The adjunctive use of light-activated disinfection (LAD) with FotoSan is ineffective in the treatment of peri-implantitis: 1-year results from a multicentre pragmatic randomised controlled trial

**Purpose:** To evaluate possible benefits of the adjunctive use of light-activated disinfection (LAD) in the treatment of peri-implantitis.

**Materials and methods:** A total of 80 patients with at least one implant affected by peri-implantitis defined as at least 3 mm of bone loss on baseline radiographs in the presence of signs of infection (pus exudation and/or soft tissue swelling and/or soft tissue redness) were non-surgically or surgically treated for peri-implantitis and 50% of them were randomly allocated to receive an additional LAD treatment (FotoSan) according to a parallel group design at four different centres. Only one implant per patient was considered. Outcome measures were implant failures, recurrence of peri-implantitis, complications, peri-implant marginal bone level (RAD) changes, probing pocket depth (PPD) changes and number of re-treatment sessions recorded by blinded assessors. Patients were followed up for 1 year after treatment.

**Results:** Five treated patients did not fit the original inclusion criteria: 4 because they were not affected by the present definition of peri-implantitis and 1 due to being treated with antibiotics. However, they were included according to an intention-to-treat-analysis concept. Nine patients of the LAD group were treated surgically versus 10 control patients. After 1 year, 3 patients dropped out, all from the LAD group. One implant treated with the LAD therapy failed versus none of the control group. Four complications occurred: 3 in 3 patients of the LAD group and 1 in the control group. Recurrence of peri-implantitis defined as 2 mm of peri-implant bone loss or more recorded on standardised periapical radiographs was observed in 6 patients, 3 from each group. In total, 29 implants were re-treated 1 to 4 times in the LAD group versus 33 implants 1 to 4 times in the control group; the difference was not statistically significant. Peri-implant marginal bone levels remained stable up to 1 year with no statistically significant differences between groups (0.13 mm favouring LAD therapy, 95% CI of difference -0.47 to 0.72; P = 0.68). PPD significantly reduced in both groups, and at 1 year there were no significant differences between groups (difference 0.19 mm favouring LAD therapy, 95% CI of difference -0.70 to 1.07; P = 0.68). There were significant differences between centres for the number of re-treatment sessions delivered, PPD changes, plaque and marginal bleeding 1 year after treatment, but not for implant failures, complications, RAD changes and recurrence of peri-implantitis. The results did not change when removing the 5 patients who did not match the original inclusion criteria.

**Conclusions:** Adjunctive use of LAD therapy (FotoSan) with mechanical cleaning of implants affected by peri-implantitis did not improve any clinical outcomes when compared to mechanical cleaning alone up to 1 year after treatment.
One of the complications that may occur in patients rehabilitated with implant-supported prostheses is peri-implantitis. This complication, if not successfully treated, can lead to implant failures. Peri-implantitis can be defined as a plaque-induced chronic infection with loss of supporting bone around a functioning implant. Peri-implantitis, defined as marginal bone loss of 3 mm or more in combination with bleeding on probing and/or pus, was diagnosed in 16% of patients rehabilitated with machined Brånemark implants followed up for 9 to 14 years after loading. Implants with a very rough surface are at higher risk for being affected by peri-implantitis. Peri-implantitis is difficult to treat and the long-term prognosis of implants affected by it remain uncertain.

There are many different therapies for peri-implantitis, however none have shown clearly better results than others. Among the therapeutic approaches used to treat implants affected by peri-implantitis, there is the so-called LAD (light-activated disinfection) also called PACT (photodynamic antimicrobial chemotherapy) and often abbreviated as photodynamic therapy. In principle, LAD involves three elements: harmless visible light, a non-toxic photosensitiser and oxygen. The treatment is based on a combination of a photosensitiser (a substance that can be photoactivated, usually toluidine blue O) and light with a suitable wavelength. The photosensitiser agent attaches to the membranes of microorganisms and absorbs energy from the light. It thereby releases energy to oxygen, which is transformed into highly reactive oxygen species like ions and radicals that kill microorganisms. LAD can be effective against bacteria, as well as other types of microorganisms like viruses, fungi and protozoa. No negative side effects have been noted, since the applied photosensitisers have less affinity for mammalian cells. As a result, LAD might be advantageous compared to chemical disinfectants and antibiotics.

