

Periowave Photodisinfection System

Received.....11.10.08 Scientific Review..... 11.24.08 IAOMT Board Review.....03.26.09 Reevaluation or Revision.....	Periodontal Therapy Periowave™ Photodisinfection System	Approval.....03.26.09 Provisional Approval No Opinion No Approval
--	---	---

Explanation of IAOMT position: Thorough periodontal disinfection – well done SR

Name of Scientific Review: Periowave™ Photodisinfection System
Alternative name(s) of Scientific Review: Photodynamic Therapy for the Treatment of Periodontal Disease
This Scientific Review is related to: Dentistry and Medicine
This Scientific Review is a: Equipment and Procedure
Purpose of the Scientific Review: To facilitate the disinfection of periodontal pockets and initiate healing by eliminating many of the pathological microorganism species known to be causative in periodontal disease.
<p>Scientific Review History: Lasers have been shown to be effective for killing all types of pathogens. With the subsequent development and use of photo-initiator chemicals or dyes to selectively target pathogens known to be associated with periodontal disease, products and procedures were developed that could effectively disinfect infected periodontal pocket sulcus sites without the use of heat. This non-heat process alleviates the potential for tissue damage and therefore the need for either anesthesia or post-operative wound healing while still maintaining effective microbial kill statistics.</p> <p>This therapy, known as Photodynamic Therapy or PDT, employs a non-toxic dye, called a photosensitizer, and a low intensity visible light which, in the presence of oxygen, combine to produce cytotoxic species that are able to effectively kill all forms of microbes. Infections of the mouth are mostly localized in nature but if left untreated can lead to potentially life-threatening medical conditions. As most mouth infections are readily accessible to the products and procedures of PDT, they are therefore well suited to treatment by this modality. Applications of PDT in dentistry are growing rapidly for the treatment of oral cancer, bacterial and fungal infections, and the photodynamic diagnosis of the potential transformation of oral lesions. Periowave™ is a PDT system specifically designed and engineered for the treatment of periodontal infections and is certified for sale and use in Canada for this purpose.</p>
<p>A <u>brief</u> description of the Scientific Review: After the appropriate scaling and debridement of a patient, a proprietary photosensitizing solution is injected into an infected periodontal pocket site. The photosensitizing solution is able to selectively attach to targeted species of pathogens in the desired treatment area. A non-thermal diode laser attachment is then inserted into the pocket and illuminated for a 60 second interval to activate the solution. This photoactivation of the solution leads to the formation of reactive oxygen species which are able to break the cell walls structures of the targeted pathogens, and as in the case of the Periowave™ system, eliminate the pathogens associated with periodontal disease. This effectively disinfects the sulcus and or diseased periodontal pockets being treated, and promotes the successful healing of the affected surgical site.</p>
<p>A <u>specific</u> description of this Scientific Review: Biofilms play a very important and potentially destructive role in periodontal disease. They are structured communities of microorganisms that live within an encapsulated or</p>

enclosed mucilaginous, polymeric matrix secretion. This mucinous, gel like secretion permits the biofilms to attach to tooth surfaces and the epithelium of the sulcus, and acts as a protective barrier to assaults from both exogenous, (eg. antibiotics), and endogenous, (host immune responses), sources. In periodontal disease, the unique protective properties of the biofilm are even more significant, due to the secluded nature of the host site in which these microbes live, (the periodontal pocket), and makes definitive treatment of periodontal disease more difficult. While most of the 500+ known sulcular species of bacteria are thought to be commensals, (neither helping nor harming the host), there are a number of pathogenic species that are capable of triggering an immune response, even in relatively low numbers. The presence of even small numbers of disease associated microorganisms therefore, is cause for concern. Treatment modalities include the use of antibiotics, the physical manipulation of the biofilms, and the use of chemical or antimicrobial solutions to disinfect or eliminate the biofilm. A recent innovation for the treatment of biofilms/pathogens in periodontal disease is the use of lasers. Photodynamic periodontal therapy is only one out of a number of these techniques that was developed for the elimination of microbial pathogens. The Photodynamic Periodontal Therapy protocol, or PDT protocol, is a two step procedure, involving the topical application of a chemical photosensitizer, followed by the selective illumination of the target lesion with the laser light source.

Periowave™ is a PDT protocol that has been designed and marketed utilizing this technology. In the Periowave™ protocol, a non-thermal diode laser light that maintains temperatures and energy levels below destructive doses for normal hard and soft tissues is utilized. The laser light cannot by itself eliminate pathogenic species associated with periodontal infections. When the laser light is combined however, with a matching wavelength-specific photosensitizing dye, a unique chemical reaction is initiated. In the presence of oxygen, the transfer of energy from the laser light to the photosensitive dyes activates them and they are then able to transfer this energy to available oxygen molecules, generating reactive oxygen species. These reactive oxygen species have the capacity to damage proteins, lipids, nucleic acids, and other cellular components. It is these reactive oxygen species that are cytotoxic to, and can effectively kill, many if not all of the pathogens associated with periodontal disease. Photodynamic periodontal therapy, (PDT) is capable of effectively killing bacteria, including both wild and antibiotic resistant strains, viruses, yeasts, and parasites. These photosensitizing dyes by themselves are non-toxic to human hard and soft tissues and alternatively by themselves are not cytotoxic to pathogens. As chemical dyes however, they can be matched to selectively attach to only the desired pathogen species and thus avoid the potential for attachment to, and the subsequent destruction of, cells of the host organism when photoactivated. PDT has this unique advantage of dual selectivity, in that the photosensitizers can be targeted to very specific pathogenic organisms, and in addition, the illumination procedure can be localized to only the area of concern. This selectivity for microbes over host cells, the accurate delivery of the photosensitizers to the affected areas, and the dose adjustment abilities, help minimize side effects and give PDT an advantage over conventional therapies. The dyes can be controlled to selectively adhere to only pathogenic species of microbes leaving desirable bacterial species intact. It is not necessarily desirable to kill the entire microbial flora in the sulcus, as this could leave a patient open to other opportunistic infections.

When used in combination with normal routine scaling and root planning procedures, photodisinfection is shown to have significant improvements in post-operative healing success over the use of scaling and root planning alone. Photodisinfection procedures done in conjunction with scaling and root planning have been shown to statistically decrease the periodontal pocket depths of infected sites better than scaling and root planning alone. Photodisinfection has shown great promise as well, as an effective therapy for controlling bone loss in furcation areas in periodontitis.

Chemical antibacterial agents and mouthwashes are increasingly being used in prophylactic and therapeutic regimes for dental plaque-related diseases. As these agents are difficult to maintain at the therapeutic concentrations in the oral cavity and can be rendered ineffective by resistance development in the target organisms, there is a need for alternative therapies. Many pathogens are becoming resistant to antibiotics through their over-use in either systemic or topical applications. The continued reliance of antibiotics and antiseptic agents creates the potential for mutagenic processes of these microbes or the selective resistance of microbial cells. PDT procedures are an effective alternative to these traditional treatment therapies as the method of action is from oxidative reactive processes and does not lead to bacterial-resistance. As microbial cell death is primarily a consequence of membrane photodamage, the risk for either the onset of mutagenic processes and or the selection of photoresistant cells has not been seen. This approach is therefore a useful alternative to antibiotic and antiseptics in eliminating periodontopathogenic bacteria while at the same time conserving the dwindling supply of antimicrobial agents that

are effective in the treatment of serious systemic infections.

The specific Periowave™ Protocol for disinfection of infected periodontal pockets, as per the manufacturer is:

1. Irrigation: After traditional scaling and debridement, Periowave™ photosensitizing solution is irrigated into an infected periodontal pocket. To thoroughly irrigate each treatment site with Periowave™ photosensitizer solution; place the irrigation cannula at the base of the treatment site pocket and slowly deliver the solution while gently moving the cannula back-and-forth in a mesiodistal direction. Continue to irrigate the pocket until a small quantity of solution can be seen flowing over the free gingival margin. Only one treatment area or site should be irrigated at a time to prevent gingival crevicular fluids from flushing out sensitizer solution out of the pockets of concern before the illumination step can be completed.

