctive antimicrobial treatment. The clinical parameters, plaque index (PI), gingival index (GI), BOP, PD and clinical attachment level (CAL) were recorded at baseline and after 1, 3 and 6 months. *Results:* At baseline, there were no significant differences between test and control sites for any of the investigated parameters. The average reduction of PD and improvement in CAL was greater in the VUS + CHX chip sites than in sites treated with the VUS alone at 1, 3 and 6 months ($P < 0.05$). The mean reductions on PD and CAL were 0.7 and 0.6 mm for the control sites and 2.2 and 1.9 mm for the test sites, respectively. Also, the mean reduction in BOP scores were higher in the VUS + CHX chip sites compared to VUS alone at 1, 3 and 6 months ($P < 0.05$). PI scores were not significantly different between VUS + CHX chip sites and VUS alone sites at any

visit. *Conclusion:* These data suggest that CHX chip application following SRP with the tested ultrasonic device is beneficial in improving periodontal parameters in patients on SPT.

Key words: adjunctive therapy; chlorhexidine chip; clinical trial; supportive periodontal treatment; ultrasonic device

Introduction

The most important goal of supportive periodontal therapy (SPT) is the long-term maintenance of gingival and periodontal health obtained after active periodontal treatment. In a number of clinical studies, scaling and root planing has been shown to be an effective treatment for maintaining successful results (1–4). However, although mechanical treatment significantly decreases the prevalence and levels of subgingival microorganisms, it does not necessarily eliminate all periodontal pathogens (5). Therefore, several biodegradable local delivery systems containing different antibacterial agents were proposed as an adjunct to mechanical therapy or even as a monotherapy (6). The goal of local drug delivery systems is to maintain effective concentrations of therapeutic agents to penetrate the biofilm in the periodontal pocket for long periods, which might be difficult to achieve due to the fact that the gingival crevicular fluid present in a 5-mm periodontal pocket is replaced about 40 times an hour (7). Chlorhexidine (CHX), which has been formulated into a number of products, is a potent antibacterial substance. Its efficacy as a topical mouthrinse to inhibit dental plaque and gingivitis has been well established (8, 9); however, its access to the periodontal pocket and the subgingival flora is limited (10).

A biodegradable CHX chip (PerioChip®, Dexcel Pharma GmbH, Alzenau, Germany) for the controlled delivery of CHX to the periodontal pocket has been introduced. This bioabsorbable CHX chip enables slow subgingival release of 2.5 mg CHX within the periodontal pocket, maintaining an average drug concentration in the gingival crevicular fluid greater than 125 μg ml^{-1} for 7–10 days (11). The concentration of the drug remains above the minimum inhibitory concentration for more than 99% of the subgingival microorganisms from periodontal pockets (8). The results of several clinical trials have shown that the use of the CHX chip in conjunction to scaling and root planing is effective in reducing probing depth (PD), clinical attachment loss, and bleeding on probing (BOP) over a 6- to 9-month period (12, 13). In addition, the use of the controlled release CHX delivery system during maintenance therapy allows greater improvement in clinical signs of periodontitis (14). The results of a multicentre clinical trial reported that routine periodontal maintenance therapy together with the adjunctive use of the CHX chip resulted in a continual and clinically significant reduction in PD over a 2-year period (15). As yet, in all these studies the potential value of the CHX chip was determined by using it as an adjunct to mechanical scaling and root planing with hand instruments immediately following the initial treatment phase or within a periodontal maintenance programme. However, lately power-driven instruments, such as sonic and ultrasonic scalers, have been proposed to mechanize and simplify the procedure of scaling and root planing. Numerous studies have reported on the comparative clinical outcome of sonic and ultrasonic versus manual instrumentation (16–18). The authors found that debridement of 4–7 mm pockets with sonic and ultrasonic instrumentation was as successful for healing of diseased periodontal sites as was scaling with hand instruments. Furthermore, several studies reported on an increased efficiency of subgingival debridement with both sonic and ultrasonic scalers, as manual instrumentation generally takes longer to achieve the same clinical results (19, 20). Therefore ultrasonic instrumentation must be regarded as a valuable substitute for conventional scaling with hand instruments. Recently, a new type of ultrasonic instrument for tooth debridement was introduced (VUS) (Vector™-ultrasonic system; Dürr Dental, Bietigheim-Bissingen, Germany). Ultrasonic vibrations are generated at a frequency of 25 kHz, and the horizontal vibration of the device is converted by a resonating ring in vertical vibration, resulting in a parallel movement of the working tip to the root surface. Furthermore, the energy from the instrument is transmitted to the root surface and the periodontal tissues by a suspension of water and hydroxyapatite (HA) particles. The results from a recent study, evaluating the healing of human intrabony defects following non-surgical periodontal treatment with the piezo-driven ultrasonic device clinically and histologically, have shown a significant gain of clinical attachment after 6 months (21). The histological evaluation revealed that healing was predominantly characterized by the formation of a long junctional epithelium along the instrumented root surface. In another recent study, non-surgical