A recent randomised controlled trial (RCT) compared the adjunctive use of LAD (phenothiazine chloride activated by diode laser) with adjunctive local antibiotic therapy (minocycline microspheres) in non-surgically treated implants (mechanical debridement with titanium curettes and glycine-based powder air-polishing) affected by initial peri-implantitis (bone loss between 0.5 to 2 mm at pockets that showed bleeding on probing) for 6 months after treatment in 20 patients per group. Treatment was repeated at 3 and 6 months at all sites that were still bleeding on probing. No statistically significant differences were observed between the two groups with the exception of more plaque at LAD treated sites (not clinically significant) after 6 months. This trial was designed in a way that could not provide an answer about whether LAD therapy could be advantageous as an adjunctive therapy to mechanical debridement alone in the treatment of peri-implantitis. Therefore, the present authors designed an RCT aimed at evaluating the potential efficacy of adjunctive use of LAD therapy to mechanical debridement. Preliminary results of this trial at 4 months after loading did not show any significant clinical improvements through the use of the FotoSan 630 instrument (CMS Dental, Copenhagen, Denmark). However, it could be possible that a 4-month follow-up period is too short to observe the potential advantages of adjunctive-use LAD therapy, and that repeated applications over longer time periods could show an additional clinical benefit by using this therapeutic approach.

The aim of this multicentre randomised controlled trial of parallel group design was to evaluate possible benefits of the adjunctive use of LAD in the treatment of peri-implantitis. At protocol stage, it was planned to follow the patients up to 5 years after initial treatment of peri-implantitis. The present article is reported according to the CONSORT statement to improve the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

Conflict-of-interest statement: CMS Dental A/S, the manufacturer of the LAD device (FotoSan) tested in this investigation, agreed to partially support this trial, however, the data belonged to the authors. When results became available, the FotoSan manufacturer did not honour the financial agreement.
Materials and methods

Patient selection

Any patient having at least one implant affected by peri-implantitis, being at least 18 years old and able to sign an informed consent form was eligible for inclusion in this trial. Peri-implantitis was defined as bacterial plaque-induced inflammation of the marginal peri-implant tissues with bone loss. To be eligible, patients had to have at least one osseointegrated implant that lost at least an average of 3 mm of peri-implant bone from the baseline (implant placement). Ideally, this should have been documented by assessing the baseline radiographs at implant placement. However, since for some patients no baseline radiographs were available because they were originally treated by other dentists, the present authors used the most coronal portion of the implant collar for bone level implants as a reference point, and in cases of transmucosal implants each investigator estimated marginal bone loss by subjectively deciding the reference point where bone was likely to be at implant placement. In addition to at least 3 mm of peri-implant bone loss, the following clinical signs had to be present at the study implants to be included in the trial: pus exudation and/or soft tissue swelling and/or soft tissue redness. Probing pocket depth (PPD) was not used as a discriminatory criteria for including patients in the study. In the presence of more than one eligible implant, the one with the most severe degree of peri-implantitis was included in the study.

Exclusion criteria:

- mobile implants
- any implant that lost less than 3 mm of peri-implant bone from implant placement
- any implant not showing clear clinical signs of inflammation (pus exudate and/or soft tissue swelling and/or redness)
- any implant considered to be untreated by the operator (radiographs and a written explanation to be provided)
- any medical conditions that had an absolute contraindication to subgingival debridement (written explanation to be provided)
- patients who received systemic or topical antibiotics at the included implant site over the previous 3 months

Patients were divided into three groups based on the number of cigarettes they declared to consume per day at time of recruitment: non-smoker, moderate smoker (≤10 cigarettes per day) or heavy smoker (>10 cigarettes per day).

Patients were recruited and treated by four different doctors in one university setting (Dr De Angelis) and three private practices (Drs Camurati, Felice, Grusovin) using similar procedures. Each doctor/centre treated 20 patients (10 in each group). The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were followed. All patients received thorough explanations and signed a written informed consent form prior to being enrolled in the trial. Originally, six centres agreed to participate in the study, but two centres did not recruit any patients.

At protocol stage it was decided that patients who lost 3 to 5 mm of peri-implant bone were to be treated with a non-surgical approach and that patients who lost more than 5 mm of peri-implant bone were to be surgically treated. Only after surgical or non-surgical debridement of the implant affected by peri-implantitis were patients randomly allocated to receive or not adjunctive LAD therapy.