2. Illumination: The non-thermal diode laser light tip is inserted into the periodontal pocket and activated to illuminate the solution filled treatment area for a 60 second period. To achieve optimum results, the tip should be walked around the treatment area defect during illumination in both an apico-coronal and mesio-distal direction, without allowing the tip to rise above the gingival crest. Reactive oxygen species formation follows. These reactive oxygen species; 1). damage bacterial cell membranes facilitating the killing of these pathogenic bacteria, and 2). are capable of inactivating the virulence factors associated with these pathogens. Any pockets greater than 4 mm that present with bleeding on probing should be re-treated at 3 to 6 weeks to prevent the re-establishment of biofilms during the healing process. Very deep pockets, implant sites, and refractory pockets have a better healing response after a second application of the treatment protocol at the initial treatment appointment.

Periowave™ is ideally targeted for patients with bleeding on probing and all pockets of 4 - 9 mm length that bleed on probing. Periowave™ should only be used following a thorough scaling and root planing debridement and after any moderate to severe post-instrumentation bleeding has been controlled. Successive, (recall), treatments may benefit from light manual debridement prior to treatment. Each defect should be treated separately, and contralateral sides of each tooth checked, especially at interproximals, as these sites may benefit from additional photodisinfection as well. Long-term results may be significantly enhanced by a follow-up treatment 3-6 weeks after the first treatment. Patient outcomes should include a reduction or elimination of bleeding on probing, an improvement in gingival tissue tone and texture, and a reduction in pocket depth.

Manufacturer(s):

Ondine Biopharma Corporation
#910 - 1100 Melville Street
Vancouver, BC, V6E 4A6

Periowave™ is strictly a minimally invasive therapy for the destruction of pathogenic flora. The unit currently sells for under \$5,000.00 Canadian which is the equivalent of about \$4,000.00 U.S. and with all the attachments, kits, etc, is only about \$7,000.00 Canadian - total. It has the potential to be a simplified tool for the entire dental team of a biological dental office, i.e. as it is marketed, for the **hygienist** to use in office, and without dentist supervision to effect a **disinfection** of the sulcular/diseased pocket areas. It has the ability to be one more tool in a limited family of effective treatment modalities, (i.e. versus drug or chemical therapies), for the average dentist to help his periodontally compromised patients achieve better oral health.

Distributors:

Henry Schein Canada, Patterson Dental Canada Inc., or Sinclair Dental Co. Ltd.

Scientific Literature:

Andersen R, Loebel N, Hammond D, Wilson M., Treatment of periodontal disease by photodisinfection compared to scaling and root planning. J Clin Dent. 2007; 18(2): 34-38