periodontal therapy with the piezo-driven ultrasonic system was compared with that of hand instruments. The results have provided evidence that non-surgical periodontal therapy with the piezo-driven ultrasonic system may lead to comparable clinical improvements than those obtained with conventional hand instruments (22).

To our knowledge, until now, there are no data available evaluating the clinical outcomes of the CHX chip in conjunction with this novel ultrasonic system. Therefore, the purpose of the present study was to determine the possible effect of the CHX chip on clinical parameters of periodontitis, when used as adjunctive therapy to non-surgical treatment with a new type of ultrasonic instrument in a cohort of recall patients.

Material and methods

Patient selection

This trial was designed as a split-mouth, single-blinded, randomised prospective study of 6-months duration. The protocol of this study was approved by the institutional review board of ethics on human research and written informed consent was obtained from all subjects. The study was in accordance with the Helsinki Declaration of 1975, as revised in 1983. Twenty chronic periodontitis patients, seven males and 13 females, aged 20–60 years (mean age 42.0 ± 5.6 years) participated in the study. Patients were considered eligible if they had at least four pockets ≥5 mm with persistent BOP, a minimum of 15 or more natural teeth and completed non-surgical phase of periodontal therapy at least 3 months prior to baseline. Exclusion criteria included: pregnancy, antibiotics or any form of periodontal treatment in the previous 3 months, teeth with furcation involvement, smoking, allergy to CHX and history of systemic disease that could affect the progression or treatment of periodontitis. No peri-implant sites were included in the study.

Treatments

An outline of the present study treatments is presented in Fig. 1. All participants received supragingival scaling and a prophylaxis of all teeth 2 weeks prior to the study. At baseline, clinical measurements were performed and patients were randomly assigned to one of the two treatment groups; subgingival debridement with the novel ultrasonic system (VUS-control sites) using straight and curved metal curettes and a polishing fluid (HA particles <10 μm) according to the instructions given by the manufacturer alone or subgingival debridement with the VUS followed by placement of a CHX chip (VUS plus CHX chip-test sites). The Vector^{TM} straight probe was used for the instrumentation of all vestibular and oral surfaces, whereas the according Vector^{TM} curette was used for the cleaning of the approximal surfaces. Instrumentation of all target sites was performed until the operator felt that the root surfaces were adequately debrided and planed without any setting of time standards. Following debridement, all pockets were thoroughly rinsed with sterile saline to remove the HA. In the test sites, the CHX chip was inserted into subgingival sites according to the manufacturer's guidelines. Patients were advised not to use dental floss for 7 days to avoid displacement of the CHX chip and to avoid the use of chemotherapeutic mouthrinses during the study period. At 3 months, all pockets that remained ≥5 mm in depth received subgingival retreatment with the VUS and additional application of a CHX chip at the test sites.

