Observations on healing of human tooth extraction sockets implanted with bioabsorbable polylactic-polyglycolic acids (PLGA) copolymer root replicas: A clinical, radiographic, and histologic follow-up report of 8 cases

P. N. Ramachandran Nair, BVSc, DVM, Dr.Odont.h.c.,a and Jens Schug, DMD,b Zurich, Switzerland

UNIVERSITY OF ZURICH CENTER OF DENTAL AND ORAL MEDICINE

Objective. The objective was to conduct a clinical, radiographic, and histologic follow-up of alveolar socket healing in 8 human cases in which the extraction sockets of the involved teeth were treated with biodegradable root replicas before metallic implants were placed.

Study design. Chair side prepared solid and porous forms of root replicas made out of polylactic-polyglycolic acids (PLGA) copolymer were utilized. Five patients were treated with the solid form and 3 with the porous form of the replicas. The cases were followed up at regular intervals postoperatively, and standardized photographs and radiographs were taken. The cylindrical core of biopsies that were removed with trephine for placement of titanium implants were processed and examined by light and transmission-electron microscopy.

Results. Both forms of the root replicas were well tolerated and biodegraded by the body. There were no histologically observable pathological tissue reactions at the time of implant application. However, the solid form seemed to cause an initial decalcification of the bone surrounding the extraction sockets that was subsequently repaired along with the bone healing of the extraction sockets. Such initial decalcification of the alveolar process was not observed in the cases that were treated with the porous form of root replicas. There was wide variation in the osseous component of the trephine-harvested biopsies in both treatment groups that suggests inconsistency in bone healing of the alveolar sockets.

Conclusion. The 2 forms of root replicas under investigation were found to be biocompatible and biodegradable. But the compact solid form may cause an initial temporary lactic acid induced decalcification of the alveolar process, which makes it unsuitable for regular clinical application as compared to the granular porous form. The observed inconsistent and unpredictable bone regeneration calls for further research to develop more optimal replica materials.


The use of osseointegrated prostheses has become an important treatment mode in edentulous patients. The prerequisite for an expected long-term prognosis of such implant surgery is the presence of sufficient volume of healthy bone at the implant recipient site, a requirement that depends on the nature of postextraction healing and rehabilitation of the alveolar process. The histologic and histochemical events of human alveolar socket healing in undisturbed extraction wounds have been reviewed and described. A striking feature of the extraction socket healing is the life-long catabolic remodeling of the residual alveolar process that results in removal of a large volume of bone structure. This unique atrophy of the alveolar process has been described as reduction of residual ridges (RRR) and is considered to be a "chronic progressive, irreversible and disabling disease" of multifactorial origin. Although the causes and tissue dynamics of the process are poorly understood, both systemic and local factors have been suggested to be involved. The rate of RRR is rapid in the first 6 months of tooth extraction and takes place mostly in the areas of the jawbones where the roots of the extracted teeth are situated. Consequently, the size of the alveolar process is substantially reduced in buccolingual and coronoapical directions, particularly in the anterior maxilla. The remodeled alveolar process cannot properly accommodate cylindrical implants, thereby causing functional and esthetic problems of implant restoration. Therefore, it is essential to maintain or achieve the original dimensions of the alveolar process for successful long-term outcome of the treatment.

In order to preserve the height, width, and contour of the alveolar process, various prophylactic and post-extraction therapeutic measures have been attempted with widely varying outcomes. In general, all measures that minimize injury to the alveolar process and surrounding soft tissues during tooth extraction also minimize bone resorption during the wound healing process. The postextraction therapeutic measures include (a) physiologic preservation of the alveolar process.
by retention of the natural roots, (b) application of prefabricated semianalogous root form implants, and (c) modified versions of guided tissue regeneration (GTR) techniques. In the latter, alloplastic bone substitutes\textsuperscript{7-17} and bone or bone derivatives of isogenic,\textsuperscript{1,18-20} allogenic,\textsuperscript{7,11,21,22} and xenogenic\textsuperscript{23-26} origin have been used as osseoinductive and/or osteoconductive materials.

