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# Regeneration Procedures in Immediate Transmucosal Implants: An Animal Study

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The aim of the present study was to evaluate bone regeneration around nonsubmerged implants placed immediately in extraction sites in the canine mandible using a combination of synthetic hydroxyapatite (HA) and collagen membranes. Ten beagle dogs were used in this study. After the second and third mandibular premolars were extracted, hollow-screw implants were placed in the distal extraction sockets. In each animal, one site received no treatment (control site), while other defects received randomly 1 of the following treatments: grafting with porous HA in the peri-implant region, collagen membrane adapted to the implant cervical collar covering the peri-implant defects, or a combination of the 2 treatments, ie, HA grafting and membrane placement. After 4 months of healing, block biopsies were obtained and prepared for histologic analysis using the cutting-grinding technique. The histometric evaluation took into account the number of integrated screw threads, the extent of bone-to-implant contact, and the density of peri-implant bone. At sites covered by membrane alone or by membrane and HA, the number of integrated threads was statistically higher than sites treated only with HA. The extent of bone-to-implant contact was significantly different between treatments. However, the use of bioabsorbable materials did not significantly enhance peri-implant bone regeneration in immediate implantation.

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**Key words:** bioabsorbable material, bone regeneration, dental extraction, titanium dental implants

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Replacing a missing tooth or a tooth affected by chronic periodontitis as early as possible is an acceptable therapeutic approach. To date, several studies are available documenting this immediate implant placement technique.<sup>1-5</sup> However, some authors<sup>6,7</sup> have noted similar difficulties associated with this therapy:

- Tooth sockets should be meticulously debrided.
- Buccal and/or lingual fenestrations, especially in the anterior region, complicate immediate implant placement.
- Primary anchorage of implants is directly proportional to the quantity and quality of osseous tissue at the apical part of the implant.
- Peri-implant mucosa should be healthy, without any inflammation, to favor primary wound closure.
- Nonsubmerged implants should be protected from functional loading during the osseointegration period.

Several authors<sup>8-10</sup> have described the advantages of immediate implantation: The tooth socket's bony walls will not undergo the same amount of resorption as when implantation is delayed, implant positioning is optimized, and the time necessary for prosthetic rehabilitation is

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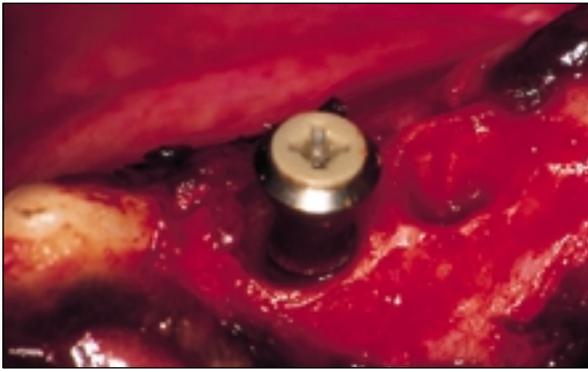
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**Fig 1** The implant is placed in the distal socket of a mandibular premolar. The first 2 to 3 threads are exposed.

diminished. In most cases, the discrepancy between the tooth socket and the implant's diameter results in a coronal peri-implant bony defect, affecting the implant's primary stability and possibly the level of osseointegration. This type of defect has been treated in rabbits,<sup>11</sup> dogs,<sup>12</sup> and humans<sup>3</sup> by guided bone regeneration. In most instances, nonresorbable membranes alone or associated with bone grafts have been used.<sup>13-16</sup> However, the use of nonsubmerged implants in a 1-phase surgical technique is not fully compatible with the use of nonbioabsorbable membranes that are to be removed through a second surgical procedure. Therefore, when using immediate nonsubmerged implants, only absorbable biomaterials lend themselves to a single-stage surgical protocol.

The purpose of the present study was to evaluate by histometry the bone-to-implant contact of nonsubmerged implants placed immediately after extraction in the tooth sockets of beagle dogs using absorbable biomaterials as defect fillers.