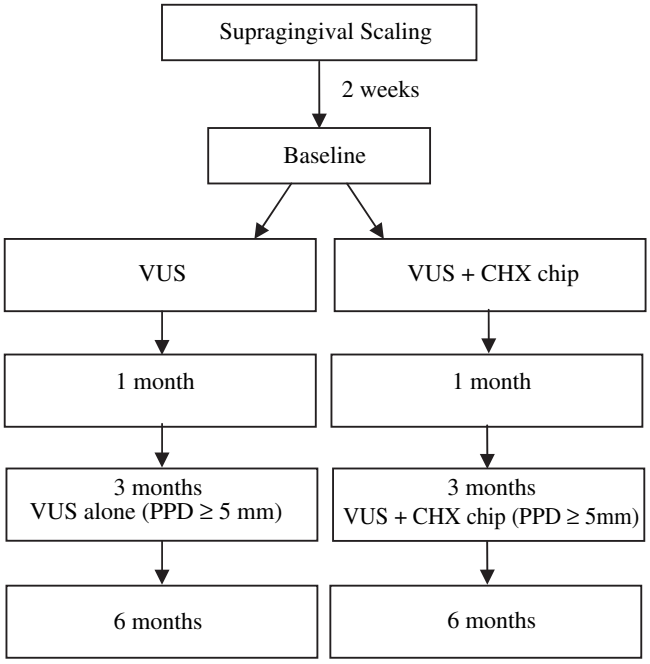

Fig. 1. Schematic outline of the study.

Clinical recordings

All clinical measurements were performed by a single calibrated examiner who was not involved in providing treatment during the study. Five patients, each showing 10 teeth (single and multirooted) with PD >6 mm on at least one aspect of each tooth, were used to calibrate the examiner. The examiner evaluated the patients on two separate occasions, 48 h apart. Calibration was accepted if measurements at baseline and at 48 h were similar to the millimetre at > 90% level.

The evaluations of clinical parameters were performed at baseline and 1, 3 and 6 months after treatment. The periodontal examination included the assessment of plaque index (PI), gingival index (GI), PD, gingival recession (GR), clinical attachment level (CAL) and BOP at six sites per tooth using a manual periodontal probe (PCP 15; Hu-Friedy Co., Chicago, IL, USA).

Statistical analysis

All statistical analyses were performed using SPSS (11.0 for Windows, Chicago, IL, USA). For the clinical parameters, PI, GI, PD, GR and CAL data were expressed as mean values ± standard deviation. Comparison between baseline and 1, 3 and 6 months were investigated using the paired *t*-test. The changes within the treatment groups were analysed using the Wilcoxon test. *P*-values <0.05 were considered as statistically significant.

Results

All patients who were enrolled in the present study (seven males and 13 females, mean age: 42.0 ± 5.6 years) completed the 6-month evaluation, and the data were included in the statistical analysis. A total of 80 sites were treated and evaluated at the end of 6 months, 40 with the VUS alone and 40 with VUS plus CHX chip.

At baseline, there was no statistically significant difference between the VUS alone and the VUS + CHX chip sites for any of the investigated parameters ($P > 0.05$) (Table 1).

Baseline mean PD in the VUS alone sites was 6.3 and 6.2 mm in the VUS plus CHX chip sites. The reduction of PD for both sites was statistically significant at 1, 3 and 6 months compared with the baseline ($P < 0.05$) (Table 2). The PD was reduced after 1 month to 5.7 mm in the VUS alone sites and to 4.9 mm in the VUS plus CHX sites. At the 3-months examination, the VUS sites showed a mean reduction of 0.6 mm as compared to 1.8 mm for the VUS + CHX chip sites. After 6 months, the total mean reductions in PD were 0.7 mm in the VUS alone sites versus 2.2 mm for the VUS plus CHX chip sites, respectively. There was a statistically significant difference ($P < 0.05$) with respect to PD reduction between the two treatment sites at all three re-examinations (1, 3 and 6 months). In addition, the percentage of sites with a reduction of PD ≥2 mm was significantly greater in the VUS + CHX chip sites than in the VUS sites alone at 1, 3 and 6 months ($P < 0.05$) (Fig. 2). Both treatment sites demonstrated an improvement in CAL values at 1, 3 and 6 months (Table 3). However, the VUS + CHX chip sites had a significantly greater gain in CAL at 1, 3 and 6 months compared to the VUS alone sites ($P < 0.05$). For the VUS sites, the mean gain in CAL at 3 months amounted to 0.5 mm compared to 1.6 mm in the VUS + CHX chip sites. After 6 months, the mean gain in CAL was 0.6 mm in the VUS alone sites and 1.9 mm in the

Table 1. **Baseline clinical data**

	VUS (mean ± SD)	VUS + CHX chip (mean ± SD)
PPD	6.3 (0.9)	6.2 (1.0)
CAL	7.2 (1.4)	6.9 (1.6)
BOP	67%	71%
PI	1.0 (0.8)	1.3 (0.9)
GI	1.1 (0.9)	1.2 (0.8)