Based on the successful use\textsuperscript{27,28} of biodegradable osteosynthesis devices in the internal fracture fixation in maxillofacial and orthopaedic surgeries, Suhonen et al\textsuperscript{29} hypothesized that custom-made biodegradable root replicas placed as immediate implants in extraction sockets could preserve the dimensions of the alveolar processes. Experiments in rabbits\textsuperscript{29} revealed that insertion of custom made biodegradable root replicas into the extraction sockets of second maxillary incisors prevented palatal collapse of the implanted area. In a human case it was later reported\textsuperscript{30} that ridge height could be successfully preserved during 21 months of radiographic observation by immediate postextraction application of a polylactic acid (PLA) root replica into the extraction socket of 1 maxillary incisor in a 42-year-old woman.

The purpose of this communication is to report on the clinical, radiographic, histologic, and fine structural follow-up observations of postextraction socket healing in 8 human cases in which the extraction sockets of the involved teeth were treated with 2 forms of biodegradable root replicas before titanium implants were placed.

**MATERIALS AND METHODS**

Eight human patients whose clinical data are summarized in Table I were studied. They were treated in accordance with the Helsinki declaration. Informed consent of each patient was obtained after explaining the clinical procedures, risks involved, and benefits and clarifying all questions raised by the patients. A total of 8 biopsies derived from clinically healed extraction sockets of teeth that were implanted with root replicas after varying periods of tooth extraction were histologically investigated.

**Preparation of the root replicas**

In general, the roots of extracted teeth were copied chair-side to provide solid or porous root replicas. After extraction, the teeth were rinsed briefly in running cold water and the soft tissue attached to the root surface was removed mechanically. The solid root replicas were prepared from polylactic-polyglycolic acids copolymer (PLGA85:25; Resomer RG858; Boehringer Ingelheim, Germany) granules. The granules were placed in glass vials, sterilized with y-radiation (25 kGy) and heated in the vials at 130°C. The resulting melt was then poured into the root-impression mold. By cooling, the polymer solidified into solid root replicas for application into patients. The porous replicas were prepared with PLGA75:25 (Resomer RG756, Boehringer Ingelheim) as described elsewhere.\textsuperscript{31} Briefly, porous PLGA75:25 granules (500-800 μm) were poured into the root-impression mold. The mold containing the granules was then placed into a high-pressure vessel and exposed to a CO\textsubscript{2} atmosphere (50 bar) for about 30 seconds. The CO\textsubscript{2} acts as a solvent\textsuperscript{32} for the polymer so that the granules glue together to form a root-shaped body. The replicas reveal a porosity of 50% (v/v) with an average pore-diameter of 200 μm.

**Clinical procedures**

After extracting the teeth, each patient was first treated for a period varying from 4 to 12 months (Table I) with one of the biodegradable root replicas that were prepared by the chair side as described above. The root replicas were inserted into the alveoli immediately after careful extraction of the teeth so as to avoid damaging the alveolar processes. Five of them received the solid and 3 the porous form of the root replicas (Table I). Thereafter, the edges of the gingival wounds were held together by sutures so that the replicas remained in the alveoli. The sutures were removed after 10 days of application. The patients were clinically examined at 1, 3, and 6 months postoperatively. Standardized photographs and radiographs were taken during recalls until single implants (Institute of Straumann AG, Waldenburg, Switzerland)

