**Abstract:** It is hypothesized that active treatment of peri-implantitis (PI) leads to re-stabilization of dental implants. The aim was to assess whether or not dental implants can re-stabilize following treatment of PI. To address the focused question, MEDLINE/PubMed and Google-Scholar databases were explored from 1977 up to and including August 2013. Any disagreements between the authors were resolved via discussion. Articles published only in English were included. Hand searching was also performed. Thirteen experimental studies were included. The treatment regimes adopted in these studies comprised of antibiotic therapy, guided bone regeneration (GBR), laser therapy, use of bone matrix proteins with membrane, conventional flap surgery and mechanical debridement. In four studies, GBR promoted new bone formation; whereas two studies showed photosensitization therapy (in combination with either mechanical debridement or GBR) to regenerate bone around peri-implant defects. Six studies reported that mechanical debridement in conjunction with antibiotic therapy promoted re-stability of dental implants. In one study, recombinant human bone matrix protein-2 with a collagen membrane helped promote re-stabilization of dental implants. New bone formation may occur to some extent around dental implants following treatment for PI; however, a “complete” re-stability may be difficult to achieve without GBR.

**Keywords:** dental implants, osseointegration, peri-implantitis, treatment
The aim of the present study was to assess whether or not dental implants can re-stabilize following treatment of PI.

Materials and Methods

Rationale and focused question

To our knowledge from indexed literature, there is no absolute explanation regarding what re-stability is or represents. Therefore, re-stability was interpreted as a complete recurrence of osseointegration (with new bone formation) around previously contaminated dental implant surfaces.

The addressed focused question was: “Can dental implants re-stabilize following treatment of PI?”

Eligibility criteria

The following eligibility criteria were imposed: 1) Original articles; 2) Experimental studies; 3) Histologic studies; 4) Reference list of pertinent original and review studies; 5) Intervention: Re-stability of dental implants after treatment of PI; and 6) Articles published only in English-language. Letters to the editor, historic reviews and unpublished articles were excluded.

Search strategy

The authors searched the MEDLINE/PubMed (National Library of Medicine, Bethesda, Maryland) and Google Scholar databases for appropriate articles addressing the focused question. Databases were searched from 1977 up to and including August 2013. Titles and abstracts of articles that satisfied the eligibility criteria were screened by the authors and checked for agreement. The full-text of the articles judged by title and abstract to be relevant were read and independently assessed against the eligibility criteria. Various combinations of the following keywords were used: “dental”, “implant”, “inflammation”, “oral”, “osseointegration”, “re-osseointegration”, “re-stability”, “re-integration”, “re-integration”, “peri-implantitis”, “periimplantitis”, “therapy” and “treatment”. Hand searching of the reference lists of original and review studies that were found to be relevant in the previous step was also performed.

The initial search yielded 23 articles. Four studies, which did not abide by the eligibility criteria were excluded, as shown in the Appendix. In total, 13 studies [16, 22–33] were included and processed for data extraction (Table I). The pattern of the current review was customized to mainly summarize the pertinent information.

Results

Characteristics of included studies

All studies [16, 22–33] were conducted at universities or healthcare centers. In these studies [16, 22–33] titanium dental implants were used. Thirteen experimental studies [16, 22–33] were included. Amongst these studies [16, 22–33], 12 studies [16, 22–30, 32, 33] were performed on dogs and one study [31] was performed on rhesus monkeys. In these studies [16, 22–33] the number of dental implants inserted ranged between 3 and 41. In 12 studies [16, 22–30, 32, 33] dental implants were placed in the mandible prior to PI induction; whereas in one study [31] the implants were placed in the maxilla and mandible before the induction of experimental PI. The treatment regimes adopted for the management of PI encompassed antibiotic therapy, guided bone regeneration (GBR), CO₂ laser therapy, conventional flap surgery and mechanical debridement. Four studies [22, 23, 25, 30] reported that GBR protocols for the treatment of PI play a significant role in re-stabilization of dental implants. Two studies [23, 25] showed that photosensitization therapy (using gallium-aluminum-arsenide diode laser) in combination with mechanical debridement and GBR reduces peri-implant inflammation and promotes re-stabilization of dental implants. Six studies [24, 26–29, 32] reported mechanical debridement with adjunct antibiotic therapy eliminates PI and promotes re-stabilization of infected dental implants. One study [31] reported that recombinant human bone matrix protein-2 (rhBMP-2) when used with a collagen membrane (carrier) helps in the resolution of PI and promotes re-stabilization compared to when the carrier is used alone. Fluorescence microscopic results by Stübinger et al. [33] demonstrated that air-powder abrasion of dental implants with adjunct CO₂ laser irradiation facilitates re-stabilization of dental implants as compared to when air-powder abrasion is used alone to treat PI (Table I).