Table 2. **Mean (±SD) reduction in PD (mm) from baseline for VUS alone sites and VUS plus CHX chip sites**

Treatment	Month 1	Month 3	Month 6
VUS alone	0.6 (0.5)	0.6 (0.5)	0.7 (0.6)
VUS plus CHX Chip	1.3 (0.6)*	1.8 (0.8)*	2.2 (0.8)*

*$P < 0.05$.
CHX, chlorhexidine; PD, probing depth; VUS, Vector™-ultrasonic system.

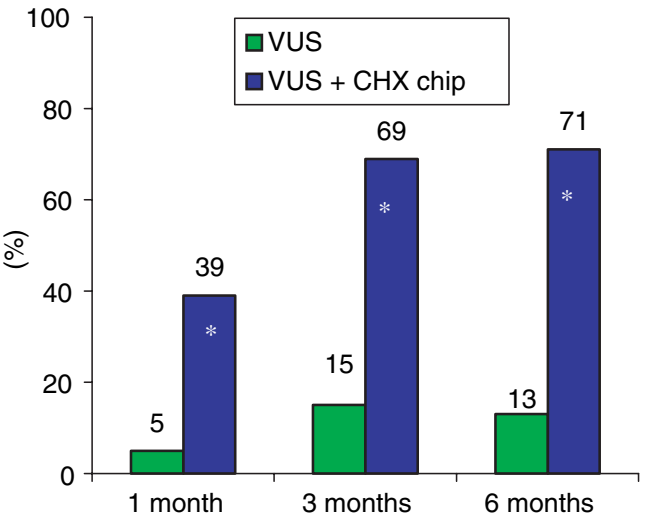

Fig. 2. Percentage of sites presenting PD reduction of ≥2 mm at 1, 3 and 6 months. *Statistically significant difference between the sites ($P < 0.05$).

Table 3. **Change (mean ± SD) in CAL from baseline for VUS alone sites and VUS plus CHX chip sites**

Treatment	Month 1	Month 3	Month 6
VUS alone	0.4 (0.5)	0.5 (0.8)	0.6 (0.7)
VUS plus CHX Chip	1.2 (0.7)*	1.6 (1.0)*	1.9 (1.1)*

*$P < 0.05$.
CAL, clinical attachment level; CHX, chlorhexidine; VUS, Vector™-ultrasonic system.

Table 4. **Frequency distribution of BOP in VUS alone sites and VUS plus CHX chip sites**

	VUS + CHX chip			VUS alone		
BOP	Month 1	Month 3	Month 6	Month 1	Month 3	Month 6
Presence	45%*	44%*	29%*	61%	54%	58%
Absence	55%	56%	71%	39%	46%	42%

*$P < 0.05$.
BOP, bleeding on probing; CHX, chlorhexidine; VUS, Vector™-ultrasonic system.

Table 5. **Plaque index score at 1, 3 and 6 months**

Treatment	Month 1	Month 3	Month 6
VUS alone	1.0 (0.6)	1.1 (0.7)	1.1 (0.7)
VUS plus CHX Chip	0.9 (0.8)	0.9 (0.7)	0.9 (0.8)

No statistically significant difference between the treated sites ($P > 0.05$).
VUS, Vector™-ultrasonic system; CHX, chlorhexidine.

VUS + CHX chip sites. The improvements in BOP were significantly reduced at 1, 3 and 6 months for the VUS + CHX chip sites compared to baseline ($P < 0.05$) (Table 4). At the 1, 3 and 6 months re-examination, the VUS + CHX chip sites demonstrated statistically significant lower bleeding scores than the VUS alone sites ($P < 0.05$). The mean BOP reduction at 6 months was 42% for VUS + CHX chip sites and 9% for VUS alone sites, respectively. PI scores were similar in both treatment sites at baseline. There was a reduction in PI values during the study period, but PI scores were not significantly different between the treatment sites at any visit ($P > 0.05$) (Table 5). Both groups showed a reduction in GI values during the study period. At the 6 months visit, the VUS + CHX chip treated sites exhibited greater improvement in GI scores than the VUS sites alone ($P < 0.05$).

