Application of PAD in clinical dentistry and the literature evidence

Liviu Steier takes a closer look at Photo Activated Disinfection and its uses in differing areas of clinical dentistry

Spread of antibiotic resistance among pathogenic bacteria is alarming the medical science. Inappropriate prescription of antibiotics in the dental profession could add to this. Oral bacterial infection can commonly be considered of local origin. Several attempts have been undertaken in dentistry to try and maintain antimicro bial treatment regimens restricted locally.

The combination of dyes and visible light has proven to kill microorganisms about 100 years ago. Harmless dyes sensitive to light are delivered locally (soft and hard tissue) and exposed to light at certain predetermined wavelength are highly successful in disinfection. Key is presence of oxygen to excited state of the Photosensitiser enhancing transfer of electrons to the ground state of molecular oxygen resulting in reactive oxygen like singlet oxygen and hydroxyl radicals. The latest two have lethal effect on pathogenic microorganisms. The process described is called photo activated disinfection when related to dentistry. Resistance to Photo Activated Disinfection (PAD) has been researched in periodontology but could not be induced artificially (Lauro et al. 2002).

Dai et al. (2009) reviewed literature on Photodynamic therapy (PDT) in regards to localised infections. Key points of interest were:

- Photosensitisers and their interaction with different bacterial strains.
- Photodynamic therapy at different tissue structures.

As a result one can state that bactericidal action was achieved by neutral or cationic PS molecules on Gram positive flora when compared to cationic in combination with non cationic ones on Gram negative (Nitzan et al. 1992, Merchat et al. 1996,). Santamaria et al. (1972) listed more than 400 compounds demonstrating photosensitising properties. Usacheva et al. has proven in 2001 that: "TB exhibits a greater bactericidal activity than MB against most bacteria in dark and light conditions."

Cohen et al. (1995) cited by Meisel et al. (2005) summarised the photobiological principles of light involved in the process:

- The Grotthus-Draper law: discusses the wavelength of light requested
- TheStark–Einsteinlaw:discusses the amount of absorbed light
- The Bunsen – Roscoe law: discusses intensity and duration of light applied

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Meisel and Kocher identified in their review 2005 the "prerequisites and further demands" in regards to PAD in Periodontology: suitability of the photosensitising dyes, optimisation of efficacy, determination of irradiation device as well as exposure time, etc.

Today PAD can be regarded as a helpful adjutant in biofilm management. Its indication in clinical dentistry varies from Cariology to Periimplantitis covering Endodontics and Periodontology.

Application in Perio

Use of PAD in Periodontology is multifaceted as an adjutant after non-surgical or in conjunction with surgical approaches.

Interestingly, Azarpazhooh et al (2010) performed a systematic review and meta analysis for the use of PAD in Periodontology and concluded: "PDT as an independent treatment or as an adjunct to SRP was not superior to control treatment of SRP. Therefore, the routine use of PDT for clinical management of periodontitis cannot be recommended."

Once one understands mechanisms of action of PAD, as briefly discussed above, and starts to critically appraise the systematic review performed by the group of Azarpazhooh et al. a major shortcoming becomes eminent – there was no appraisal of the studies included, in regards of suitable selection of photosensitiser, adequate light source and timing. Correct conclusion would have referred to the kind of PS used and the question if photobiological principles of light have been disregarded.

It is sad to admit that even applying the highest criteria for appraisal according to the Cochrane library one may generate confusing conclusions if authors are not familiar with the review topic.

In 2009, Ramos de Oliviera et al. managed to demonstrate a statistically significant reduction in TNF -a level 30 days following treatment when PAD used without SRP. Similar results were achieved by Braham et al.(2009).

An in vivo study by Sigusch et al. (2010) showed "that the adjuvant application of the described PDT method is appropriate to reduce periodontal inflammatory symptoms and to successfully treat infection with F. nucleatum."

The results of Allan et al. (2007) using Toluidine blue "indicate that PDT may be an effective alternative to conventional modalities in the treatment of periodontal disease."

Andersen et al. (2007) compared the use of Pad to SRP and concluded that "Within the limits of the present study, it can be concluded that SRP combined with photodisinfection leads to significant improvements of the investigated parameters over the use of SRP alone."