### Materials and Methods

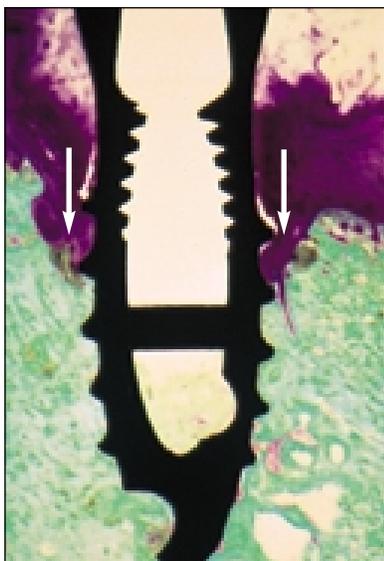
This study was conducted according to good laboratory practices as specified by the United States Food and Drug Administration.<sup>17</sup> After a period of housing, 10 adult beagle dogs with a mean age of 5 years were operated under general anesthesia. A full-thickness flap was elevated in the region of mandibular premolars, the second and third premolars were extracted, and the corresponding distal sockets received 8-mm-long, 2.8-mm-diameter nonsubmerged hollow-screw titanium implants (Straumann AG, Waldenburg, Switzerland). In each dog, each of 4 implants had 2 or 3 of the

most coronal threads exposed (Fig 1). Each peri-implant defect was treated randomly with one of the following modalities: no treatment (control sites), grafting with porous hydroxyapatite (HA) (Pred, Paris, France), covering with a collagen membrane (Colética, Lyon, France), or with a combination of HA grafting and collagen membrane placement. The flaps were subsequently replaced and tightly sutured around the cervical surface of the implants. Postoperatively, each animal received an analgesic and 0.5 g of amoxicillin for 4 days. Apart from keeping the dogs on a soft diet for 14 days after surgery, no other precautionary measures were taken.

**Histologic Preparation.** Four months after surgery, the animals were perfused under general anesthesia, and after sacrifice, block biopsies including the mandibular premolar region were harvested. After fixation in 10% neutral phosphate-buffered formalin, specimens were dehydrated in alcohols and embedded in resin (Heraeus Kulzer, Wehrheim, Germany). Using the cutting-grinding technique, 2 to 3 sections 30  $\mu$ m thick were obtained in a mesiodistal direction for each implant and stained using basic fuchsin and light green for examination under light microscopy. A histometric study was performed on all sections using an image analysis system (Optilab, Graftek, France) coupled with a camera on a microscope, the examiner being unaware of the allocation of treatment modalities to different sites. Several parameters were measured:

- The number of threads in contact with bone in relation to the total number of threads on the implant (n%),
- The surface of peri-implant bone between threads in relation to the surface between the contour of all implant threads (s%), and
- The density of peri-implant bone, ie, the ratio between the surface of bone between threads on one hand and the total surface between the contour of the threads in contact with bone on the other (d%).

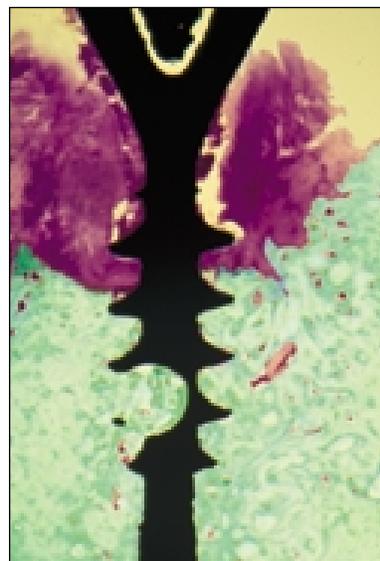
Measuring s% and d% led to the quantitative and qualitative evaluation of the integration. Likewise, counting the threads (n%) was key to assessing the degree of regeneration at the peri-implant defects. The results of measurements were expressed as means ( $\pm$  SD) and statistically compared among different therapies (Kruskal-Wallis and paired *t* test, *P* < .05).



**Fig 2** Site treated with a collagen membrane. The bone crest shows a crater-like defect (*arrows*) and 2 threads are visible. Otherwise, bone density is normal (original magnification  $\times 10$ ).



**Fig 3** Control site. Bone regeneration is partial and different between the 2 sides of the implant. All of the threads are covered on one side, while 2 threads are exposed (*arrows*) on the other side. The contour of the bone crest is irregular (original magnification  $\times 8$ ).

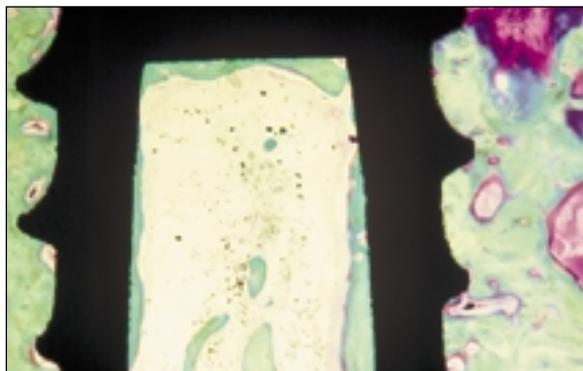


**Fig 4** Site filled with HA. The section does not encompass the hollow part of the implant. Only the first thread is exposed. The biomaterial is not visible on the section (original magnification  $\times 10$ ).

## Results

There were no postsurgical complications or infections. However, of the 40 implants placed, 8 were lost, 5 of which were in control sites and 3 in HA-grafted sites. In addition, 3 of the 32 remaining implants showed mobility.

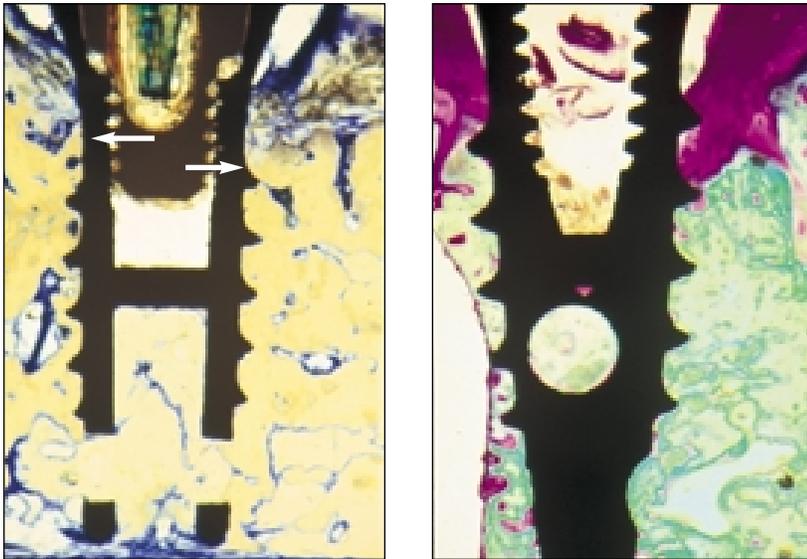
Histologic sections revealed a wide range of bone-to-implant contact among various implants. In a few instances, all exposed threads after implant placement were covered only by the mucosa because of the lack of bone regeneration (Fig 2). For a few implants, only their apical part was in contact with bone, and the hollow part of the implant was sometimes filled by soft tissue. More often, variable bone-to-implant contact, unequal between mesial and distal surfaces, allowed the initially exposed threads to be covered (Figs 3 and 4). The profile of the bone crest at the implant function was crater-like (Figs 2 and 3), whereas the hollow part was weakly filled by bone (Fig 5). Finally, a few implants demonstrated bone-to-implant contact at the end of partially completed regeneration of the initial peri-implant circular bony defect, the osseous tissue having variable densities (Figs 6 and 7). Bacterial deposits



**Fig 5** Enlargement of the hollow part of the implant shown in Fig 3. The hollow part is only weakly colonized by osseous tissue (original magnification  $\times 25$ ).