The most frequent adverse events in the CHX chip treated sites were gingival discomfort (three sites) and gingival swelling (one site); however, these side-effects resolved spontaneously within a few days without requiring any medication. There was no difference in the frequency of adverse events between the two treatment procedures at any of the treatment intervals.

Discussion

The present study evaluated the efficacy of a CHX chip as an adjunctive treatment to a newly developed ultrasonic device in SPT. Previous studies demonstrated that the adjunctive use of a CHX chip to traditional scaling and root planing at sites with a PD ≥5 mm provided significantly greater reductions of PD at both 6 and 9 months (12, 13). These additional benefits could also be observed when the CHX chip was applied during the maintenance periodontal therapy (14). However, some recent studies did not confirm these results (23, 24).

In the present study, the reduction in PD and CAL obtained in the VUS plus CHX chip sites was greater than those obtained in the VUS sites alone at 1, 3 and 6 months. The VUS plus CHX chip sites showed a mean PD reduction of 2.2 mm and a mean CAL gain of 1.9 mm at 6 months post-operatively. A comparison with clinical results obtained after the adjunctive use of the CHX chip to mechanical debridement using conventional ultrasonic systems or hand instruments (e.g. Gracey curettes) is difficult as all previously published studies on the use of the CHX chip focused on its effects when used as an adjunct to conventional scaling and root planing and immediately following the initial treatment phase.

In our study, the reduction in PD and improvement in attachment levels in the VUS + CHX sites were greater than that observed in other studies evaluating the adjunctive use of the CHX chip to scaling and root planing using hand instruments or conventional ultrasonic scalers (12–14). This may be due to deeper PD at baseline in the present study. Clinical studies have demonstrated that the reduction of PD and gain of CAL is greater in deeper pockets following scaling and root planing (25). Furthermore, the differences may be related to disparity in pocket management. In the present study, all residual sites at 3 months were systematically retreated with the VUS, followed by CHX chip placement in the test sites. In contrast, the studies by Soskolne *et al.* (12), Jeffcoat *et al.* (13) and Heasman *et al.* (14) did not expose residual control sites to additional therapy, except supragingival prophylaxis. Another important factor is the different period of time scheduled for scaling and root planing which was not limited in the present study, and may have induced a quality difference in mechanical debridement. The better clinical results might also be due to the excellent motivation of the patients and the different mode of mechanical debridement using a piezoelectric ultrasonic scaler. In contrast to our study, Grisi *et al.* (26) reported that the CHX chip did not provide any clinical benefit beyond that achieved with conventional scaling and root planing after a 9 month period. This may be due to their low mean PD baseline values of 5.2 mm leaving a lower potential for clinical improvements. Furthermore, their evaluation period of 9 months was longer than in the present study. In a previous study, a PD reduction of 2 mm has been considered as a clinically relevant change (13). The proportion of sites showing PD reduction ≥2 mm in the present study was higher for the

VUS + CHX chip sites in comparison to the VUS sites alone. These findings are in agreement with previous studies (12, 23). In all the studies, SRP alone was used as the positive control arm providing a mean reduction in PDs between 0.65 and 0.78 mm after 6 months (12–14). In comparison, our 6 month data showed for the control sites a mean reduction in PDs of 0.7 mm using a piezoelectric ultrasonic scaler for mechanical root debridement. These findings are also in accordance with the results reported by Sculean *et al.* (22) demonstrating a mean PD decrease of 0.6 mm following treatment with the VUS after 6 months at sites with initial PDs of >6 mm. There was no statistically significant difference between the tested ultrasonic device and hand instrumentation (22). Several other studies have demonstrated that ultrasonic instrumentation achieves equal or superior treatment outcomes when compared with hand instruments (16–19). As subgingival instrumentation is performed repeatedly during SPT, it is crucial to prevent root damage because the cumulative effect of substance removal by scaling may result in severe root damage over time (27). Kawashima *et al.* (28) suggested that the VUS scaler produces a smooth root surface with minimal loss of tooth substance and is therefore a reasonable choice for gentle periodontal maintenance treatment. An *in vitro* study examining the effectiveness of scaling and root planing using the VUS with the fluid polish demonstrated minimal damage of the root surface with preservation of more cementum and a tight attachment of fibroblasts on the root surface in contrast to a conventional ultrasonic scaler (29). Nyman *et al.* (30) concluded that excessive removal of root cementum is not necessary and that the exclusive removal of the biofilm is sufficient for the removal of contaminants. In a recent study, it could be demonstrated that the amount of root substance removal with the VUS was significantly dependent on the choice of the irrigation fluids (31). Using the polishing fluid, the amount of root substance removal has been shown to be similar to a conventional ultrasonic device but lower than with hand instruments (31). However, the piezo-driven ultrasonic device in polishing mode has been shown to be sufficient to remove subgingival biofilm (32), which is a prerequisite for chemotherapy. In the present study, it is impossible to estimate to what extent the used polishing fluid, containing HA, influenced the clinical outcomes and the efficacy of the CHX chip. Further studies are needed in order to clarify this issue.

