

Minimally Invasive Laser Decontamination MILD®—A New Procedure for the Treatment of Marginal Periodontopathies and Periimplantitis

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Even though the concept of photodynamic therapy had already been discovered and described for the first time in 1900 by Paul Ehrlich, the method became generally accepted only hesitantly. Hermann von Tappeiner, a dermatologist from Munich, had defined the clinical approach of the photodynamic therapy as early as 1904.

But it took almost a century until medical science recognized the usefulness of this form of therapy and tried to integrate it into their treatment.

Today, anti microbial photodynamic therapy is used primarily for the treatment of tumors and, since the beginning of the 1990s, also increasingly in dentistry.

Here, it is periodontal and periimplantitis treatments that are of particular interest for their use in photodynamic therapy.

Confusing are, however, the mere vast number of sensitizers, laser wavelengths and parameters, therefore the recommendations of the authors for these uses sometimes differ considerably. An Austrian company broke new ground, not only manufacturing the low-level laser itself but also offering the photo sensitizer still required.

That supplier goes even a step further and offers the aPDT as a "complete module" for the integration of this concept in dental practice. In comparison to the already mentioned "flood of sensitizers and laser parameters", in this case a strict protocol is specified.

After an initial euphoria, the interest in photodynamic therapy has considerably and quickly cooled off, and hopes for stimulating effect for the entire laser dentistry failed to materialize.

Aside from the still poor documentation of the method regarding the verification of effective results in dentistry, the relatively high price for the described "complete method" might also have contributed to this fact.

Despite this development, photodynamic therapy still commands a high appeal and interest for dental professionals, still offering an option for an actual minimally invasive procedure!

Accordingly, our goal was to develop a method, which

- is based on detailed fundamental research
- does not have an antimicrobial effect by the use of the sensitizer itself
- does not leave sensitizer remains on teeth and implants
- delivers long-lasting results.

This method, developed by a successful team is referred to as "MILD – Minimally Invasive Laser Decontamination" and will be introduced in the following text in detail.

General information regarding the concept of antimicrobial photodynamic therapy

Idea and fundamentals of the PT concept

According to the underlying evidence-based periodontological data, the biofilm becomes the focus of interest in periodontology and therefore also in PT. The PT is based on the interaction between a stain (sensitizer), laser light, and pathogenic germs: Those pathogenic (mostly gram-negative anaerobic) bacteria are stained with a special photosensitizer, followed by laser light application in the low-level range (previously referred to as "soft laser"), and the singulett oxygen released in the process damages the membrane of the bacteria to such an extent that it is not compatible with the further survival of the germ.

Pretreatment

Almost all relevant working groups, which rendered outstanding services to the PT in the last several years like [Siegusch [Germany], Neugebauer [Germany], Bogaerts [Belgium], Sculean [Netherlands], and Frentzen [Germany] call for a thorough pretreatment prior to PT. This is both true for patients suffering from the periodontal disease, as well as for patients with periimplantitis having manifested itself on their artificial tooth posts. The following pretreatment steps are generally described in literature (independent of the sensitizer and the PT method favored):

- Depuration and patient instructions
- Findings, precision cleaning and subsequent utilization of PT
- Checkup after seven days (if bleeding is persistent on probing: repeat PT)
- Recall (the first one after six to eight weeks, after that in quarterly intervals).

Present long-term observations in PT

The active principle of PT in dentistry has been described in many publications by Prof Dörtbudak (Vienna University, Austria) since the beginning of the 1990s (still with the photo sensitizer Toluidine Blue

used at that time). With the rediscovery of PT, and most importantly based on the activities of Helbo Company, dental practices increasingly switch to this treatment option.

Initial long-term data—quite naturally—are reported primarily from the country this method originates from, Austria, and here, the study by Mrs. Schütze-Gössner (representative practice for Helbo Company in Salzkammergut, Austria) particularly deserves to be mentioned: In 2006, this Austrian dentist was able to report the following long-term observations regarding the benefits of PT achieved in her practice.