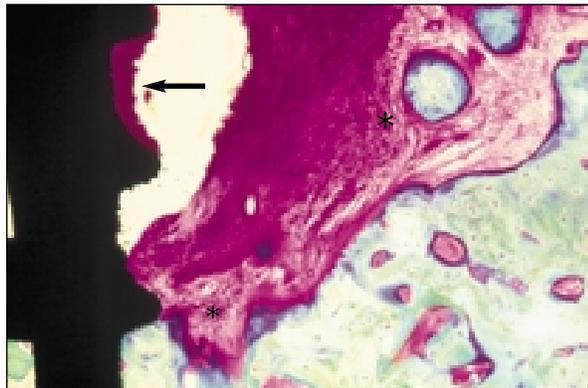
were observed at the cervical region and exposed threads of some implants, facing a mucosa infiltrated by inflammatory cells (Fig 8).

Statistical analysis of the histometric measurements was different if the lost implants were excluded from the study ( $n = 32$ ), or if on the contrary, they were taken into account ( $n = 40$ ), their values were considered as zero (0%). The number



**Fig 6** (Left) Another site treated with a collagen membrane. Peri-implant bone regeneration has been effective and the bone crest (arrows) is clearly situated at a more coronal level than the first thread. Bone density is less important in the apical and hollow parts of the implant (toluidine blue, original magnification  $\times 10$ ).

**Fig 7** (Right) Site treated with a combination of HA and membrane. After healing, the extent of bone-to-implant contact results in the bony coverage of the implant apart from 1 thread exposed on one side (original magnification  $\times 13$ ).



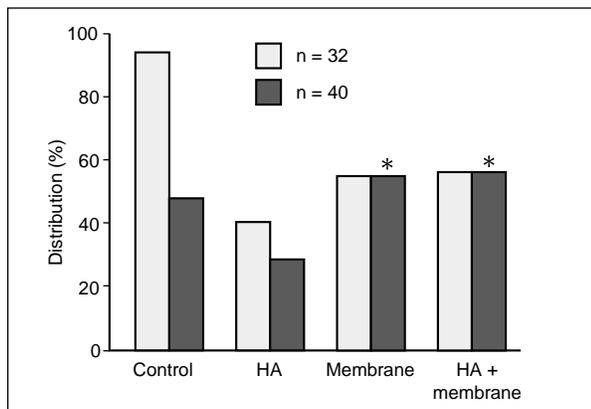
**Fig 8** Enlargement of the crestal region shown in Fig 3. Several threads are exposed and partially covered by bacterial deposits (arrow), and the mucosa presents an inflammatory infiltrate (asterisk). The sharp, uneven contour of the bone crest suggests active remodeling (original magnification  $\times 25$ ).

of bone-contacting threads (Fig 9, Table 1) was not statistically different (Kruskal-Wallis,  $H = 6.06$ ,  $P > .10$ ) when compared globally between the 4 different therapies when lost implants were excluded ( $n = 32$ ). On the contrary, when including all implants ( $n = 40$ ), the number of bone-contacting threads covered by membrane alone ( $53.8 \pm 34\%$ ) and that of the sites treated with a combination of HA and membrane ( $54.4 \pm 39.4\%$ ) was statistically higher than the number of bone-contacting threads at sites treated by HA alone ( $26.8 \pm 35.7\%$ , paired  $t$  test,  $P < .05$ ). The peri-implant osseous surface (Fig 10, Table 2) was statistically different (Kruskal-Wallis,  $H = 7.8$ ,  $P < .05$ ) when globally compared between the 4 treatment modalities and taking into account the number of successful implants ( $n = 32$ ). However, when all

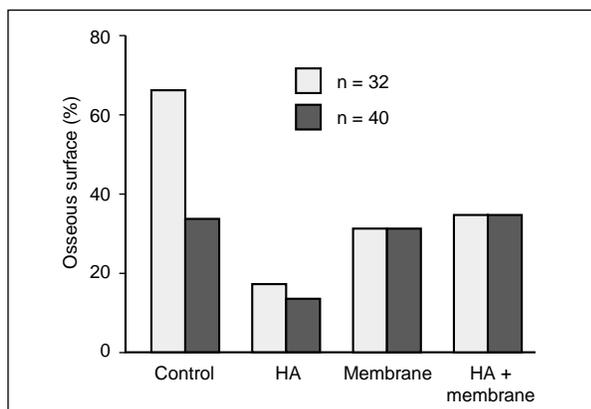
implants ( $n = 40$ ) were taken into consideration,  $2 \times 2$  comparisons (paired  $t$  test) did not show any significant statistical difference ( $P > .05$ ). Finally, the bone density (Fig 11, Table 3) was not significantly different in any case.