Conclusion

In conclusion, the results of the present study show that the adjunctive application of the CHX chip to SRP with the tested ultrasonic device is beneficial in improving clinical periodontal parameters in patients on SPT. However, further longitudinal studies with the inclusion of more study subjects with other types of periodontal disease are needed to investigate the changes of the subgingival microbiota.

Acknowledgement

The present study was supported by Dexcle Pharma GmbH, Alzenau, Germany.

References

1 Ramfjord SP, Knowles JW, Nissle RR, Shick RA, Burgett FG. Results following three modalities of periodontal therapy. *J Periodontol* 1975; **46:** 522–526.
2 Badersten A, Nilveus R, Egelberg J. Effect of non-surgical periodontal therapy. (VIII) Probing attachment changes related to clinical characteristics. *J Clin Periodontol* 1987; **14:** 425–437.
3 Isidor F, Karring T. Long-term effect of surgical and non-surgical periodontal treatment. A 5-year clinical study. *J Periodontal Res* 1986; **21:** 462–472.
4 Kaldahl WB, Kalkwarf KL, Patil KD, Dyer JK, Bates RE. Evaluation of four modalities of periodontal therapy. Mean probing depth, probing attachment level and recession changes. *J Periodontol* 1988; **59:** 783–793.
5 Haffajee AD, Cugini MA, Dibart S, Smith C, Kent RL Jr, Socransky SS. The effect of SRP on the clinical and microbiological parameters of periodontal diseases. *J Clin Periodontol* 1997; **24:** 324–333.
6 Rams TE, Slots J. Local delivery of antimicrobial agents in the periodontal pocket. *Periodontol* 2000; **10:** 139–159.
7 Goodson JM. Pharmacokinetic priciples controlling efficacy of oral therapy. *J Dent Res* 1989; **68:** 1625–1632.
8 Stanley A, Wilson M, Newman HN. The *in vitro* effects of chlorhexidine on subgingival plaque bacteria. *J Clin Periodontol* 1989; **16:** 259–264.
9 Loe H, Schiott CR. The effect of mouth rinses and topical application of chlorhexidine on the development of dental plaque and gingivitis in man. *J Periodontol Res* 1970; **5:** 79–83.
10 Pitcher G, Newman H, Strahan J. Access to subgingival plaque by disclosing agents using mouthrinses and direct irrigation. *J Clin Periodontol* 1980; **7:** 300–308.
11 Soskolne WA, Chajek T, Flashner M *et al.* An *in vivo* study of the chlorhexidine release profile of the PerioChip™ in the gingival crevicular fluid, plasma and urine. *J Clin Periodontol* 1998; **25:** 1017–1021.
12 Soskolne WA, Heasman PA, Stabholtz A *et al.* Sustained local delivery of chlorhexidine in the treatment of periodontitis. *J Periodontol* 1997; **68:** 32–38.
13 Jeffcoat MK, Bray KS, Ciancio SG *et al.* Adjunctive use of a subgingival controlled-release chlorhexidine chip reduces probing depth and improves attachment level compared with scaling and root planing. *J Periodontol* 1998; **69:** 989–997.
14 Heasman PA, Heasman L, Stacey F, McCracken GI. Local delivery of chlorhexidine gluconate (PerioChip™) in periodontal maintenance patients. *J Clin Periodontol* 2001; **28:** 90–95.