Milanezi de Almeida et al. (2008) induced periodontal bone loss in rats by ligature and treated with PAD. Their conclusion: "PDT may be an effective alternative for control of bone loss in furcation areas in periodontitis." Kömerik et al. (2003) researched the lethal action of Toluidine blue as PS on Porphyromonas Gingivalis and concluded "The results of this study show that Toluidine blue-mediated lethal photosensitisation of P. gingivalis is possible in vivo and that this results in decreased bone loss. These findings suggest that photodynamic therapy may be useful as an alternative approach for the antimicrobial treatment of periodontitis."

Application for treatment of Peri-implantitis

Hayek et al (2005) published a study comparing conventional therapy versus PAD for treatment of ligature induced periimplantitis in dogs. They concluded that the non invasive PAD technique could be used to reduce pathological microorganism in peri-implantitis.

Shibli et al. (2003) examined the efficacy of PAD application alone in ligature induced peri-implantitis in dogs and concluded that complete elimination of pathogens was achieved in some cases.

Dörtbudak et al. (2001) researched microbial decontamination on peri-implantitis affected IMZ implants in vivo and identified a significant reduction

Figı - SRP - Pocket debridement using US

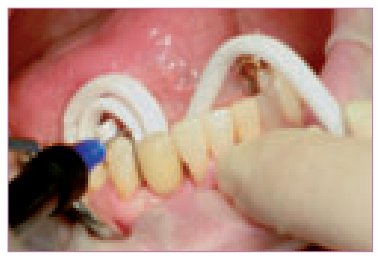

Fig2 - Instillation of the PS (Toluidine blue) into the pocket

Fig3 - Tip of light source (Aseptim Plus, Denfotex) in situ

Fig4 - Application of light (120 sec)

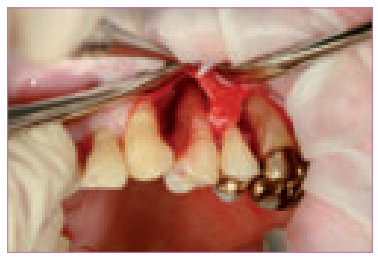

Fig5 - Clinical picture showing advanced bone loss. Teeth involved demonstrated no mobility. Tooth 24 received a RCT

Fig6 - PAD disinfection once mechanical debridement completed and prior to GBR

Fig7 - Clinical picture showing localised peri-implantitis. Similar to the case above once mechanical debridement completed PAD disinfection applied prior to GTR

after PAD application.

Baron et al (2000) reviewed 29 papers on regenerative methods in regards to regeneration of peri-implantitis affected sites and concluded: "Of all tested treatment methods, the combination of guided bone regeneration and augmentation with demineralised freeze-dried bone resulted in the most favorable results regarding bone gain and reosseointegration."

Application in Cariology

Williams et al (2002) researched the bactericidal efficacy of Toluidine blue and variable energy on Streptococcus mutans. The results were extremely encouraging: "The system was highly effective in killing TBO-treated Streptococcus mutans NCTC 10449 in stirred planktonic suspension, killing at least 109 cfu/ml. Antibacterial action increased as the delivered energy dose increased."

The study of Lima et al. (2009) "evaluated the effect of PACT (Photodynamic antimicrobial therapy) on dentine caries produced in situ." They came to the following conclusions: "PACT was effective in killing oral microorganisms present in dentine caries produced in situ and may be a useful technique for eliminating bacteria from dentine carious lesions before restoration."

Steier et al. researched the efficacy of PAD bovine root canal dentine previously infected with Enterococcus Faecalis monoculture Biofilm.

Especially with today's trends of minimalistic intervention and using adhesive dentistry the use of PAD may prevent excessive hard tissue removal and help maintain great amounts of dentin. Major benefit of course is the conservation on tooth vitality.

Application in Endodontics

An in vivo study performed by Bonsor et al. (2006) concluded that "Results indicate that the use of a chelating agent acting as a cleaner and disrupter of the biofilm and photo-activated disinfection to kill bacteria is an effective alternative to the use of hypochlorite as a root canal cleaning system."

Another in vivo study published as well in 2006 by the group of Bonsor researched the ability of PAD to compliment conventional RCT disinfection and concluded that "The PAD system offers a means of destroying bacteria remaining after using conventional irrigants in endodontic therapy."