## Discussion

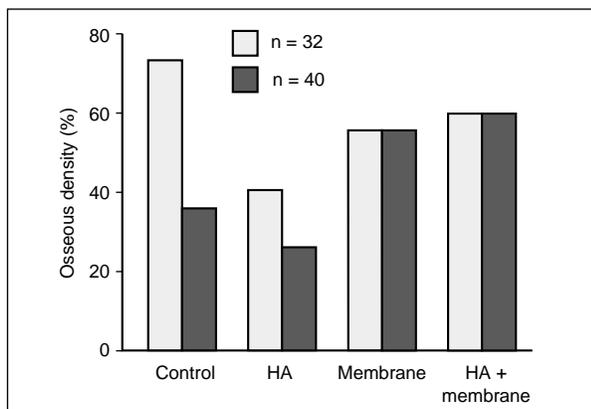
Most of the studies on immediate implant placement report clinical trials; animal studies involving histologic assessments are less numerous,<sup>18-22</sup> and publications related to the immediate placement of nonsubmerged implants are even more scarce.<sup>9,23,24</sup> To enhance osseous integration of implants in extraction sites, and at the same time accommodate a single-stage surgical protocol, bioabsorbable collagen membranes could be used.



**Fig 9** Mean distribution of bone-contacting threads, expressed as percentages. For n = 32, no statistically significant difference was seen between the treatments (Kruskal-Wallis,  $P > .10$ ). Asterisks indicate significant differences with HA for n = 40 (paired  $t$  test,  $P < .05$ ).



**Fig 10** Mean peri-implant osseous surface, expressed as percentages. For n = 32, statistically significant differences were observed between all treatments (Kruskal-Wallis,  $P < .05$ ). For n = 40, no statistically significant differences were seen (paired  $t$  test,  $P > .05$ ).



**Fig 11** Mean peri-implant osseous density, expressed as percentages. For n = 32 and n = 40, no statistically significant differences were seen between treatments (Kruskal-Wallis,  $P = .10$ ; and paired  $t$  test,  $P > .05$ ).

**Table 1** Distribution of Bone-Contacting Threads

Treatment	n = 32	n = 40
None (control)	92.6 ± 10.5	46.3 ± 49
HA	38.3 ± 37.4	26.8 ± 35.7
Membrane	53.8 ± 34.0	53.8 ± 34.0
HA + membrane	54.4 ± 39.4	54.4 ± 39.4

**Table 2** Peri-implant Osseous Surface

Treatment	n = 32	n = 40
None (control)	70.2 ± 22.2	35.1 ± 39.9
HA	19.0 ± 22.6	13.3 ± 20.6
Membrane	32.2 ± 27.3	32.2 ± 27.3
HA + membrane	34.4 ± 31.0	34.4 ± 31.0

**Table 3** Peri-implant Osseous Density

Treatment	n = 32	n = 40
None (control)	76.0 ± 18.0	38.0 ± 41.8
HA	41.6 ± 25.2	29.1 ± 28.8
Membrane	58.3 ± 29.0	58.3 ± 29.0
HA + membrane	61.2 ± 32.4	61.2 ± 32.4

These membranes have previously been documented for both guided tissue regeneration<sup>25-27</sup> and guided bone regeneration.<sup>28-30</sup> Regarding space-maintaining biomaterials, there are no studies demonstrating the superiority of one biomaterial over others, or even the necessity for their use in case of immediate implantation.<sup>18-21</sup> However, well-known osteoconductive properties of HA<sup>31-33</sup> and the authors' experience with this biomaterial<sup>34,35</sup> prompted the use of a porous and relatively resorbable HA to support the collagen membrane, the exceptional presence of this biomaterial on histologic preparations confirming its good resorbability. Histometric analysis of bone-to-implant contact is often performed using linear bone-to-implant contact (BIC).<sup>15,18,19,22</sup> However, the surface and density measurements of bone between threads allow the evaluation of integration beyond only the BIC, the latter not always but often representing only a limited portion of the area between threads.