Clinical procedures

Independent outcome assessors at each centre took baseline PPD measurements using a PCP-15 periodontal probe (Hu-Friedy, Leimen, Germany) with light pressure at the deepest point of the study implant, rounded to the nearest mm. They also recorded presence of plaque (plaque index; PI) and marginal bleeding on gentle probing (marginal bleeding index; MBI) at 4 sites of the study implants as the number of affected sites. Detailed and personalised oral hygiene instructions were given and, whenever needed, possible overhangs and over-contoured prostheses were corrected. Sites with a peri-implant marginal bone loss of ≤5 mm were to be treated non-surgically and those with a bone loss >5 mm were to be treated surgically. Regenerative procedures and the use of systemic or topical antibiotics were not allowed.
Patients rinsed with chlorhexidine mouthwash 0.2% for 1 min prior to the intervention and were treated under local anaesthesia using articaine with adrenaline 1:100,000. The time required to complete the debridement of the implant surface was recorded.

In the case of the non-surgical approach (peri-implant marginal bone loss between 3 and 5 mm), the implant surface was debrided with a hand and/or mechanical instrument for the time that the clinician considered sufficient to have it properly cleaned. Investigators were allowed to use the type of instrument they preferred among the following: stainless steel curette/tip, titanium curette/tip, gold-plated curette/tip, plastic curette/tip, teflon-plated curette/tip, hand curette, ultrasonic scaler, piezo-electric scaler or sonic scaler.

In the case of the surgical approach (peri-implant marginal bone loss >5 mm), a full-thickness flap was elevated and the defect was carefully curetted to remove all granulation tissue. Bone removal could be performed at the discretion of the investigator. The implant surface was carefully debrided as previously described. In addition, the investigator decided whether to eliminate or reduce the unsupported implant threads and/or to polish the implant surface.

Only after having thoroughly mechanically cleaned the implant surface were operators informed whether the site was to receive or not adjunctive LAD therapy by opening a sequentially numbered sealed envelope corresponding to the patient recruitment number. The pocket of patients to be treated with LAD therapy was overfilled with a medium viscosity gel active agent (toluidine blue O at 0.1 mg/ml) contained in syringes. The 23 mm-long perio tip of the FotoSan 630 instrument (CMS Dental) was then inserted at 4 points around the implant and light was delivered for 20 s at each site. Sutures were given when needed.

After the intervention, baseline standardised periapical radiographs were taken using a customised stent. In case of an unreadable radiograph, the radiograph was taken again. The following recommendations were given only to surgically treated patients: to take ibuprofen 400 mg in the presence of pain, use chlorhexidine mouthwash 0.12% for 1 min twice a day for 2 weeks and to refrain from interdental cleaning in the treated area for 2 weeks. Gentle wiping with a soft brush was started after the first week.

Patients were seen at 1 week (when present, sutures were removed), 1 and 4 months, and every 4 months thereafter for maintenance with supragingival prophylaxis with a rubber cup for the entire duration of the study. PI and MBI were recorded dichotomously as presence or absence at 4 sites of the study implants at 4 months and 1 year post-treatment. Presence of complications/adverse events at the study implants were also recorded at each maintenance visit. According to the investigators’ clinical judgement, implants still affected by peri-implantitis could be re-treated following the treatment that was originally allocated to them (i.e. those implants allocated to adjunctive LAD treatment received adjunctive LAD therapy, and the others debridement only). Re-treatment was mandatory in cases where clinical signs of inflammation were present: pus exudate and/or soft tissue swelling and/or soft tissue redness. Local or systemic antibiotics, laser or any other antimicrobials in the pocket could not be used, however surgery could be repeated if deemed necessary. At protocol stage it was decided that once the 1-year post-treatment follow-up was completed, if patients allocated to adjunctive LAD treatment showed statistically better results (less marginal peri-implant bone loss, and/or shallower PPD, and/or lower MBI) than those debrided only, all patients were to receive adjunctive LAD treatment for the remaining duration of the study. Since no statistically significant differences were observed, patients continued to be re-treated according the treatment that was originally allocated to them.