<table>
<thead>
<tr>
<th>Case</th>
<th>Tooth</th>
<th>Birth</th>
<th>Replica insertion</th>
<th>Trepanning</th>
<th>Age/Sex</th>
<th>Observation (months)</th>
<th>Remarks</th>
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<tr>
<td>HG</td>
<td>7 (12)</td>
<td>08/31/66</td>
<td>12/01/98</td>
<td>11/10/99</td>
<td>34/F</td>
<td>11</td>
<td>Solid</td>
</tr>
<tr>
<td>SNV</td>
<td>9 (21)</td>
<td>07/23/42</td>
<td>10/01/96</td>
<td>04/16/97</td>
<td>55/F</td>
<td>6</td>
<td>Solid</td>
</tr>
<tr>
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<td>02/17/28</td>
<td>03/31/99</td>
<td>01/12/90</td>
<td>72/F</td>
<td>9</td>
<td>Solid</td>
</tr>
<tr>
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<td>3 (16)</td>
<td>07/16/51</td>
<td>07/13/98</td>
<td>01/13/99</td>
<td>48/F</td>
<td>6</td>
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</tr>
<tr>
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<td>11/05/62</td>
<td>04/21/99</td>
<td>01/12/90</td>
<td>38/F</td>
<td>8</td>
<td>Porous</td>
</tr>
<tr>
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<td>20 (35)</td>
<td>11/22/45</td>
<td>05/07/98</td>
<td>01/15/99</td>
<td>54/F</td>
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<tr>
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<td>07/13/59</td>
<td>06/14/99</td>
<td>06/14/90</td>
<td>41/M</td>
<td>12</td>
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<td>09/29/48</td>
<td>04/13/99</td>
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<td>51/F</td>
<td>4</td>
<td>Porous</td>
</tr>
</tbody>
</table>

*Highlighted cases are illustrated and described in the results.

†FDA tooth indices in parenthesis.
were placed into trephine-drilled bone-beds. The trephine-bur-harvested cylindrical biopsies were processed for light and transmission-electron microscopy.

**Tissue processing**

Immediately after removal, the biopsies were fixed by immersion in a solution consisting of glutaraldehyde and paraformaldehyde for a period of 1 week. Thereafter, the specimens were decalcified in 0.25 mol/L ethylenediamine tetracetic acid (Titriplex-III; Merck, Damstadt, Germany) and 4% glutaraldehyde, subdivided in the axial plane into 2 halves, postfixed in 1.33% OsO4, dehydrated in ascending grades of ethanol, and embedded in epon. From each epon block, 1- to 2-μm thick survey sections and from selected blocks serial sections were prepared using glass or histodiamond knives (Diatome AG, Biel, Switzerland) and the Reichert Ultracut E microtome (Leica, Glattbrugg, Switzerland). The sections were stained in periodic acid-Schiff (PAS) and methylene blue-Azur II and photomicrographed in a Dialux 20 photomicroscope (Leica) equipped with the digital camera Progress C14 (Senoptik, Eching, Germany) and a digital imaging system (ImageAccess; Imagic, Glattbrugg, Switzerland). The sections were studied in a light microscope for any physical and/or pathobiological changes in the biopsies. Thereafter, areas in the epon blocks were determined for ultra-sectioning. Such selected tissue sites were target-trimmed and thin-sectioned with the Reichert Ultracut E microtome (Leica). The thin sections were double- contrasted with lead and uranium salts and examined in a Philips EM400T transmission electron microscope (Philips, Endoven, The Netherlands).

Because of the small sample sizes and nonstandardized variables involved in the cases, no attempt was made to quantify the tissue components of the biopsies by stereologic means because it was unlikely to have resulted in statistically reliable data.

**RESULTS**

The healing of the postextraction wounds of all the patients was uneventful and satisfactory by qualitative clinical and radiographic assessments at regular intervals. Clinically, the gingival heights and widths appeared to maintain the respective preoperative dimensions as can be judged by standardized photographic and radiographic means. However, some of the patients who received the solid form root replicas revealed an initial decline of radiodensity of the alveolar processes surrounding the extraction sockets that was subsequently replenished. Histologic examination of the trephine-harvested biopsies revealed considerable variation in the density of the trabucular bone at the implant sites. These clinical observations and histologic variations are described and illustrated in detail for 2 sample cases each for the recipients of the solid and of the porous replicas.

**Solid replica recipients**

*Case HG.* The right maxillary second incisor (tooth 7) of a 34-year-old female patient was involved in this case. The tooth had extensive cervical resorption (Fig 1, A). It was scheduled to be replaced with a titanium implant and was removed by careful extraction. Within minutes of tooth removal, the alveolus was closed by inserting a solid PLGA root replica that was prepared chair-side as described above (Fig 1, B-D). A control radiograph taken immediately thereafter showed a radiolucent alveolus delimited by a distinct radiodense line representing the alveolar bone (Fig 1, E). Clinically, the gingival healing was uneventful, and at the time of suture removal, 10 days postoperatively, no signs of microbial infection, exudation, or dehiscence of the wound were observed.

Three months after the extraction, a clear decline in the radiodensity of the alveolar process was observed. Concurrently the radiolucent area that was limited to the alveolus seemed to expand into the spongiosa of the alveolar process (Fig 1, F). However, by 11 months postextraction the radiolucency disappeared and a radiodensity reminiscent of a healthy alveolar process appeared uniformly in the vertical and horizontal planes of the interdental bone between teeth 6 and 8 (Fig 1, G). There was no observable ridge reduction, and a bone bed that was sufficient for insertion of the titanium implant was present (Fig 1, H). Histologically, the trephine-harvested core of tissue (Fig 1, I and J) showed loose trabecular bone separated by soft connective tissue that was devoid of any inflammatory cellular infiltration. No osteoclastic activity or other pathological features could be observed around the bony trabeculae.

*Case UR.* The right maxillary second premolar (tooth 4) of a 72-year-old female was scheduled to be replaced by an implant. The crown of the tooth was completely damaged (Fig 2, A), the root was carefully extracted and the alveolus was closed minutes thereafter by inserting a chair-side-prepared solid PLGA root replica as described above. Clinically, the gingival wound healed without complications (Fig 2, B). A control radiograph taken immediately after insertion of the root replica revealed a radiolucent alveolus with ill-defined radiodense contour (Fig 2, C). By 6 months post operatively the alveolar socket appeared to be filled with a radiopaque tissue except for the cervical most portion of the alveolus. The trephine-harvested cylindrical shaft of tissue showed similar histologic features (Fig 3, A) as those described for Case HG (Table I). No signs of bone resorption or inflammation of the intertrabecular soft tissue could be observed. The trabecular bone was lined.
Fig 1. Radiographic (A) and photographic (B) records of the right maxillary second incisor (tooth 7) of a 34-year-old female patient before (A) and the socket after tooth extraction (B). Note the cervical resorption of the incisor (A). A PLA replica (RP in C) of the extracted root of the tooth (RO in C) in position immediately after insertion into the extraction socket (D). Radiograph does not reveal the PLA replica (E). Control radiograph taken 3 months postinsertion of the replica (F) reveals partial dissolution of the radiodense contour of the alveolar socket and extension of the radiolucency. By 11 months postextraction, there is complete (G) bone healing of the extraction socket and the surrounding alveolar bone. Note the definite titanium implant in position (H) well within the bone-healed extraction socket 11 months postextraction. Histologically (I), trabecular bone (BO in I) separated by soft connective tissue (SC) can be seen in the trephine-harvested biopsy (J). (Original magnification: I × 30.)
on the outer aspect by cuboidal osteoblast-like cells and contained intact osteocytes within the bone (Fig 3, B and C).

Porous replica recipients

Case SCV. The biopsy originated from a 38-year-old female patient. The first left mandibular molar (tooth 19), scheduled for replacement by an implant, was extracted with regular oral hygiene, aseptic, and postextraction measures. A chair-side-prepared porous PLGA replica of the distal root was inserted into the extraction socket and the gingival wound closed as described above. There was uneventful healing of the gingiva. However, a macroscopically distinguishable reduction in the bucco-oral width of the gingival segment of the extracted tooth could be observed in occlusal view between 1 week (Fig 4, A) and 6 months (Fig 4, B) of postextraction respectively. The lateral photographs (Fig 4, C and D) taken concurrently did not reveal any observable reduction of gingival margin in the axial (apical-coronal) plane of the tooth. Radiographic records (Fig 4, E) taken immediately before extraction showed apical radiolucencies of the tooth which was more pronounced for the mesial root. The control radiograph taken 6 months post extraction (Fig 4, D) reveals increased radiographic density due to bone healing of the extraction socket.