She presented a total of 20 female and male patients, who underwent PT (at Helbo also referred to as aPDT) and the subsequent recall in a time period of 29 to 54 months. Teeth, which could not be preserved, were extracted before the start of the therapy; germ tests were, however, only done on eleven from 20 patients. In two patients, despite the use of PT additional flap operations were required.

In short, Schütze-Gößner reports about positive clinical parameters following the completion of aPDT without secretion accumulation in the pockets and BOP persistence in only 1.7% of all cases.

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Regarding general guidelines and methodology this study does not meet general requirements for a systematic study leading to verifiable conclusions.

Other more recent bibliographical references also originate from Germany but those tend to cover shorter observation time periods (four weeks up to a year). The extraordinary clinical benefits of the method are always highlighted in those reports, leading to considerable improvement in the clinical (inflammation) reaction:

Siegusch

In several publications assistant professor Siegusch (Germany) could confirm the minimally invasive procedure of the photodynamic therapy, as well as a considerable improvement of all clinical parameters following recent PT in marginal periodontopathy. He attributes high importance and an enormous future potential to the method.

Neugebauer

The first German academic publications originated from the Cologne Working Group with Neugebauer and Zöller, who used PT alongside their "classic field" of periodontology within the scope of a periimplantar lesion for the improvement of wound healing, reporting unconditionally positive results.

Sculean

Professor Sculean (Netherlands) assesses the perceived value of the photodynamic therapy slightly more soberly when reporting at the annual AGLZ conference in Düsseldorf that PT can contribute to the improvement of periodontal health.

Bogaerts

At the ISLD 2006 in Berlin, a Belgian working group including Bogaerts and colleagues reported, among other things, a distinct germ-killing effect of photodynamic therapy following simultaneous low heating. This working group ruled out damage to the dental pulp caused by PT.

Eberhard

As a "master thesis" for obtaining the academic title of "M.Sc.—Master of Science", Eberhard presented a study to his colleagues, demonstrating the results of a long-term analysis of patients treated with PT.

With the predominant number of patients treated, one-time use of PT already led to treatment success. A small number of patients had to repeat treatment and sometimes additional medical aids were required.

Stoll, Bähr and Bach

This Freiburg working group confirmed a significant improvement of the clinical parameters fol-

lowing PT but pointed out a clearly verifiable bactericidal effect of photo sensitizer Phenotiazine (HelboBlue) and sensitizer remaining attached to implants and teeth with deep defects, which were not removable.

Minimally invasive laser decontamination—MILD®

I—The philosophy of MILD procedure:

The goal of the MILD diode laser with a wavelength of 810 nm in combination with a sensitizer is the tackling of the biofilm and interruption of the QUORUM SENSING (cell-to-cell communication of bacteria starting at a certain number).

Precisely, the prevention of the last process is of a big importance according to the opinion of many periodontologists because the bacteria's cells divide every 20 minutes. According to the inaugurator of PT in dentistry, Austrian microbiologist Dörtbudak, the procedure leads to light-induced deactivation of cells, microorganisms and molecules. The mechanisms of this action would, in case it proves its value in periodontology and the treatment of periimplantitis, later make the application of MILD in the therapy of tumors and in endodontology appear even more meaningful at a later point in time.

II—Assumed side effects of MILD procedure:

MILD procedure must not be carried out on patients with iodine allergies because PS Indo Cyanine Green could trigger an allergic reaction in these patients.

Furthermore, a time-limited green coloring of the gingiva, which came into contact with the PS, is expected. Permeable filling edges must also to be paid close attention to because they could become colored permanently.

III—Documentation of the Basics

a) The wavelength

The goal was to develop a protocol for PT with the diode wavelength of 810 nm as established in dentistry. Diode lasers with 810 nm wavelengths are used in the hard laser field for soft tissue surgery since 1994 and for decontamination in periodontology and implantology. This wavelength has been well documented for long-term periods, amongst others, in the only 10-year study about the use of laser light decontamination in periimplantitis and in the treatment of marginal periodontopathies.

b) The sensitizer

INDOCYANINE GREEN is used as a photosensitizer, the pathogenic bacteria being stained and sensitized by this photosensitizer and subsequently totally eliminated by laser light. Indocyanine green is used in human medicine as an intra-

venous infusion for checking the effectiveness of the blood circulation in the heart, for monitoring blood circulation, for assessing the function of the liver, and is available as a concentrate, which has to be diluted.

c) Absorption characteristics

At the NTA meeting in Isny, research regarding the absorption maximum of the potential sensitizer was performed by the study group with Professor Dr Donges. The tests showed an absorption maximum at approx. 800 nm. Therefore the sensitizer matches the wavelength of the used diode laser (810 nm).

d) Achieving an optimal active component concentration

In order to determine the optimal sensitizer concentration, two test runs in combination with microbiological examinations were performed. The first series of test runs were done with 1:10, 1:20, 1:30 and 1:40 dilutions.

Those dilutions produce a clearly dark-green sensitizer, which was applied on microbiological agar plates, which, in turn, were irradiated with laser light, following the rinsing and removing of excessive dye. The findings from those dilutions and the used laser parameters, however, did not generate positive results (see section microbiological examinations), there were effects associated with the inhibition of germinal growth caused by the sensitizer itself and also manifestations caused by heat damage, which were achieved by high sensitizer concentration in combination with laser light (high absorption). After evaluating these results and followed by a phase of reevaluation, another test run with using a 1:100 dilution was undertaken. This concentration in combination with the appropriate laser light parameters generated satisfactory microbiological results. Therefore the 1:100 dilution was determined to be the ideal concentration of the active component of the MILD sensitizer.

d) Testing for antimicrobial effects of the sensitizer itself

Following the evaluation of our own research with a sensitizer from a popular PT supplier, it had to be determined that an antimicrobial effect can already be achieved with that particular PS. This germ killing effect was confirmed by the German subsidiary of the manufacturer but is definitely inferior to the results achieved by simultaneous application of laser light and sensitizer. When diluting the sensitizer ICG used by us, a clearly germ killing and germ growth inhibiting effect could also be established in dilutions of up to 1:40 by applying the sensitizer alone. With higher dilutions starting from 1:100, those effects could not be observed any longer.

e) Avoidance of sensitizer residuals on the surfaces of teeth and implants following MILD procedure

In our own research we noticed sensitizer residuals on the roots of teeth and on implants, following previous treatment according to the PT principles of that manufacturer. Those sensitizer residuals could be observed in regions and in the area of the deepest defects of supporting tissue of tooth and implant parts not worth preserving. After an intensive discussion, the reduced metabolism in those regions causing an acidic environment with corresponding low re absorption and degradation turnover was considered to be the underlying factor. In the course of the research presented, patients, who had teeth not worth preserving or where artificial tooth posts were pending for explantation were asked if they would be agreeable to participate in MILD therapy for testing purposes. The therapy was performed following the guidelines of the respective protocol and was subsequently followed by the removal of non-rescueable teeth/implants. These teeth were evaluated clinically and were subsequently assessed using a raster electron microscope. In these cases, sensitizer residuals on the rough implant surfaces were observed in dilutions ranging from 1:10 to 1:50. With dilutions of 1:100 and higher (based on the basic, original solution) it was not possible to clinically detect sensitizer residuals on teeth or on implants or detecting them using a raster electron microscope neither.

f) Determining efficient dilutions for the base sensitizer solution

The ICG concentrate was used as an original solution 1:10 in water, exactly how it is used in human medicine.