Williams et al. (2006) tested the efficacy of PAD on Fusobacterium nucleatum, Peptostreptococcus micros, Prevotella intermedia and Streptococcus intermedius and concluded that "PAD killed endodontic bacteria at statistically significant levels compared to controls."

Garcez et al (2008), in an in vivo study, researched the "Antimicrobial Effects of Photodynamic Therapy on Patients with Necrotic Pulps and Periapical Lesion" and their results suggested "that the use of PDT added to endodontic treatment leads to an enhanced decrease of bacterial load and may be an appropriate approach for the treatment of oral infections."

The research hypothesis of Bergmans et al. (2007) was: "To test the hypothesis that photoactivated disinfection (PAD) has a bactericidal effect on pathogens inoculated in root canals, with emphasis on biofilm formation/destruction." Their conclusions were: Photo-activated disinfection is not an alternative but a possible supplement to the existing protocols for root canal disinfection as the interaction between light (diode laser) and associated dye (TBO) provides a broad-spectrum effect."

The research goal of Garcez et al. (2006) was "To compare the effectiveness of antimicrobial photodynamic therapy (PDT), standard endodontic treatment and the combined treatment to eliminate bacterial biofilms present in infected root canals."

Their results: "Endodontic therapy alone reduced bacterial bioluminescence by 90 per cent while PDT alone reduced bioluminescence by 95 per cent. The combination reduced bioluminescence by >98 per cent, and importantly the bacterial regrowth observed 24 hours after treatment was much less for the combination ($P<0.0005$) than for either single treatment."

The in vitro study of Soukos et al. (2006) ended with the conclusion that "PDT may be developed as an adjunctive procedure to kill residual bacteria in the root canal system after standard endodontic treatment."

Pinheiro et al. (2007) study was to "evaluate photodynamic therapy in deciduous teeth with necrotic pulp by means of fully quantifying viable bacteria, before and after instrumentation and after the use of photodynamic therapy". They concluded that "Photodynamic therapy is recommended as adjunct therapy for microbial reduction in deciduous teeth with necrotic pulp."

When using Methylen blue as PS, Fimple et al. (2008) concluded "that PDT can be an effective adjunct to standard endodontic antimicrobial treatment when the PDT parameters are optimised."

The research group around Lim (2009), calling the PAD process "Light Activated Disinfection" (LAD) used "biofilms of Enterococcus faecalis at two different stages of maturation" and extracted teeth. The results of the study showed "Sodium hypochlorite and improved LAD showed the ability to significantly inactivate bacteria in four-day-old biofilms when compared to the control and LAD ($p < 0.05$). Inactivation of bacteria from deeper dentine was higher in improved LAD than sodium hypochlorite. In four-week-old biofilms, a combination of chemomechanical disinfection and improved LAD produced significant bacterial killing compared to either chemomechanical disinfection or improved LAD alone."

'Confirming treatment efficacy is a demanding and highly time-, resource-and finance-consuming process.'

Souza et al (2010) compared the efficacy of Methylen blue and Toluidine blue as an adjuvant in root canal disinfection. Their conclusions were "These in vitro results suggest that PDT with either MB or TB may not exert a significant supplemental effect to instrumentation/irrigation procedures with regard to intracanal disinfection. Further adjustments in the PDT protocol may be required to enhance predictability in bacterial elimination before clinical use is recommended." It may be noted that the culture media for E. faecalis may play a role in the different outcomes.

Based on current knowledge and evidence the author suggests the implementation of PAD in root canal disinfection once conventional protocol completed.

Conclusion

PAD is not at all a new concept. It has proven it s efficacy in action over almost the last hundred years. New microbiologic knowledge is continuously compensated with advanced research in light emitting sources. Intensive work is committed into the identification process of correlating adequate PS to specific bacterial infection, enhancing dye penetration, adjusting light exposure time, etc.

On the other side numerous new applications arise. Confirming treatment efficacy is a demanding and highly time-, resource-and finance-consuming process. Rewards are amazing taking under consideration the huge added benefits in regards of antibiotic resistance. DT

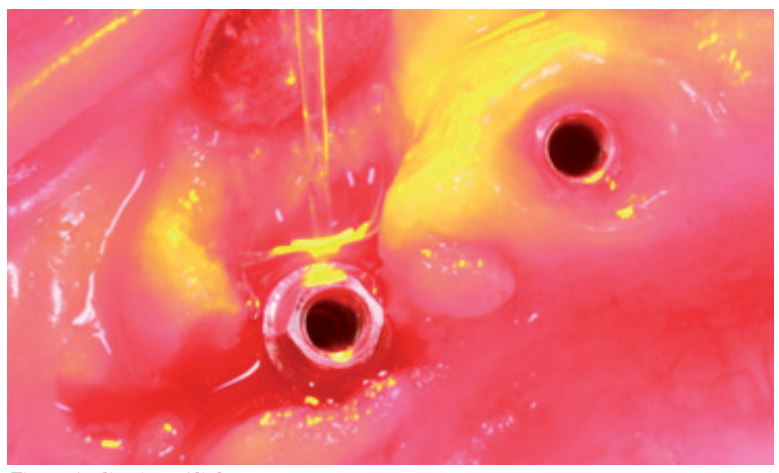

Fig8 – Application of light source

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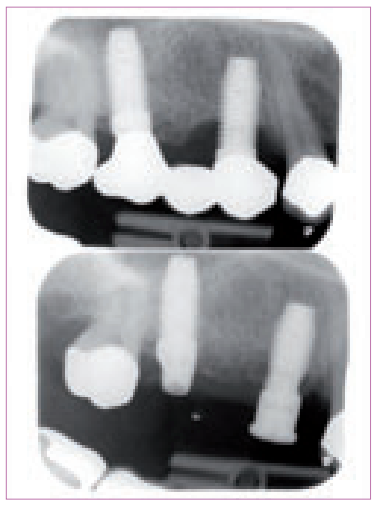


Fig9 – Pre-operative and post-operative (six-month recall) radiographs of a peri-implantitis affected and treated implant. The treatment involved implantplastic

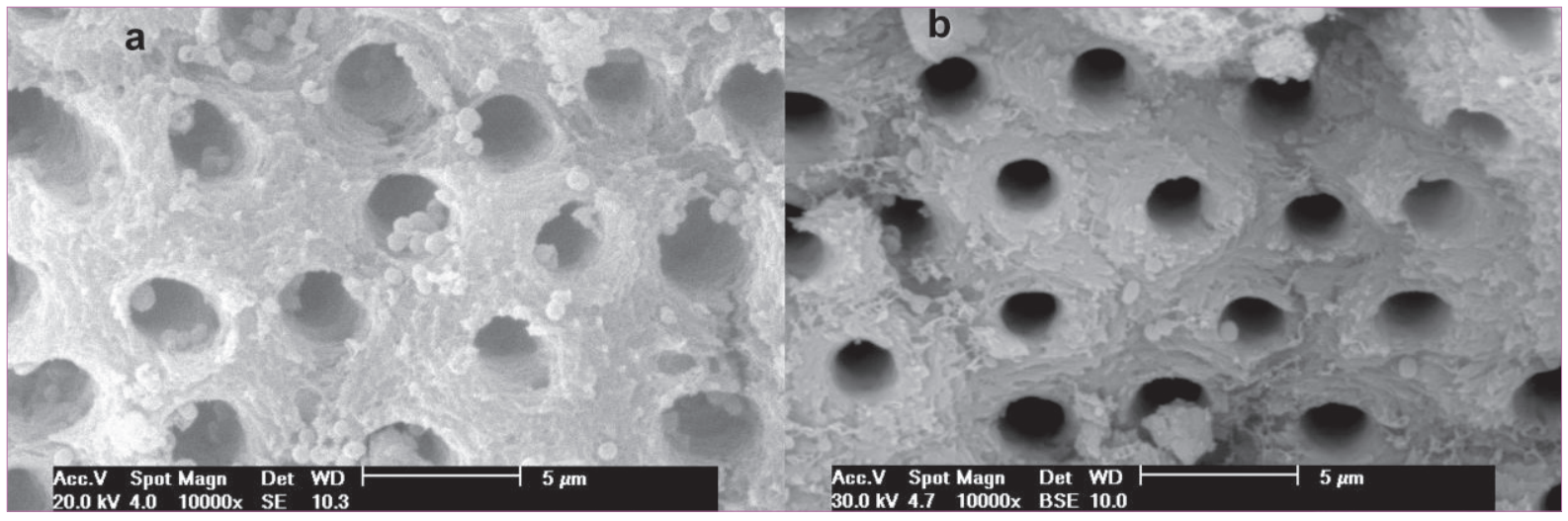


Fig10 – (a&b) A cross-sectional view of the dentinal tubules a - before PAD activation (control group) b - after PAD activation – SEM 10000x