Case NJ. The right maxillary second premolar (tooth 4) with extensive coronal decay (Fig 6, A) was to be replaced by an implant in a 41-year-old male patient (Table I). The diseased tooth was extracted and the alveolus was treated as described above. The
Fig 3. Low-magnification overview photomicrograph (A) of a midaxial section of the trephine bur-harvested cylindrical tissue shaft from the replica-implanted extraction socket of the tooth shown in Fig 2. The rectangular demarcated areas in A and B are magnified in B and C, respectively. Note the newly formed trabecular bone (BO) separated by soft connective tissue. The circular demarcated area in C is magnified in the insert in B. Note the osteocyte (OC) within the bone. (Original magnifications: A ×30, B ×75, C ×225.)
postextraction healing of the gingival wound was satisfactory (Fig 6, B). A control radiograph taken immediately after insertion of the chair-side-prepared porous PLGA root replica (Fig 6, C) revealed a radiolucent alveolus delimited by a radiodense line representing the alveolar bone (Fig 6, D). At 6 months postinsertion of the root replica, a control radiograph showed filling of the alveolus-bottom with a radiodense material and persisting radiolucency of the cervical portion of the alveolus (Fig 6, E). The premolar site was trephine-drilled and a definite implant was placed 12 months postextraction. Histologically, the trephine-harvested biopsy (Fig 6, F and G) revealed both osseous and soft connective tissue. However, unlike the biopsies described for the previous 3 cases, the bone was not distributed uniformly within the central
Fig 5. Low-magnification photomicrograph (A) of an axial histologic section of the cylindrical tissue core from the replica implanted extraction socket of the tooth shown in Fig 4. The demarcated areas in A and B are magnified in B and C, respectively. Note the newly formed dense trabecular bone (BO) separated by soft connective tissue (SC). The transmission electron micrograph (D) reveals an intact osteocyte (OC) within the newly formed bone. (Original magnifications: A ×20, B ×65, C ×125, D ×5,750.)
axial plane of the biopsy but was surrounding an area resembling an alveolar cavity filled with delicate soft connective tissue.

**DISCUSSION**

This report presents clinical, radiographic, histologic, and fine structural qualitative observations on postextraction healing of 8 alveolar sockets that were treated with the 2 forms of biodegradable root replicas before definite implants were placed.

There has been several attempts to prevent postextraction atrophy of the alveolar ridge so as to maintain or regenerate (augment) the alveolar process when they were seriously diminished due to periodontal or other diseases before extraction of the affected tooth. Most of the publications were human case...
or animal studies\(^9\),\(^12\),\(^17\),\(^19\),\(^21\),\(^36\),\(^39\) in which bone grafts or bone substitutes were used to preserve or augment the alveolar process with varying and often conflicting outcomes. In several cases histologic examination of the tissues removed during implant surgery was also done.\(^1\),\(^7\),\(^10\),\(^11\),\(^16\)–\(^19\),\(^21\),\(^23\),\(^25\),\(^26\),\(^39\) However, the treatment outcome of the cases presented here cannot be objectively compared with those of the above cited reports.

To our knowledge, there are only 2 publications in the literature,\(^29\),\(^30\) in which the extraction sockets were treated with biodegradable root replicas. The final radiographic outcomes in all of the 8 cases reported here broadly agreed with that of the 2 previous reports.\(^29\),\(^30\) In the pioneer study in rabbits,\(^29\) it was revealed that insertion of custom-made root replicas made out of polyglycolic acid (PGA) into the extraction sockets of second maxillary incisors prevented palatal collapse of the implanted area. Collateral control sockets that did not receive any root replicas showed clear collapse of the area. The idea of using biodegradable root replicas was extended to a human patient\(^30\) in whom 1 extraction socket was treated with a chair-side-made solid PLGA root replica. Based on radiographic follow-up it was reported that ridge height could be preserved during 21 months of observation and with time the radiographic density of the cancellous bone increased in the replica-implanted area.

However, in some of the 5 cases in which the solid PLGA root replicas were used and reported here, the radiographic healing of the extraction sockets and remodeling of the bone surrounding them were more eventful as those stated in the previous report.\(^30\) In certain cases there were initial decline in the radiodensity of the alveolar processes surrounding the extraction socket that resulted in total disappearance of the radiodense contours of the respective alveolar bone (Fig 1, \(F\) and \(G\)). This is suggestive of an initial expanding demineralization of the bones that surrounded the root replica. However, such initial decline in the radiodensity of the alveolar process were not observed in the 3 cases in which the porous form of root replicas were used.

It is known that hydraulic degradation of the PLGA copolymers results in the release of lactic acid monomers that are oxidized to pyruvic acid.\(^15\) The latter eventually enters the citric acid cycle and is metabolized to yield energy, \(\text{CO}_2\), and water. The release of organic acids from the solid PLGA root replicas might have been in quantities that could not be immediately metabolized by the body that possibly resulted in the initial demineralization of the bone surrounding the solid replicas. This was visualized as the initial decline in the radiodensity of the bone. Unlike the solid form PLGA mass, the porous form of the root replicas were composed of copolymer particles that were glued together so as to leave plenty of interconnected spaces that reduced the overall quantity the polymer components in the latter. As a result, the amount of lactic acid released from the porous form may be substantially lower than that from the solid form replicas. Further, body cells that were involved in the socket healing process might have entered the network of spaces in the porous replicas,\(^9\) resulting in a more efficient recycling and repair process.

Histologic findings of the biopsies harvested several but varying months after tooth extraction, at the time of insertion of the definite implants, suggest healing of the extraction sockets without complications. Absence of inflammatory and foreign-body giant cells in the biopsies indicate a complete biodegradation of the root replicas during the period of observation. The normal fine structure of the osteocytes suggests healthy regeneration of bone in the alveolar socket. However, the relative volume of bone within the biopsies, as can be qualitatively and subjectively assessed from 2-dimen-
sional tissue sections, varied substantially in both groups of patients that were treated with the solid and porous forms of root replicas. For instance, the biopsy from Case SCV (Fig 5) revealed an optimal bony trabecular distribution, but the socket healing in Case NJ (Fig 6) was mostly accomplished by soft connective tissue. This suggests inconsistency in bone regeneration of the extraction sockets. The reasons for the inconsistent bone healing of the extraction sockets are unknown.

A quantitative determination of the volume densities of the various tissue components of the biopsies was not attempted, because it was unlikely to have resulted in statistically reliable or biologically more meaningful data owing to the limitations of the material, such as the smallness of the sample sizes and noncomparable variables involved. The number of cases could not be increased owing to technical reasons. It may be further pointed out that the reported observations were on 8 patients who were under regular dental health care. They were not subjects of an experimental study. Therefore, it was ethically not possible to provide controls.

Nevertheless, a conclusion may be drawn that the 2 forms of root replicas under observation were biocompatible and biodegradable. The initial lactic acid-induced decalcification of the alveolar process by the solid form of root replica and the inconsistent bone regeneration call for further research to develop optimal materials that can be applied in human patients after adequate animal experimentation.

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REFERENCES


Reprint requests:
Dr. P.N.R. Nair
Institute of Oral Biology
Oral Structures & Development (OSD)
Plattenstrasse 11
CH-8028 Zurich
Switzerland

nair@zzmk.unizh.ch