**Outcome measures**

This study tested the null hypothesis that there were no differences between the two procedures against the alternative hypothesis of a difference.

Outcome measures:

- Implant failures (primary outcome measure): any mobile or fractured implant that was not restorable. In principle, the investigators were not allowed to remove any stable implants, however it was recognised that there could be some special circumstances in which implant removal was indicated. When this was the case, the investigator had to justify in writing and to document with clinical pictures and radiographs the decision to remove the implant.
• Recurrence of peri-implantitis (primary outcome measure): defined as additional bone loss of at least 2 mm documented by standardised periapical radiographs with the presence of at least one of the following infection/inflammatory signs: pus exudation and/or soft tissue swelling and/or redness. This outcome was reported at 1 year after treatment and will be reported again at 3 and 5 years after treatment.

• Complications and adverse events (primary outcome measure): any complication (fistula, suppuration, swelling, abscess, abutment loosening, etc.) and adverse events (allergic reactions, etc.).

• Re-treatments (primary outcome measure): number of subgingival re-treatment sessions required during and outside maintenance.

• Changes in radiographic marginal bone levels (RAD) (secondary outcome) evaluated on standardised intraoral radiographs taken with the paralleling technique just after peri-implantitis treatment (baseline) and 1, 3 and 5 years after initial treatment. Digital or conventional standardised intraoral radiographs were obtained according to the paralleling technique using commercially available film holders (Rinn XCP; Dentsply Rinn, Elgin, IL, USA) and individual stents made of hard silicone and used for bite registration (Occlufast, Zhermack Spa, Badia Polesine, Italy) to standardise repositioning of the film holders. In case of an unreadable radiograph, the radiograph had to be taken again. Conventional radiographs were scanned, digitised in JPG, converted to TIFF format with a 600 dpi resolution and stored in a personal computer. Marginal bone levels were measured using the Scion Image software program (Scion Corporation, Frederick, MD, USA). Measurements of the mesial and distal bone crest levels adjacent to each implant were made to the nearest 0.5 mm. Reference points for the linear measurements were: a fixed reference point on the implant collar that was decided and recorded by the independent and blinded outcome assessor (Dr Michele Campailla) when evaluating the first postoperative radiographs and the most coronal point of bone-to-implant contact. Bone levels were measured at both mesial and distal sides and averaged. Bone levels at single implants were averaged at group level.

• Changes in PPD (secondary outcome): the deepest PPD at each study implant was recorded to the nearest mm just prior to the intervention and at 4 months, and 1, 3 and 5 years thereafter. At each centre there was a local blinded outcome assessor who recorded all outcome measures. These assessors were not calibrated between them. The only exception was the RAD change evaluation, which was performed by a single blinded outcome assessor (Dr Michele Campailla).

### Statistical analyses

The sample size was calculated to detect a 1 mm difference in mean marginal bone level changes between the two groups. A total of 49 patients had to be included in each group with 90% power, assuming that the common SD was 1.500 using an independent sample t test with a 0.050 two-sided significance level. It was planned to include 60 patients per group to compensate for possible dropouts. Each of the six original centres had to recruit 20 patients, 10 of them to be randomly allocated to each group. Unfortunately, due to the early withdrawal of two centres, the planned sample size could not be achieved. Six computer-generated restricted random lists were created. Only one investigator (Dr Esposito), who was not involved in the selection and treatment of the patients, knew the random sequence and had access to the random list stored in a password protected portable computer. The random codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Only after the study implants had been thoroughly mechanically cleaned and smoothed, if considered necessary, were the envelopes opened sequentially. Therefore, treatment allocations were concealed to the investigators in charge of enrolling and treating the patients.

All data analysis was performed according to a pre-established analysis plan by a biostatistician with expertise in dentistry who analysed the data without knowledge of the group codes following an intention-to-treat concept. The patient was the statistical unit of the analyses. Differences in the proportion of patients with implant failures, complications and number of re-treatments (dichotomous outcomes) were compared between the groups.
using the Fisher exact probability test. Differences of means at patient level for continuous outcomes (PPD changes) between groups were compared by independent sample t tests and within groups by paired t tests. Dichotomous and continuous outcomes were also compared between the four centres using the chi-squared test and one way analysis of variance, respectively. Sensitivity statistical analyses were repeated excluding five patients who did not fully match the original inclusion criteria. All statistical comparisons were conducted at the 0.05 level of significance.

**Results**

During initial monitoring it was noticed that two of the original six centres were not recruiting and therefore were excluded. In total, 83 patients were screened at the four remaining centres and 80 patients were consecutively enrolled in the trial. Three patients were not included by Dr Grusovin since they were unable to attend a 5-year follow-up. All patients were treated according to the allocated interventions. One patient (Dr Grusovin) from the LAD group died from cancer just before the 4-month evaluation. One patient of Dr Grusovin’s from the control group did not attend the 1-month recall. Two patients from Dr Camurati’s centre allocated to the LAD group dropped out 6 months after treatment, one because the patient moved away and the other because the patient decided to change dentist. The data of all remaining patients were evaluated in the statistical analyses. The main deviations from the protocol are as follows. Two patients from each group were recruited without having visible signs of infection at recruitment with the exception of bleeding on probing (Dr De Angelis). One patient took antibiotics after recruitment, 1 week before peri-implantitis treatment, to treat a case of tonsillitis (Dr Grusovin). Two patients (one from Dr Camurati’s centre, then allocated to the control intervention, and one from Dr Grusovin’s centre, then allocated to adjunctive LAD therapy) were treated non-surgically despite having bone loss >5 mm because they refused surgical treatment. The centre with Dr Felice took periapical radiographs that were not standardised, and the same occurred with 4 patients (2 per group) in Dr Grusovin’s centre. Finally, one patient (LAD group, Fig 1) of Dr Felice who developed an abscess 11 months after initial treatment was treated with antibiotics, when the patient should have been re-treated with the allocated intervention.

Patients were recruited and treated from May 2010 to January 2012. The follow-up of all patients was to 1 year after peri-implantitis treatment. Patient demographics, implant characteristics and the use of various types of instruments are presented in Table 1. There were no apparent significant baseline imbalances between the two groups. Nineteen implants were surgically treated. During surgery, osteoplasty was never performed,
9 implants had their unsupported threads removed and all surgically treated implants had their surfaces smoothed. There were no differences between groups for time needed to complete implant debridement (10.7 min for LAD-treated implants and 12.0 min for control implants).

After debridement and randomisation, 40 patients had one implant treated with adjunctive LAD and 40 without adjunctive LAD.

Plaque and marginal bleeding scores recorded preoperatively at 1 week, and at 1, 4 and 12 months are reported in Tables 2 and 3, respectively. Both plaque and bleeding indexes significantly improved over time and there were no significant differences between the two groups at any time period.

One implant belonging to the LAD group failed 11 months after initial treatment. It was affected by an abscess and was treated with Augmentin 3 times/day for 5 days and Corsodyl gel 1% 3 times/day for 10 days. After 10 days, the implant was mobile and removed. The difference in proportions was not statistically significant (40 patients in the control group and 37 in the LAD group; Fisher exact test \( P = 0.49 \); difference = 0.026; 95% CI -0.024 to 0.076).

Table 1  Patient and intervention characteristics.

<table>
<thead>
<tr>
<th></th>
<th>LAD [n = 40] (%)</th>
<th>Control [n = 40] (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females</td>
<td>21 (53)</td>
<td>21 (53)</td>
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<tr>
<td>Mean age at implant insertion (range)</td>
<td>58.0 (36–79)</td>
<td>60.2 (25–80)</td>
</tr>
<tr>
<td>Smoking up to 10 cigarettes/day</td>
<td>9 (23)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Smoking more than 10 cigarettes/day</td>
<td>5 (13)</td>
<td>4 (10)</td>
</tr>
<tr>
<td>Implants in maxilla</td>
<td>11 (28)</td>
<td>18 (45)</td>
</tr>
<tr>
<td>Implants in mandible</td>
<td>29 (73)</td>
<td>22 (55)</td>
</tr>
<tr>
<td>Implants in incisor position</td>
<td>8 (20)</td>
<td>14 (35)</td>
</tr>
<tr>
<td>Implants in canine position</td>
<td>6 (15)</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Implants in premolar position</td>
<td>5 (13)</td>
<td>8 (20)</td>
</tr>
<tr>
<td>Implants in molar position</td>
<td>21(53)</td>
<td>12 (30)</td>
</tr>
<tr>
<td>Initial bone loss mean (SD)</td>
<td>4.40 (1.58)</td>
<td>4.73 (2.11)</td>
</tr>
<tr>
<td>Years from implant placement: mean (SD)</td>
<td>5.65 (3.06)</td>
<td>6.13 (3.85)</td>
</tr>
<tr>
<td>Implant surgically treated</td>
<td>9 (23)</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Preoperative mean PPD (deepest pockets only): mean (SD)</td>
<td>6.23 (1.62)</td>
<td>6.45 (2.15)</td>
</tr>
<tr>
<td>Preoperative plaque index at 4 sites: mean (SD)</td>
<td>2.18 (1.53)</td>
<td>2.15 (1.64)</td>
</tr>
<tr>
<td>Preoperative bleeding index at 4 sites: mean (SD)</td>
<td>2.95 (1.32)</td>
<td>2.68 (1.25)</td>
</tr>
<tr>
<td>Scaling with manual instruments only</td>
<td>6 (15)</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Scaling with ultrasound instruments only</td>
<td>24 (60)</td>
<td>24 (60)</td>
</tr>
<tr>
<td>Scaling with both manual and ultrasound instruments</td>
<td>10 (25)</td>
<td>10 (25)</td>
</tr>
<tr>
<td>Used stainless steel instruments</td>
<td>40 (100)</td>
<td>36 (90)</td>
</tr>
<tr>
<td>Used titanium instruments</td>
<td>0 (0)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Used plastic instruments</td>
<td>0 (0)</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Time employed to clean the implant surface mean (SD)</td>
<td>10.68 (6.68)</td>
<td>12.03 (7.35)</td>
</tr>
<tr>
<td>Unsupported threads removed</td>
<td>3 (8)</td>
<td>6 (15)</td>
</tr>
<tr>
<td>Number of prosthetic adjustments necessary</td>
<td>3 (8)</td>
<td>4* (10)</td>
</tr>
<tr>
<td>Complications</td>
<td>2 (5)</td>
<td>1 (3)</td>
</tr>
<tr>
<td>Number of implants re-treated once to 1 year</td>
<td>16</td>
<td>16</td>
</tr>
<tr>
<td>Number of implants re-treated twice to 1 year</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Number of implants re-treated 3 times to 1 year</td>
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<td>2</td>
</tr>
<tr>
<td>Number of implants re-treated 4 times to 1 year</td>
<td>6</td>
<td>9</td>
</tr>
</tbody>
</table>

*Only one prosthetic adjustment was actually performed.
Four complications were registered in 4 patients, 3 from the LAD group and 1 from the control group. The difference in proportions was not statistically significant (40 patients in the control group and 37 in the LAD group, Fisher exact test $P = 0.35$; difference = 0.056; 95% CI 0.044 to 0.16). Complications in the adjunctive LAD therapy group were 1 postoperative wound dehiscence (Dr De Angelis), 1 postoperative swelling (Dr Grusovin) and the abscess occurred at 11 months after initial treatment (Dr Pietro Felice). One patient from the control group experienced postoperative swelling and moderate pain (Dr Grusovin). Apart from the abscess, which determined the failure of the implant, the remaining complications resolved spontaneously.

Recurrence of peri-implantitis, defined as 2 mm or more of additional bone loss from post-treatment baseline to 1 year after treatment recorded on standardised intraoral radiographs, occurred in 6 patients, 3 from each group. The difference in proportions was not statistically significant (40 patients in the control group and 37 in the LAD group; Fisher exact test $P = 1.00$; difference = 0.006; 95% CI -0.12 to 0.13).

Twenty-nine LAD-treated implants versus 33 control implants were re-treated at least once over the 1-year follow-up (Table 1), the difference was not statistically significant (40 patients in the control group and 37 in the LAD group; Fisher exact test $P = 78$; difference = -0.04; 95% CI -0.22 to 0.14).

Just after treatment, RADs were 4.5 mm at LAD implants and 4.9 mm at control implants (Table 4). One year after treatment, mean bone levels remained substantially stable for both groups ($P = 1.00$ and $P = 0.54$ for LAD and control implants, respectively). When comparing the two groups, there was no statistically significant difference in RAD changes after 1 year ($P = 0.68$).

Just before treatment, PPDs were 6.23 mm at LAD implants and 6.45 mm at control implants (Table 5). There was a significant reduction in PPD after 1 year for both groups ($P = 0.001$ for LAD and $P = 0.003$ for control implants). When comparing the two groups, there was no statistically significant difference in PPD changes after 1 year ($P = 0.68$).

The comparison between the four centres is presented in Table 6. There were statistically significant differences in the number of re-treatment sessions delivered ($P = 0.03$), PPD changes ($P < 0.001$), plaque ($P < 0.001$) and marginal bleeding ($P < 0.001$) at 1 year, but not for implant failures, complications, recurrence of peri-implantitis or RAD changes.
Once excluded, the 5 patients who were included despite not being in strict adherence to the inclusion criteria did not change the results.

### Discussion

This 1-year follow-up report confirmed the initial findings observed at 4 months post-loading, i.e. that the adjunctive use of an LAD therapy with implant surface debridement for the treatment of implants affected by peri-implantitis is ineffective. One year after initial treatments, both interventions improved the clinical outcomes in a statistically significant way (Table 4), but no additional benefits were observed in the LAD group versus the control. Interestingly, the only implant that failed was treated with adjunctive LAD therapy, though this observation is likely to be coincidental. Exactly the same number of implants from both groups were affected by recurrence of peri-implantitis defined as the loss of 2 mm or more of peri-implant marginal bone level.
on standardised periapical radiographs. Since all radiographs were evaluated by a single blinded and independent examiner, it can be concluded that no advantage was derived from the adjunctive use of LAD therapy with FotoSan.

While it is unlikely that a clinically and statistically significant difference between the two treatments will appear over time, it is still of interest to follow these two cohorts of patients, as originally planned, to acquire additional data on the prognosis of these treatment modalities of peri-implantitis since some studies have suggested a poor medium prognosis for implants treated for peri-implantitis.

The main limitation of the present trial was the lack of a placebo control. During protocol preparation, the present authors attempted to find some sort of placebo dye. However, they all appeared somewhat effective on bacteria when the light was activated so we had to abandon this idea and run the trial without a placebo dye.

There were consistent statistically significant differences between the four different centres regarding the number of re-treatment sessions delivered, PPD changes, and level of plaque and marginal bleeding 1 year after treatment reflecting different levels of oral hygiene and possibly lack of calibration between the blinded outcome assessors from the various centres. These differences and trends might be at least partly explained by the different ability of the clinicians to treat the patients, to instruct them in maintaining a good level of oral hygiene and by the heterogeneity of the patient populations. One centre (Dr De Angelis) for instance was a university clinic and another (Dr Grusovin) a private specialist centre in periodontology. In any case, is difficult to provide a reliable explanation for these differences. When looking closer at the data there is one centre (Dr Felice) that despite obtaining the best oral hygiene levels (reflected by the lowest levels for plaque and marginal bleeding) also reported the lowest improvements in pocket probing reduction, which appears to be contradictory compared to the outcome of the other centres. These apparent differences between various centres were not confirmed when all radiographs were evaluated by a single blinded outcome assessor. Since the bone level assessments performed by a single outcome assessor on standardised periapical radiographs can be considered more reliable than probing pocket depths, this observation suggests that the outcome of patients from different centres was more homogeneous than appeared at a superficial evaluation.

This trial was to be sponsored by CMS Dental, the manufacturer of FotoSan, however as soon as the company realised that adjunctive LAD therapy with FotoSan was ineffective they stopped honouring the financial commitments with the investigators. Possibly this was an unsuccessful attempt to avoid data publication and negative advertising. Since the investigators were the owners of the data, it was decided to publish the data anyway. It was considered unethical to avoid data publication, since clinical research is performed also to understand whether the therapies that our patients receive are effective or not. While no side effects were associated with the adjunctive use of Fotosan, the lack of any clinical benefit may question its clinical utility at least under the conditions this trial was conducted.

In the present multicentre investigation, because both interventions were tested in real clinical conditions and patient inclusion criteria were broad, the results can be generalised with confidence to a wider population with similar characteristics.

### Conclusions

The use of adjunctive LAD therapy (FotoSan) with mechanical cleaning of implants affected by peri-implantitis did not improve any clinical outcomes when compared to mechanical cleaning alone up to 1 year after treatment.
References