- Bhatti M, MacRobert A, Henderson B, Shepherd P, Cridland J, Wilson M, Antibody-Targeted Lethal Photosensitization of *Porphyromonas gingivalis*., *Antimicrob. Agents and Chemotherapy*; 2000 Oct; 44(10): 2615-2618
- Bhatti M, MacRobert AJ, Meghji S, Henderson B, Wilson M., A study of the uptake of toluidine blue O by *Porphyromonas gingivalis* and the mechanism of lethal photosensitization. *Photochem Photobiol* 1998 Sep; 68(3): 370-376
- Bhatti M, MacRobert AJ, Meghji S, Henderson B, Wilson M., Effect of dosimetric and physiological factors on the lethal photosensitisation of *Porphyromonas gingivalis* in vitro. *Photochem Photobiol* 1997 Jun; 65(6): 1026-1031
- Calzavara-Pinton PG, Venturini M, Sala R., A comprehensive overview of photodynamic therapy in the treatment of superficial fungal infections of the skin., *J Photochem Photobiol B*. 2005 Jan 14;78(1) :1-6
- de Almeida JM, Theodoro LH, Bosco AF, Nagata MJ, Oshiiwa M, Garcia VG., Influence of photodynamic therapy on the development of ligature-induced periodontitis in rats., *J Periodontol*. 2007 Mar; 78(3):566-575
- de Almeida JM, Theodoro LH, Bosco AF, Nagata MJ, Oshiiwa M, Garcia VG., In vivo effect of photodynamic therapy on periodontal bone loss in dental furcations., *J Periodontol*. 2008 Jun;79(6): 1081-1088
- de Almeida JM, Theodoro LH, Bosco AF, Nagata MJ, Bonfante MJ, Garcia VG., Treatment of Experimental Periodontal Disease by Photodynamic Therapy in Rats With Diabetes., *J Periodontol*. 2008 Nov;79(11): 2156-2165
- Demidova TN, Hamblin MR, Photodynamic therapy targeted to pathogens. *Int J Immunopathol Pharmacol*. 2004 Sep-Dec;17(3):245-254
- Demidova TN, Hamblin MR, Effect of cell-photosensitizer binding and cell density on microbial photoinactivation. *Antimicrob Agents Chemother*. 2005 Jun;49(6):2329-2335
- Dobson J, Wilson M., Sensitisation of oral bacteria in biofilms to killing by light from a low-power laser. *Arch Oral Biol* 1992 Nov; 37(11): 883-887
- Hamblin MR, Hasan T., Photodynamic therapy: a new antimicrobial approach to infectious disease? *Photochem Photobiol Sci*. 2004 May;3(5):436-50. Epub 2004 Feb 12
- Hayek RR, Araujo NS, Gioso MA, Ferreira J, Baptista-Sobrinho CA, Yamada AM, Ribeiro MS., Comparative study between the effects of photodynamic therapy and conventional therapy on microbial reduction in ligature-induced peri-implantitis in dogs. *J Periodontol*. 2005 Aug;76(8):1275-1281
- Jori G., Photodynamic therapy of microbial infections: state of the art and perspectives. *J Environ Pathol Toxicol Oncol*. 2006;25(1-2):505-519
- Jori G, Fabris C, Soncin M, Ferro S, Coppellotti O, Dei D, Fantetti L, Chiti G and Roncucci G., Photodynamic Therapy in the Treatment of Microbial Infections: Basic Principles and Perspective Applications. *Lasers Surg Med*. 2006 Jun; 38(5):468-481
- Komerik N and MacRobert AJ., Photodynamic therapy as an alternative antimicrobial modality for oral infections. *J Environ Pathol Toxicol Oncol*. 2006; 25(1-2) : 487-504
- Komerik N, Wilson M, Poole S., The effect of photodynamic action on two virulence factors of gram-negative bacteria. *Photochem Photobiol*. 2000 Nov;72(5):676-680
- Konopka K and Goslinski T., Photodynamic therapy in dentistry. *J Dent Res* 2007; 86(8):694-707
- Maisch T., Anti-microbial photodynamic therapy: useful in future? *Lasers Med Sci*. 2007 Jun;22(2):83-91. Epub

2006 Nov 21

Matevski D, Weersink R, Tenebaum HC, Wilson B, Ellen RP, Lepine G., Lethal photosensitization of periodontal pathogens by a red-filtered Xenon lamp in vitro. *J Periodontol Res.* 2003 Aug;38(4):428-435

Meisel P, Kocher T., Photodynamic therapy for periodontal diseases: state of the art. *J Photochem Photobiol. B.* 2005 May 13; 79(2): 159-170

Pfitzner A, Sigusch BW, Albrecht V, Glockmann E., Killing of periodontopathogenic bacteria by photodynamic therapy. *J Periodontol.* 2004 Oct;75(10): 1343-1349

Reszka KJ, Denning GM, Britigan BE., Photosensitized oxidation and inactivation of pyocyanin, a virulence factor of *Pseudomonas aeruginosa*. *Photochem Photobiol.* 2006 Mar-Apr; 82(2):466-473

Sakar S, Wilson M., Lethal photosensitization of bacteria in subgingival plaque from patients with chronic periodontitis. *J Periodontal Res.* 1993 May;28(3):204-210

Shibli JA, Martins MC, Theodoro LH, Lotufo RF, Garcia VG, Marcantonio EJ., Lethal photosensitization in microbiological treatment of ligature-induced peri-implantitis: a preliminary study in dogs. *J Oral Sci.* 2003 Mar;45(1):17-23

Sigusch BW, Pfitzner A, Albrecht V, Glockmann E., Efficacy of thermodynamic therapy on inflammatory signs and two selected periodontopathogenic species in a beagle dog model. *J Periodontol.* 2005 Jul;76(7):1100-1105

Street CN, Gibbs A, Pedigo L, Andersen D, Loebel NG., In vitro photodynamic eradication of *Pseudomonas aeruginosa* in planktonic and biofilm culture, *Photochem Photobiol.* 2008 Jul 30

Tang HM, Hamblin MR, Yow CM., A comparative in vitro photoinactivation study of clinical isolates of multidrug-resistant pathogens. *J Infect Chemother.* 2007 Apr;13(2):87-91. Epub 2007 May 8

Teichert MC, Jones JW, Usacheva MN, Biel MA., Treatment of oral candidiasis with methylene blue-mediated photodynamic therapy in an immunodeficient murine model. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod.* 2002 Feb;93(2):155-160

Usacheva MN, Teichert MC and Biel MA., Comparison of the methylene blue and toluidine blue photobactericidal efficacy against gram positive and gram negative microorganisms. *Lasers Surg. Med.* 2001; 29(2): 165–173

Usacheva MN, Teichert MC, Sievert CE, Biel MA., Effect of Ca⁺ on the photobactericidal efficacy of methylene blue and toluidine blue against gram-negative bacteria and the dye affinity for lipopolysaccharides. *Lasers Surg Med.* 2006 Dec;38(10):946-954

Wainright M., Photodynamic antimicrobial chemotherapy (PACT). 1998 Jul;42(1):13-28

Wilson M., Bactericidal effect of laser light and its potential use in the treatment of plaque related diseases. *Int Dent J.* 1994 Apr;44(2):181-189

Wilson M., Lethal photosensitization of oral bacteria and its potential application in the photodynamic therapy of oral infections. *Photochem Photobiol Sci.* 2004 May;3(5):412-418. Epub 2004 Feb 5

Wilson M, Dobson J., Lethal photosensitization of oral anaerobic bacteria. *Clin Infect Dis.* 1993 Jun;16 Suppl 4:S414-5

Wilson M, Dobson J, Sarkar S., Sensitization periodontopathogenic bacteria to killing by light from a low-power laser. *Oral Microbiol Immunol.* 1993 Jun;8(3):182-187

Wilson M., Mia N., Sensitization of Candida albicans to killing by low-power laser light. J Oral Pathol Med. 1993 Sep;22(8):354-357

Below are the titles from three sources of information provided by the manufacturer that would indicate their successes with periodontal pocket depth reductions while utilizing their system.

- 1. Loebel N, Andersen R, Hammond D, Leone S, and Leone V, Ondine Biopharma Corporation. Non-Surgical Treatment of Chronic Periodontitis Using Photoactivated Disinfection. International Association of Dental Research, March 2006.
- 2. N.G. Loebel, R. Andersen, Y. Li, R. Shu, X. Zhang., Meta-Analysis of Three Chronic Periodontitis Trials with Periowave™ Photodisinfection, International Association of Dental Research, March 2008
- 3. A Multi-Center, Randomized, Examiner-blinded Study of Photodisinfection in the Treatment of Chronic Periodontitis.

Legal Aspects of this Scientific Review: Periowave™ has been approved for sale and use by Health Canada since March of 2006. Ondine Biopharma Corp. is currently seeking FDA approval to distribute this product in the United States.

To date there are no known drug interactions with the use of the Periowave™ system. Theoretical there may be a concern for patients with severe Glucose-6-phosphate dehydrogenase deficiency but since the Periowave™ photosensitizer is not ingested during a normal treatment procedure, this outcome would be extremely unlikely and should therefore not be at risk to cause a reaction.

Periowave™ is not contraindicated in pregnancy or lactating women.

Applicant Name: Nestor Shapka, DDS, FIAOMT		Office Phone: 780-826-5333
Mailing Address: P.O. Box 5245, 5029-50 Avenue,		Office FAX: 780-826-2947
City: BONNYVILLE		Home Phone: 780-826-2480
State of Province: Alberta	Postal Code: T9N 2G4	Home FAX:
Country: Canada		e-mail: nestor_shapka@hotmail.com
IAOMT Member #: 949		IAOMT Chapter: North American