Discussion

Osseointegration may be defined as a direct structural and functional connection between the living bone and the surface of a load-carrying implant [34]. In practice, osseointegration of dental implants is highly predictable when the implants are embedded in bone tissues [34]. Implant surface characteristics have also been shown to directly influence osseointegration [35]. With this background, “re-stabilization” may be interpreted as a complete recurrence of osseointegration following active treatment of peri-implant disorders, such as PI. After a vigilant review of pertinent literature, we observed that most of the treatment modalities adopted for the treatment of PI, caused regeneration of bone around the
<table>
<thead>
<tr>
<th>Authors</th>
<th>Study animals</th>
<th>Mean age</th>
<th>Implants with PI (n)</th>
<th>Treatment strategy</th>
<th>Main result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Javed et al. [16]</td>
<td>9 mongrel dogs</td>
<td>NA</td>
<td>6</td>
<td>Dental implants were sprayed with saline in situ</td>
<td>After three-months of treatment, animals in Group-1 showed significantly more bone-to-implant compared to animals in Group-2</td>
</tr>
<tr>
<td>You et al. [22]</td>
<td>6 mongrel dogs</td>
<td>NA</td>
<td>36</td>
<td>GBR</td>
<td>Six months after therapy, re-osseointegration was significantly higher in animals in Group-1 as compared to animals in Group-2</td>
</tr>
<tr>
<td>Shibli et al. [23]</td>
<td>5 mongrel dogs</td>
<td>2 years</td>
<td>40</td>
<td>Mechanical Debridement, lethal photosensitization’ and GBR</td>
<td>Five months after treatment, animals in Group-1 showed a better re-osseointegration around the peri-implant defect compared to animals in Group-2 (regardless of the implant surface)</td>
</tr>
<tr>
<td>Sennery et al. [24]</td>
<td>4 Beagle dogs</td>
<td>NA</td>
<td>24</td>
<td>Antibiotics and surgical therapy in smooth surfaced dental implants</td>
<td>DI re-osseointegrated to some extent in animals in Group-1 as compared to animals in Group-2</td>
</tr>
<tr>
<td>Shibli et al. [25]</td>
<td>6 mongrel dogs</td>
<td>2 years</td>
<td>36</td>
<td>Lethal photosensitization’ and GBR (all dogs)</td>
<td>After five months of treatment, PI was resolved</td>
</tr>
<tr>
<td>Wetzel et al. [26]</td>
<td>7 Beagle dogs</td>
<td>4 years</td>
<td>41</td>
<td>Antibiotics with GTR</td>
<td>After six months of healing, the amount of re-osseointegration was higher for dental implants in Group-1 as compared to those in Group-2</td>
</tr>
<tr>
<td>Persson et al. [27]</td>
<td>2 Labrador dogs</td>
<td>~1 year</td>
<td>8</td>
<td>Antibiotics, surgical debridement and pristine coronal fixture</td>
<td>After four months, animals in Group-2 failed to demonstrate re-osseointegration as compared to those in Group-1</td>
</tr>
<tr>
<td>Persson et al. [28]</td>
<td>4 Beagle dogs</td>
<td>~1 year</td>
<td>6</td>
<td>Antibiotics and surgical debridement</td>
<td>After six months, the amount of re-osseointegration was higher for dental implants in Group-1 as compared to those in Group-2</td>
</tr>
<tr>
<td>Persson et al. [29]</td>
<td>4 Beagle dogs</td>
<td>1.5 years</td>
<td>6</td>
<td>Fixtures were cleaned with an abrasive (pumice) and antibiotics</td>
<td>After 7 months of treatment, small amounts of new bone formation occurred in both groups</td>
</tr>
<tr>
<td>Hürzeler et al. [30]</td>
<td>7 Beagle dogs</td>
<td>3 years</td>
<td>3</td>
<td>Debridement and GBR</td>
<td>After 4 months of healing, animals in Group-1 showed the most significant bone generation around peri-implant defects compared to those in Group-2</td>
</tr>
</tbody>
</table>

Note: *GBR indicates guided bone regeneration.
affected dental implants; however, none of the studies demonstrated true "re-osseointegration". For example, in the Wetzel study, dental implants with both smooth (machined) and rough (titanium plasma sprayed or sand-blasted/acid-etched [SLA] coated) surfaces installed in beagle dogs [26]. PI was induced and subsequently treated using a regimen that included systemic antibiotic therapy and local debridement. In addition, the implant surfaces were cleaned and copiously irrigated with CHX. After six months of healing, biopsies were obtained and analyzed in the microscopic field. The study reported that for all types of implants used, treatment resulted in 60–80% bone-fill in the hard tissue defect [26]; however, the overall amount of re-osseointegration achieved was only 0.6 mm for the SLA surface and 0.1 mm for the machined surface. This study concluded that "true re-osseointegration appears to be difficult to achieve" [26]. Likewise, in the Persson study, treatment for PI resulted in a 72% bone fill of the bone defects at turned sites and 76% at SLA sites [28]. In this study, the amount of re-osseointegration was 22% at turned sites and 84% at SLA sites [28]. In this regard, we suggest that the term "re-osseointegration of dental implants" should be interpreted with caution.