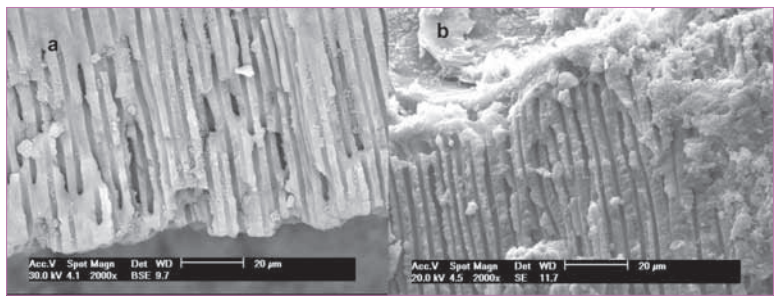


Fig11 – (a&b) The roots were split in halves, then SEM/BSE observations were made along the dentinal tubules starting from the canal wall through the tubules. The length of action of PAD was assessed (Mm) – this image shows the overall look of the control group, with e faecalis invading the whole length of the tubules. SEM 2000x; a – control, b - PAD

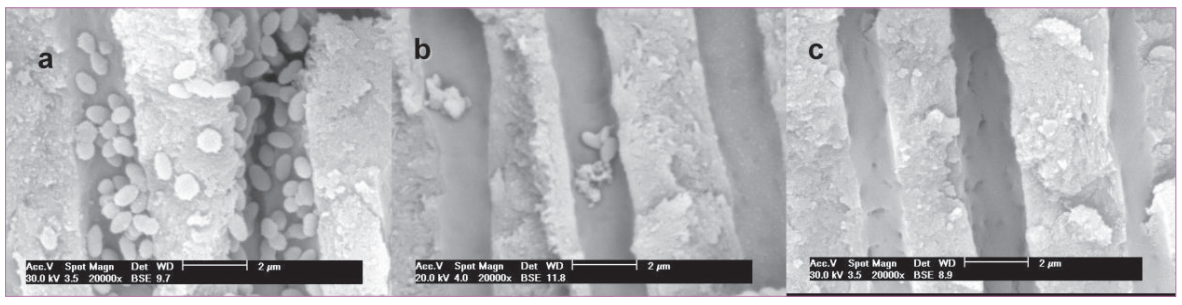
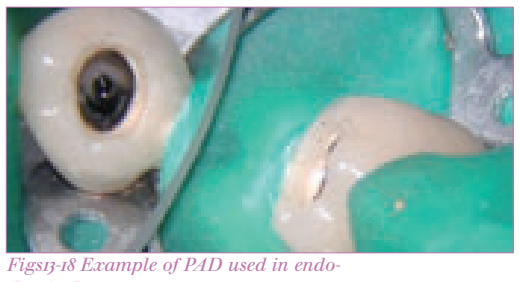


Fig12 - Assessment of the length of action of PAD was assessed (Mm) – Backscattering (BSE) SEM 20000x; a – control - e faecalis invading the whole length of the tubules; b - PAD activation – small number of e faecalis invading the tubules, with dentinal tubules free of the bacteria to a length of 20 Mm; c - PAD activation – dentinal tubules free of the bacteria to its whole length



Figs13-18 Example of PAD used in endodontic therapy

Fig 14

Fig 15

Fig 16

Fig 17

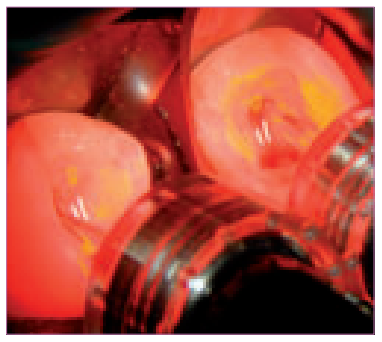


Fig 18

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