15 Soskolne WA, Proskin HM, Stabholz A. Probing depth changes following 2 years of periodontal maintenance therapy including adjunctive controlled release of chlorhexidine. *J Periodontol* 2003; **74:** 420–427.

16 Torfason T, Kiger R, Selvig KA, Egelberg J. Clinical improvement of gingival conditions following ultrasonic versus hand instrumentation of periodontal pockets. *J Clin Periodontol* 1979; **6:** 165–176.

17 Badersten A, Nilveus R, Egelberg J. Effect of nonsurgical periodontal therapy. I. Moderately advanced periodontitis. *J Clin Periodontol* 1981; **8:** 57–72.

18 Loos B, Kiger R, Egelberg J. An evaluation of basic periodontal therapy using sonic and ultrasonic scalers. *J Clin Periodontol* 1987; **14:** 29–33.

19 Dragoo MR. A clinical evaluation of hand and ultrasonic instruments on subgingival debridement. 1. With unmodified and modified ultrasonic inserts. *Int J Periodontics Restorative Dent* 1992; **12:** 310–323.

20 Copulos TA, Low SB, Walker CB, Trebilcock YY, Hefti AF. Comparative analysis between a modified ultrasonic tip and hand instruments on clinical parameters of periodontal diesease. *J Periodontol* 1993; **64:** 694–700.

21 Sculean A, Windisch P, Keglevich T, Gera I. Histologic evaluation of human intrabony defects following non-surgical periodontal therapy with and without application of an enamel matrix protein derivative. *J Periodontol* 2003; **74:** 153–160.

22 Sculean A, Schwarz F, Berakdar M *et al.* Non-surgical periodontal treatment with a new ultrasonic device (Vector^{TM}-ultrasonic system) or hand instruments. A prospective, controlled clinical study. *J Clin Periodontol* 2004; **31:** 428–433.

23 Azmak N, Atilla G, Luoto H, Sorso T. The effect of subgingival controlled-release delivery of chlorhexidine chip on clinical parameters and matrix metalloproteinase-8 levels in gingival crevicular fluid. *J Periodontol* 2002; **73:** 608–615.

24 Daneshmand N, Jorgensen MG, Nowzari H, Morrison JL, Slots J. Initial effect of controlled release chlorhexidine on subgingival microorganisms. *J Periodont Res* 2002; **37:** 375–379.

25 Ramfjord SP, Caffesse RG, Morrison EC *et al.* 4 modalities of periodontal treatment compared over 5 years. *J Clin Periodontol* 1987; **14:** 445–452.

26 Grisi DC, Salvador SL, Figueiredo LC, Souza SLS, Novaes Ab Jr, Grisi MFM. Effect of controlled-release chlorhexidine chip on clinical and microbiological parameters of periodontal sysndrome. *J Clin Periodontol* 2002; **29:** 875–881.

27 Kocher T, Fanghänel J, Sawaf H, Litz R. Substance loss caused by scaling with different sonic scaler inserts – an *in vitro* study. *J Clin Periodontol* 2001; **28:** 9–15.

28 Kawashima H, Sato S, Kishida M, Ito K. A comparison of root surface instrumentation using two piezoelectric ultrasonic scalers and a hand scaler *in vivo*. *J Periodont Res* 2007; **42:** 90–95.

29 Kishida M, Sato S, Ito K. Effects of a new ultrasonic scaler on fibroblast attachment to root surfaces: a scanning electron microskopy analysis. *J Periodont Res* 2004; **39:** 111–119.

30 Nyman S, Sarhed G, Ericsson I, Gottlow J, Karring T. Role of 'diseased' root cementum in healing following treatment of periodontal disease. An experimental study in the dog. *J Periodont Res* 1986; **21:** 496–503.

31 Braun A, Krause F, Frentzen M, Jepsen S. Removal of root substance with the Vector^{TM}-system compared to conventional debridement *in vitro*. *J Clin Periodontol* 2005; **32:** 153–157.

32 Schwarz F, Aoki A, Sculean A, Georg T, Scherbaum W, Becker J. *In vivo* effects of an Er:YAG laser, an ultrasonic system and scaling and root planing on the biocompatibility of periodontally diseased root surfaces in cultures of human PDL fibroblasts. *Lasers Med Surg* 2003; **33:** 140–147.