Tested were

- a) the change in pH
- b) the change in oxygen concentration
- c) the change in temperature in ICG solutions
- I) original solution
- II) 1:10 dilution
- III) 1:100 dilution
- IV) 1:1,000 dilution

In the basic solution and in the 1:10 and 1:100 dilutions, a significant change in the value of the pH, a significant reduction of oxygen concentration caused by the ascending oxygen following laser light application ($p = 1.0 \text{ watts/t} = 20 \text{ sec}$) could be determined.

In the original basic solution the increase in temperature in interaction with ICG and laser light was obvious with 3.2 degrees.

This increase dropped to approx. 1°C in the 1:10 and 1:100 dilutions.

With dilutions of 1:1,000 and less (only a very light green coloring of the solution could be observed), it was no longer possible to determine any verifiable effects any more.

Because of the high increase in temperature (and the results of the microbiological examinations performed at a later point in time (illegible))

g) Determination of suitable laser light parameters

A total of two test runs with different laser parameters were performed. In both test series the laser light was applied in cw-mode.

An initial analysis applying classic parameters (from the hard laser therapy) with a power output of 1.0 watts and a 20-second application of laser light did not generate any positive results in combination with sensitizer concentration dilutions ranging from 1:10 to 1:40. Either there were no actual effects of laser therapy caused by the excessive germ killing effects of the highly concentrated sensitizer alone or even—with the lowest dilutions—heat manifestations on the microbiological compounds could not be detected. Better results were only achieved only when changing to a dilution of 1:100 while at the same time the laser light was reduced to the LLLT range. The respectively best results were clearly achieved with laser light parameters of 75 mW and a duration of 15 seconds on of the application using a 1:100 dilution of the sensitizer. Longer irradiation times did not improve germ eliminating and reducing effects, shorter irradiation times, however, clearly lead to less favorable results.

Therefore, 75 mW with an application duration of 15 seconds were determined to be the ideal laser light parameters.

g) Microbiological examinations

Microbiological examinations were performed at the Institute for Hygiene and Microbiology at Freiburg im Breisgau University Hospital using four potentially periodontal pathogenic germs. These germs are

- a) *Actinobacillus actinomycetemcomitans* (A.a.) (FR68/27-7)
- b) *Porphyromonas gingivalis* (P.g.) (W381 AND Fr68/27-2))
- c) *Prevotella intermedia* (P.i.) (016/16-2).

The germs were applied to fresh agar (yeast extract, cysteine, blood agar, at A.a. also in 2 balanced sensitive test agars) using the three step streaking process (Phase I) and the flooding process (Phase II).

PHASE I:

The first part of the plates was further processed as an "empty sample" in the appropriate environment without additional manipulation.

Another part of the plates was additionally sprinkled in the center with a milliliter of ICG photosensitizer in a dilution of 1:10, rinsed with a sterile NaCl solution (0.9% buffered) following a reaction time of one minute and subsequently dried/extracted.

In the following step, the therapy laser light was applied with the parameters:

p = 1.0 watt

t = 1 minute

Wavelength: 810 nm in cw-mode.

The other half of the plates, however, was processed following the same procedure until the extraction of the diluted photosensitizer solution and subsequently rinsed; laser light application was not applied here! The A. a. test sample was incubated at 36 °C and 5–10% CO₂ for 24–48 hours, the anaerobic test samples (P.g. and P.i.), however, were further incubated under anaerobic conditions for a minimum of 48 hours.

Microbiological results of phase I

Both samples treated with sensitizer and laser light, and also the samples treated exclusively with sensitizer showed significantly slow germ growth in basically all tested germs strains, which, in terms of a quantified statement cannot be distinguished from each other.

Some of the samples had discrete lesions in terms of a heating damage in the area where the laser light fiber was placed.

There were no differences between the results in plates treated with the flooding process and between plates treated with the three step streaking process.

Conclusion phase I:

With the test set-up for phase I, no advantageous growth inhibiting effects caused by the interaction of laser light and sensitizer could be demonstrated convincingly for the bacteria tested; it could be clearly demonstrated, however, that both the laser light was overdosed and the sensitizer was concentrated too much thus causing slow growth!

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laser

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