For practical reasons, it was not possible to provide professional postsurgical plaque control for the animals; thus the dogs did not receive any toothbrushing for the entire healing period. These conditions probably contributed to the bacterial accumulation and peri-implant soft tissue inflammation possible observed on some histologic sections. In addition, in this study the use of implants in a nonsubmerged protocol exposed the implants to functional disturbances in this animal model, which could have negatively influenced their primary stability (already diminished in case of immediate implant placements). The inflammation of bacterial origin and early destabilization could explain the failure of 3 implants, with their bone anchorage level being apical to the last thread, and the loss of 8 other implants. The fact that all lost implants were situated at the control or HA-treated sites, while treatment options were allocated randomly to different sites, suggests a link between the treatment modality and the implant loss. Therefore, the statistical analysis should be performed using the total number of implants ( $n = 40$ ), with the values of measurements on lost implants being equal to zero (0%). However, 6 of the 8 lost implants were placed at sites corresponding to the second mandibular premolars, with an osseous environment different from that of the third premolars. Krump and Barnett<sup>36</sup> have shown the importance of the anatomic situation and osseous environment in obtaining sufficient primary stability during immediate implantation. If the loss of implants in the present study was related to their position in the arch, the

results should be analyzed excluding all lost implants ( $n = 32$ ).

These results, both qualitative and quantitative, show large variability. Considering all implants ( $n = 40$ ), this variability was even higher, since the value of measurements on lost implants was considered to be zero (0%). For all studied parameters, the weakest values were those obtained at sites treated only by HA. The values obtained at control sites were intermediary, slightly inferior to the values obtained at sites treated by membrane alone or by the combination of membrane and HA, for which comparable values were obtained. Although the histogram of the 3 measured parameters has similar profiles, the surface and peri-implant bone density evaluations proved to be less discriminatory than the number of bone-contacting threads. Indeed, the latter parameter allowed the detection of significant differences for sites grafted with HA and sites treated by the membrane with or without the association of HA. These results put into question the rationale for using HA, alone or as a space-maintaining material in combination with a membrane during immediate implant placement. The percentage of bone-to-implant contact, never more than 55%, demonstrated that bone regeneration at the peri-implant cervical defect is on average very limited and that the contribution of absorbable biomaterials is not crucial and determinant for bone regeneration for this indication in this experimental model.

When lost implants were discarded ( $n = 32$ ), the surface of peri-implant bone was significantly different between the 4 therapeutic modalities, more advantageous at the control sites in which the amount of bone-contacting threads showed good bone regeneration around the initially exposed threads and a remarkable level of bone-to-implant contact. The lack of studies using methodology similar to that used in this experimentation limits the possibilities for comparison. In previous studies, the percentage of bone-to-implant contact has been reported as being relatively inconstant:

- 43% for perpendicular sections to 68.8% for sections parallel to the long axis of the implant<sup>18</sup>;
- 30.5% to 64.8% after 2 to 12 months of healing<sup>18</sup>;
- 59% on average after 4 to 7 months of early placement; and
- 29% to 32% for submerged implants, without any difference between control sites and defects treated by guided bone regeneration.<sup>15</sup>

The levels of bone-to-implant contact obtained in this present study were similar to those reported by others and in some cases even better, in particular for implants placed at the control sites. In all cases, the parameter showing the weakest values has been the peri-implant bone surface measurements. However, although this parameter is rather severe, it is the best indication of the histologic level of "osseointegration" of a given implant.

### Conclusion

This study has demonstrated the possibility of placing transmucosal nonsubmerged implants in fresh extraction sites. In spite of unfavorable conditions related to this animal model, the level of bone-to-implant contact was satisfactory for most implants, although it was probably influenced by the position of each implant in the arch. The absorbable biomaterials used in this study to accommodate the single-stage surgical protocol did not result in a significant enhancement of bone regeneration around the exposed threads of implants. New studies performed under more favorable experimental conditions, especially with respect to the healing period, should confirm the advantages of immediate implant placement in a nonsubmerged approach.

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