The oral biofilm harbors microbes that may jeopardize the alveolar bone supporting natural teeth and dental implants [36, 37]. Furthermore, gram-negative microbes play a significant role in the pathogenesis of PI [38, 39]. It has been reported that regeneration of new bone occurs when dental implants are cleaned with CHX and subsequently GBR procedures performed [22, 27, 28]. In vitro studies [40, 41] have shown that CHX is adsorbed to the oxide layer of titanium surfaces thereby inhibiting microbial growth. This suggests that CHX irrigation coupled with mechanical debridement markedly reduces the pathogenic microbes around the peri-implant defects. This may in turn provide a suitable environment for GBR procedures to regenerate new bone tissues around dental implants. This seems to be an explanation for the results by Shibli et al. [23], Hürzeler et al. [30] and studies by Persson et al. [27, 28]. Nevertheless, studies have also reported that though new bone generation occurs to some extent, a "true" re-stabilization could not be regained without adjunctive GBR [23, 26–28].

The use of CO2 lasers in implant dentistry is increasing [42]. This is most probably because use of the CO2 wavelength reduces the risk of temperature-induced tissue damage as the laser is minimally absorbed in the implant surface. Furthermore, CO2 laser has also been suggested as one possible instrument for the disinfection of dental implant surfaces because of its excellent absorption on water [33, 43–45]. Romanos et al. investigated the osteoblast attachment on titanium disks after irradiation with and without CO2 laser [46]. The results demonstrated that irradiation with CO2 laser did not affect the osteoblast attachment on titanium disks [33]. CHX and subsequently GBR procedures performed on peri-implant defects. CHX irrigation coupled with mechanical debridement reduced the pathogenic microbes around the peri-implant defects. The oral biofilm harbors microbes that may jeopardize the alveolar bone supporting natural teeth and dental implants; however, none of the studies demonstrated true "re-osseointegration". For example, in the Wetzel study, dental implants with both smooth (machined) and rough (titanium plasma sprayed or sand-blasted/acid-etched [SLA] coated) surfaces installed in beagle dogs [26]. PI was induced and subsequently treated using a regimen that included systemic antibiotic therapy and local debridement. In addition, the implant surfaces were cleaned and copiously irrigated with CHX. After six months of healing, biopsies were obtained and analyzed in the microscopic field. The study reported that for all types of implants used, treatment resulted in 60–80% bone-fill in the hard tissue defect [26]; however, the overall amount of re-osseointegration achieved was only 0.6 mm for the SLA surface and 0.1 mm for the machined surface. This study concluded that "true re-osseointegration appears to be difficult to achieve" [26]. Likewise, in the Persson study, treatment for PI resulted in a 72% bone fill of the bone defects at turned sites and 76% at SLA sites [28]. In this study, the amount of re-osseointegration was 22% at turned sites and 84% at SLA sites [28]. In this regard, we suggest that the term "re-osseointegration of dental implants" should be interpreted with caution.

Table I (continued)

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<tr>
<th>Authors</th>
<th>Study source</th>
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<th>Implants with PI (n)</th>
<th>Treatment strategy</th>
<th>Main result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hanisch et al. [31]</td>
<td>4 rhesus monkeys</td>
<td>NA</td>
<td>4 rhBMP-2 with collagen sponge (carrier)</td>
<td>Carrier alone</td>
<td>After 4 months of healing, animals in Group-1 showed significant bone regeneration (40%) around peri-implant defects compared to those in Group-2 (9%)</td>
</tr>
<tr>
<td>Ericsson et al. [32]</td>
<td>5 Labrador dogs</td>
<td>1 year</td>
<td>6 Debridement and antibiotic treatment</td>
<td>Debridement without antibiotic treatment</td>
<td>Resolution of PI was observed in animals in Group-1 as compared to animals in Group-2</td>
</tr>
<tr>
<td>Stübinger et al. [33]</td>
<td>6 Beagle dogs</td>
<td>2 years</td>
<td>60 a) CO2 laser b) CO2 laser and air-powder abrasive</td>
<td>Air-powder abrasive alone</td>
<td>After 2 months, fluorescence microscopic results performed showed significantly more new bone formation around defects treated with either laser alone or laser + air-powder abrasive than those treated by air-powder abrasive alone</td>
</tr>
</tbody>
</table>

*Gallium-aluminum-arsenide diode laser; GBR = guided bone regeneration; GTR = guided tissue regeneration; CO2 = carbon dioxide; PI = peri-implantitis; rhBMP-2 = recombinant human bone morphogenetic protein-2
CO₂ laser promotes osteoblast attachment and further bone formation [46]. This may be a possible explanation for the experimental results by Stübing et al. [33], where CO₂ laser application (as an adjunct to mechanical debridement) promoted new bone formation at peri-implant defect sites. However, an understanding of the characteristics of the applied laser energy to optimize therapeutic implementation is essential since heat production as a result of CO₂ laser application may still result in lack of osseointegration [47, 48].

Conclusion

Though various treatment regimes may assist in the formation of new bone around peri-implant defects; a complete recurrence of osseointegration may be difficult to achieve.

References

28. Persson LG, Berglundh T, Lindhe J, Scanferla L: Re-osseointegration after treatment of peri-implantitis at different implant sur-

Appendix

List of excluded studies

Main reason for exclusion is shown in italics: