RADIOGRAPHIC OBSERVATIONS ON THE USE OF TWO DIFFERENT REGENERATION MATERIALS IN A SINGLE SUBJECT: CASE STUDY

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Two infrabony defects (i.e. defects in tooth supporting bone that extend into the body of the bone) in different sites in the same individual were treated surgically. Tissue regeneration was incorporated into the surgical procedures using a different material in each site (oxidized cellulose mesh and bioglass). The post surgical radiographic appearance showed increasing calcification in both sites that was not complete even at 15 months after placement. The radiographic appearance of both sites was similar but calcification was observed above the crest of alveolar bone in the oxidized cellulose mesh site that was not present with bioglass site. As calcification did not appear to be complete by 15 months after placement and it did not resemble true bone in either site, it would appear that the regenerative process was not yet complete by this time. Bone regeneration may therefore progress slowly over a protracted period of time after placement. Some evidence is present that oxidized cellulose mesh may have enhanced regenerative capacity by comparison to other synthetic bone regeneration materials such as hydroxyapatite and bioglass. No conclusions could be drawn from this single case study and further work is necessary to confirm and investigate these observations more fully.

Keywords: Guided tissue regeneration, Hydroxyapatite, Bioglass, Oxidized cellulose, Tissue regeneration, Bone formation, Biomaterials

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INTRODUCTION

Periodontal disease is a condition affecting the majority of the adult population to a greater or lesser degree. Essentially, accumulation of microbial dental plaque biofilm causes the release of toxic and irritant by-products, which causes inflammation of the gingival (i.e. gum) margins known as gingivitis. With time the inflammation becomes so established as to result in a conversion from superficial inflammation to deeper seated destructive change. This results in breakdown of the delicate seal between the gingival margins and the teeth, with formation of pockets of dental plaque infection below the gingival margins. This is known as periodontitis and is characterized by the formation of periodontal pockets. These periodontal pockets, contaminated by pathogenic plaque bacteria, cause more deep-seated inflammatory change. This results in more destruction of the attachment of the teeth to the underlying bone, but more importantly resorption of the supporting bone. As a result of increasing loss of bony support, the gingivae recede, and the teeth start to become mobile and drift out of alignment. Ultimately abscess formation and tooth loss occur.

Management of this condition is aimed at eliminating and controlling the reinfection of pathogenic bacteria in dental plaque biofilm to arrest of the condition. While eliminating plaque biofilm from periodontal pockets is often successful, recontamination does occur, and retreatment may be necessary. As a result the condition can be arrested in most cases, but in some instances retreatment is necessary to maintain health.

The major problem in periodontics is that once bone loss has occurred, it will not spontaneously regrow. This is a well known problem in many medical situations in which bone is lost, and that while the remaining bone has the capacity for regrowth, the memory matrix for the missing bone is lost, and the osteoblasts are unable to regenerate the lost bone. Therefore, in the management of periodontitis, but also other medical conditions in which bone loss is a feature, achieving regeneration of the lost bone is a primary objective outcome that has eluded clinicians. Considerable research has been directed at achieving regeneration of bone in clinical situations.

Essentially there are two ways of achieving tissue regeneration in defects in bone caused by destructive periodontal diseases: grafting/infill techniques, and guided tissue regeneration (GTR).

Achieving bone regrowth using grafting/infill techniques by demineralised freeze-dried bone has been very popular, and good results have been reported. However increasing concerns in the general population and the profession about the use of tissue-derived products has resulted in an increasing use of synthetic alternatives. Many materials have been used for this purpose, and these have included plaster of Paris (Radentz and Collings 1965) and hydroxyapatite/tri-calcium phosphate materials (Galgut 1990, 1992, 1998). Plaster of Paris was used many years ago, with little apparent success, although there has been some revival in interest in this material more recently. The hydroxyapatites and tri-calcium phosphate materials are manufactured for dental use in many different forms, which include resorbable/non-resorbable, sintered/non-sintered, and different physical structures, all of which were claimed to give superior results. However, when used clinically, it has been reported that these materials do not live up to expectations (Galgut et al. 1992; Polson and Yukna 1994; Stahl and Froum 1987; Caranca et al. 1987), and therefore the use of these materials in clinical practice has waned with time. More recently bioglasses have been developed for use in infrabony defects to encourage bone regrowth. BioGlass® was developed by Professor Larry Hench in response to a request by the American Medical Corps to develop a material to help regenerate bone for Vietnam war veterens who had suffered extensive bone damage As with all glass it is made up predominantly of silicon dioxide (SiO_2), but other substances include Na_2O, CaO, and P_2O_5, but characteristically, in a high CaO/P_2O_5 ratio, which makes BioGlass® highly bioactive in aqueous media. Results of the use of these materials clinically have been encouraging (Wilson and Low 1992; Zamet et al. 1997).

Guided tissue regeneration has been used extensively to achieve regeneration of bone and periodontal structures. This technique employs barrier membranes, placed over bony defects to preferentially promote bone growth as opposed to scar tissue formation from maturing granulation tissue. A number of different membrane materials have been used, and results of treatment using this technique have been good.

Cellulose based wound dressings were developed by Johnson & Johnson for medical use in the early 1980's, and a specific dressing to promote wound healing in dentistry called Surgicel (oxidized cellulose mesh) was produced as a post dental extraction dressing for use in the mouth. This material occluded and sealed the extraction socket wounds by absorbing blood from the wounds, which then clotted to form a semirigid blood-mesh conitinuum. The product, being extracted from seaweed contains high $CaPO_4$ concentrations which were claimed to provide the mineral basis for enhanced bone growth. In addition the material was claimed to be bacteriostatic. This material has been used to promote healing in dentistry for many years, and more recently in surgical applications (Sharma et al 2003) to control postoperative haemorrhage. Different forms of this material have also been used to aid in tissue regeneration of cartilage (Svensson et al 2005). Being licensed for use in the oral cavity, with the ability to form an infill and scaffold to support maturing granulation tissue, with natural biodegradable properties which potentially encouraged bone regeneration, and with bacteriostatic properties, oxidized cellulose mesh seemed to have ideal properties for consideration as a bone regeneration material in the treatment of periodontal defects in bone arising from the ravages of destructive periodontal diseases.

This author has published a number of case studies (Galgut 1990, 1990) utilising oxidized cellulose mesh to achieve enhanced regeneration of periodontal tissues using the GTR technique. In attempting to reduce the amount of postoperative attachment loss, a combination technique using hydroxyapatite as an infill material, followed by oxidized cellulose mesh used as a protective and exclusive membrane has been described (Galgut 1990). However, it was shown that the clinical benefit using this combination technique was limited. Subsequently, another variation of this technique has been described (Galgut 1994) in which the oxidized cellulose mesh was cut into small pieces and placed incrementally into a defect to act as a scaffold for maturing blood clot and granulation tissue, as well as over it to act as a protective membrane, using the material in a combined infill and GTR technique. A case report has been published (Galgut 1998), demonstrating that similar results can be achieved in clinical healing when using oxidized cellulose mesh in this way, as compared to bioglass. Although these case studies (Galgut 1994, 1998, 1990, 1990) have shown good results clinically, the question remains as to whether actual tissue regeneration using this material occurs, and how it compares to other materials used for this purpose.

AIM

The aim of this paper is to compare radiographically the amount of bone regrowth using oxidized cellulose mesh versus bioglass placed into two surgically exposed defects in the same patient.

MATERIALS AND METHODS

The subject for this case study was a 50 year old medically healthy Caucasian male who had been referred for periodontal treatment. On initial examination it was found that multiple periodontal pockets of infection were present, ranging from 4 to 8mm in depth, the plaque score was 75% (indicating very poor oral hygiene), and the gingival bleeding score was 16% (demonstrating the presence of high levels of active inflammation). Periapical radiographs using a paralleling technique were taken pre-operatively. The patient was referred to the practice hygienist for an initial phase of treatment, which included oral hygiene instruction, supra- and subgingival scaling, and root planing of the periodontal pockets. After completion of the initial phase of treatment, the patient was seen for further scaling and root planing of the residual pockets by the author. After four weeks the healing response was assessed, and very little reduction in probing depths had occurred in a number of pockets, predominantly tooth 23, and teeth 45, 46, and 47, although the plaque score and gingival bleeding scores had reduced to negligible levels. Surgery was therefore indicated and, as infrabony defects were present, it was decided to use a regeneration technique to promote infill of these defects. Replaced flap surgery was undertaken using local anaesthetic, taking care to preserve as much of the gingival tissue as possible. The surgical flaps were reflected, the root surfaces exposed, and residual accretions were removed. The surgical sites were then flushed with a weak solution of hydrogen peroxide to cleanse and disinfect them prior to placement of the regenerative materials. Oxidized cellulose mesh (Surgicel ®, Johnson & Johnson Ltd., Slough, U.K.) was placed using an incremental technique in the defect in tooth 23, using a technique previously described (Galgut 1994), and bioglass (Perioglass ®, US Biomaterials Corp., Florida, USA.) was placed in the defects on teeth 45, 46, and 47. The patient was instructed to brush the teeth at the surgical sites very lightly, taking care to avoid brushing the gingival margins, and to rely on the use of chlorhexidine mouthwash three times a day after meals during the initial healing period. The patient was seen one week later for removal of sutures, at which time healing was progressing satisfactory. The patient was seen three monthly thereafter for maintenance visits. As clinically observable gingival health had been achieved, with resolution of periodontal pocketing, no radiographs were taken until the fourth review appointment after surgery which was in fact 15 months after the initial preoperative radiographs.

RESULTS

The results of this case study are presented in the radiographs listed as Fig. 1 a,b (pre-operatively and 15 months postoperatively) and Fig. 2 a,b (pre-operatively and 15 months postoperatively) for infrabony defects between the teeth).

Figure 1a shows the defect in the bone surrounding the teeth pre-operatively. This was a "gutter" defect extending circumferentially around teeth, together with horizontal bone loss. This site received oxidized cellulose mesh, filling the "gutter" and covering the defect to a thickness of approximately 1.5mm above the alveolar crest. Figure 1b, a radiograph taken 15 months after placement, shows a band of partial radio-opacity extending approximately 1 mm supra-crestally around teeth, with some increase in radio-opacity in between the teeth. The increase in radio-opacity in this infra-bony defect in between the teeth is difficult to discern, because a thick plate of cortical bone was present, which masked the extent of the defect on these radiographs. Nevertheless the supra-crestal radio-opacity is clearly visible, and it should be noted that this is not as radiodense as the original alveolar bone, indicating that the radiodensity of the calcified material filling the defect, presumably bone, was not equivalent to the original alveolar bone at this point in time.

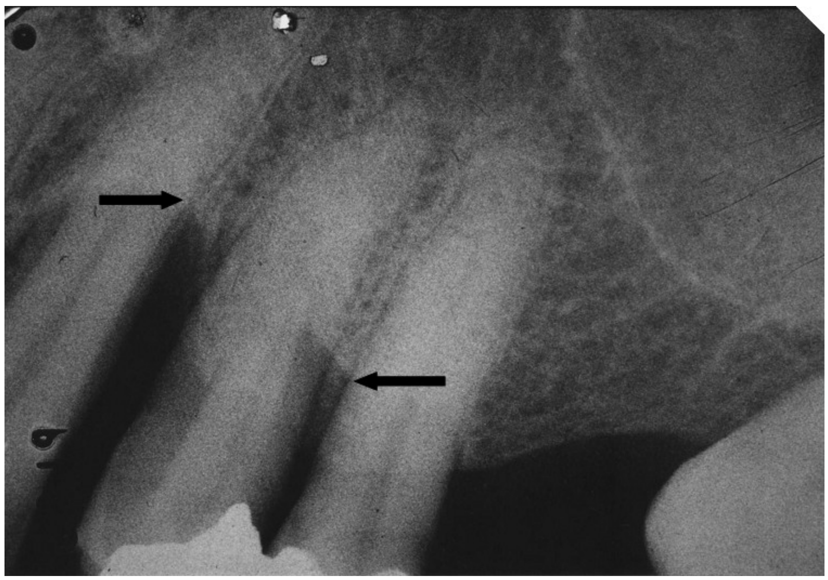

Figure 1a. Radiograph showing bone loss around several teeth with an infrabony defect between two teeth (see arrow).

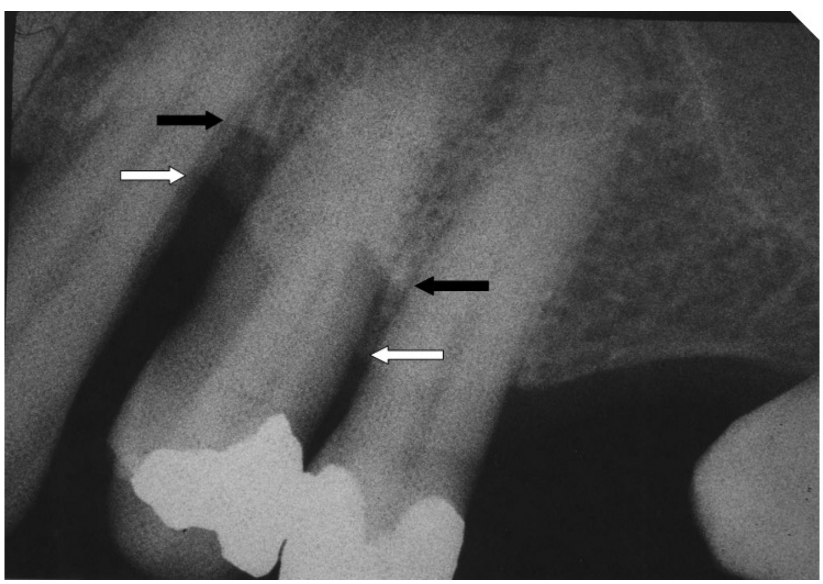

Figure 1b. Radiograph of the same site 15 months postoperatively showing infill of the infrabony defects (see arrows) and an increase in radiodensity supracrestally, which has not matured to form the radiographic characteristics of bone. (White arrows = change; black = baseline.)

Figure 2a shows other defects in a different site in the same patient pre-operatively. It can be seen that extensive horizontal and vertical bone loss had occurred.

At 15 months postoperatively (Fig. 2b) it can be seen that the defects had partially filled in. A diffuse partially radio-opaque material is visible interdentally and coronally to the bony margins of the original infrabony defect (see arrows).

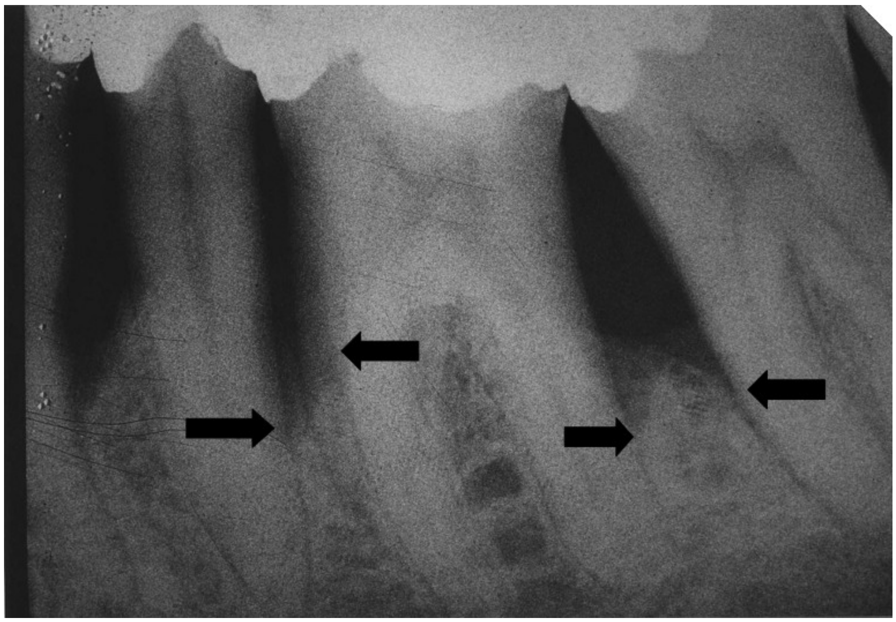

Figure 2a. Pretreatment radiograph showing bone loss and infrabony defects between several teeth.

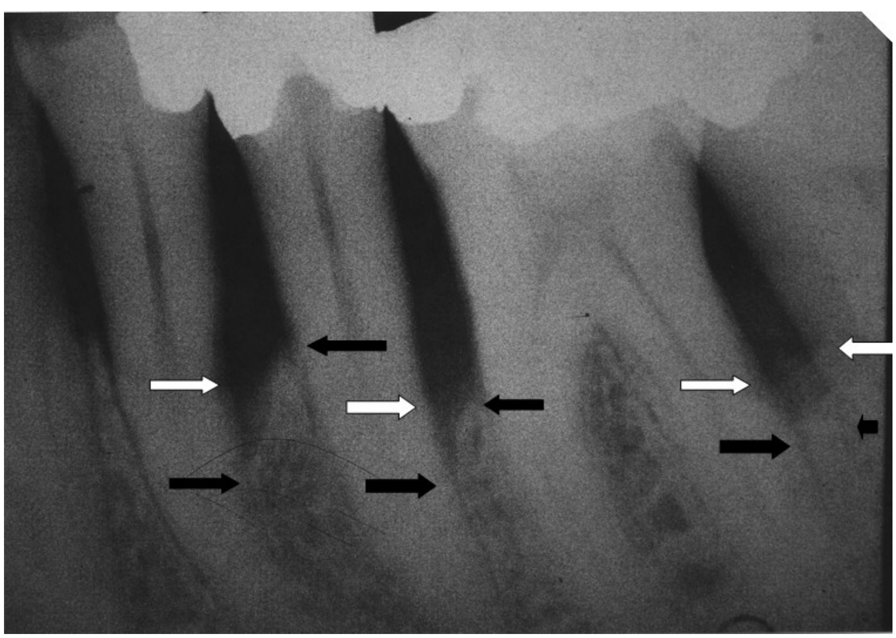

Figure 2b. Radiograph of the same site taken 15 months postoperatively showing an increase in radiodensity in the infrabony defects but only partial infill of the defects. The radiodense material is diffuse and without trabeculations indicating that it had not matured into bone. (White arrows indicate change; black arrows show baseline.)

The defect between the teeth illustrated in Figs. 2a and b show increased radio-opacity, which reduces from the bony surface of the original defect towards the coronal root surface. Furthermore, it should be noted that a clear demarcation line can be seen between the alveolar crest and the less radio-opaque material. Similarly it should be noted that no clear boundary can be determined at the coronal edge of the healing defects in the 15 monthly post-treatment radiograph. The absence of a clear edge to the partially radio-opaque material indicates an ongoing calcification process, presumably forming bone, which was not yet complete 15 months after placement. If these ill-defined areas of increased radio-opacity indicate a calcification process forming new bone, it seems as though this process was not completed by as long as 15 months after placement.

This characteristic of partial radio-opacity has been observed in both the site that received oxidized cellulose mesh and the site that received bioglass, possibly indicating that the calcification process and bone formation takes place over an extended period of time, exceeding 15 months after placement, irrespective of the material used.

DISCUSSION OF RESULTS

In this paper two sites in the same patient were treated using different defect infill materials to achieve tissue regeneration. The radiographic appearance 15 months after placement indicated some radio-opacity developing in both sites. It may be assumed that this radio-opacity is part of a calcification process that may eventually lead to bone formation. However the radiographic characteristics of neither of these materials resembled bone, as no trabeculations, lamina dura, or radiodense cortical surfaces, characteristic of true bone were visible in either of these sites. Therefore, if bone was forming, it had not completed the regenerative process in either of the treated sites by 15 months after placement.

As both sites were in the same patient, one may assume that the conditions for healing were similar, and the fact that the radiographic appearance of both sites was similar indicates that both infill materials had a similar effect of enhancing calcification, which may lead to the formation of true bone, but this process takes place over a protracted period of time.

A number of clinical studies have shown that very little difference is clinically observable in the amount of regeneration that can be achieved using either G. T. R. or graft/infill techniques (Polson 1994; Polson et al. 1994). The amount of tissue regeneration that can be achieved and the rate of tissue regeneration is dependent on a multitude of factors including postoperative contamination of the site, the cells that repopulate the wound during healing phase, the availability of nutrients, oxygen, and the appropriate cascade of growth factors within the healing wound, over which the clinician has no control (Nerem and Sambanis 1995).

Any conclusions from this case study of only two sites should be viewed with great caution, but the appearance of these sites in which two different materials were used was remarkably similar 15 months after placement both in a radiographic appearance, and the extent of the regenerative process. This observation is in agreement with other more substantial work that has concluded that calcification and bone formation occurs over an extended period of time, which may be in excess of 12 months with little observable difference between sites treated with different materials (Moon et al. 1996; Polson 1994).

An interesting additional observation was that the site that received the oxidized cellulose mesh was actually showing increased radio-opacity supra-crestally, indicating that bone may have been regenerating above the most coronal margin of the alveolar crest. This was not occurring in the bioglass site, in which the defects were only partially filled and were showing some residual angulation of the crest, characteristic of reduced, but not completely filled infrabony defects. This is a well documented observation with hydroxyapatites, which characteristically achieve calcification/infill only in the deepest parts of infrabony defects, and partial infill coronally (Galgut 1990, 1992, 1998). Therefore, although the radiodensity of both sites was similar, indicating a similar degree of calcification taking place, it was observed that the site receiving the oxidized cellulose mesh not only achieved complete infill of the site, but also has the potential to encourage regeneration supra-crestally. This may be a major advantage of this material in comparison to other synthetic bone regenerative materials. Skoog (1967) highlighted the substantial regenerative capacity of oxidized cellulose mesh in cleft palate cases where it was used to induce new bone formation where no bone previously existed. More recent work demonstrating significant reparative and regenerative properties of oxidized cellulose in gynaecological and cartilage repair procedures support the findings of this case study (Sharma et al. 2003).

Therefore it may in fact be possible to achieve enhanced bone regrowth in periodontal (and other) defects using oxidized cellulose mesh. Whether this effect can be achieved predictably in clinical practice, or this observation is a chance finding, or whether this represents some erroneous interpretation of the radiographs cannot be determined from this single site. Therefore, more work needs to be done in order to confirm this observation.

CONCLUSIONS

No definitive conclusions can be drawn from the radiographic observation of two sites in a single individual. However the interesting observation that calcification, possibly leading to bone formation takes place over an extended period of time, and is not complete by 15 months after placement is supported by other work. In both materials used in this case the calcification process seemed to be similar, an observation also supported by other published work, albeit not using oxidized cellulose for this purpose.

However, the observations that with oxidized cellulose mesh not only was complete defect fill achieved, but some supra-crestal calcification was evident on the radiographs have not been reported previously, and the subject needs to be investigated more fully in more definitive controlled clinical trials.

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