Dental Implants Placed in Extraction Sites Implanted with Bioactive Glass: Human Histology and Clinical Outcome

Michael R. Norton, BDS[1]/June Wilson, PhD[2]

Purpose: *To evaluate the clinical outcome of implants placed into sites grafted with bioactive glass.* ***Materials and Methods:*** *Seventeen consecutively treated patients were referred to a private specialist surgical practice for the repair of dentoalveolar defects, and/or ridge maintenance at the site of extraction sockets, prior to implantation. Bioactive glass available in 1 of 2 forms was utilized as an alloplastic grafting material. Bone cores were trephined out at the time of implantation and processed and examined to evaluate the tissue response under the light microscope. Implant mobility, marginal bone levels, and soft tissue health were all evaluated over a 2- to 3-year follow-up period to determine treatment success.* ***Results:*** *A total of 40 Astra Tech dental implants were placed. The overall sucess rate at the end of the study was 88.6% for implants that were in function for a mean period of 29.2 months (22 to 24 months). One patient with 5 successful implants died at 18 months after functional loading. At that time the cumulative success rate was 90%. Another patient who was diagnosed with cancer of the large bowel lost 3 implants. If this patient were excluded from the data, the cumulative success rate increases to 96.8%. Mean marginal bone loss measured 0.5 mm mesially and 0.4 mm distally over a maximum follow-up of 36 months. Human histology demonstrated that connective tissue was seen to exist without any inflammatory response, for up to 6 months. Increasing evidence of bone formation was seen in direct relation to the boactive glass material beyond this time frame.* ***Discussion:*** *The need to repair and augment dentoalveolar defects necessitates the use of autogenous bone or a substitute that may be seen to avoid the additional morbidity of a donor site procedure and without risk of cross infection. The use of bioactive glass has been proposed as a viable bone substitute. The current study draws attention to the long healing time required to achieve even a small amount of new bone incorporation into the graft, as seen histologically. However, the high rate of osseointegration and continued medium-term function of implants placed into these grafted sites would indicate that the use of bioactive glass does not prohibit osseointegration. However, it is likely that the initial integration will have derived from those areas in contact with native bone.* ***Conclusion:*** *Implants will survive for up to 3 years in sites grafted with bioactive glass, even when such grafts appear to only slowly conduct new bone growth.* (INT J ORAL MAXILLOFAC IMPLANTS 2002;17:249–257)

Key words: *alloplast, augmentation, bioactive glass, dental implants*

Dental implants have been utilized in increasing numbers since the publication of long-term data on the osseointegrated technique.[1–3] With advances in clinical skill, more difficult cases have been addressed, particularly with the aid of grafting, when the volume of dentoalveolar bone would otherwise prohibit implant placement.

Grafting materials are known to encourage new bone formation by differing means. Autogenous bone, the so-called "gold standard," can induce bone formation through osteogenesis, while allogeneic bone is said to be osteoinductive. Xenografts, such as bovine-derived bone mineral and the bioactive glasses such as Biogran (Implant Innovations, Palm Beach Gardens, FL) and Perioglas (US Biomaterials, Alachua, FL), are said to encourage the apposition of new bone by osteoconduction or osteoproduction and can only work in the presence of differentiated osteoblasts. The use of these latter materials has found increasing favor

[1]Specialist in Surgical Dentistry, Private Practice, London, United Kingdom.
[2]Consultant, Department of Materials, Imperial College, London, United Kingdom.

Reprint requests: Dr Michael R. Norton, 98 Harley Street, London W1G 7HZ, United Kingdom. E-mail: drnorton@nortonimplants.com

within dental surgery for repair of periodontal and dentoalveolar defects,[4–9] because of concerns over morbidity with donor sites and the perceptions of the public regarding the risks of cross-infection with donated human bone and xenografts.

The discovery and development of 45S Bioglass (US Biomaterials), a compound of 45% SiO_2, 24.5% Na_2O, 24.5% CaO, and 6% P_2O_5 has been shown to induce a sequential reaction that encourages bonding to hard and soft tissues.[10,11] This material and other identical compounds have been closely scrutinized through in vitro and animal studies.[12–15] However, to date the majority of human studies have used only clinical parameters such as probing depth and radiographic appearance to assess the success and incorporation of the graft,[4,5,9,16] while histology has been scarce, with only limited numbers presented in a few reports.[6,17]

Furthermore, many clinicians are now using these materials in preliminary grafting procedures prior to placing dental implants. Yet to the authors' knowledge, there are no long-term data on implant success placed into sites grafted with bioactive glass.

There has been some speculation that glass particles of a narrow particle size range may in some way be preferable to particles of a wider size range.[4] The present study set out to document histologically, clinically, and radiographically the treatment of 17 consecutive patients, who required one or more dental implants in combination with preliminary grafting using either Biogran or Perioglas bioactive glasses. The principal aim of the study was to determine the success rate for implants placed into sites grafted with bioactive glass and to report the histology of the materials when used in humans. An effort was also made to identify any difference in tissue response to the 2 products used, which have identical composition but differing particle size ranges.

MATERIALS AND METHODS

Patients were added to the study in chronologic order. All were systemically healthy at the time of consultation. Diabetics, alcoholics, and drug abusers were excluded, but smokers were included.

Seven men and 10 women, with a mean age of 47.6 years (27 to 65 years), were referred for the extraction of failed teeth, typically the result of periodontal disease, endodontic failure, or trauma. All patients were informed of the treatment protocol and signed consent was obtained.

When requested by the patient, surgery was conducted under intravenous sedation; otherwise, all procedures were conducted under local anesthetic.

All extractions, grafting, and the implant surgery were carried out under antibiotic prophylaxis of 3g amoxicillin 1 hour preoperatively and then 250 mg 3 times a day for 5 days postoperatively. All patients were asked to rinse with a 0.2% chlorhexidine gluconate mouthwash for 1 minute preoperatively and then twice a day for 1 minute, for 1 week postoperatively.

In all, 40 teeth required extraction with a mean of 2.4 teeth per patient, resulting in intact extraction sockets or sockets with loss of the buccal/labial cortical plate (Fig 1a).

Extractions were facilitated by means of a periotome and gentle elevation, with every effort made to ensure maintenance of the labial cortical plate, when present. All sockets or defects were thoroughly debrided with aggressive curettage, followed by intramarrow perforation with a round bur through the cortical lining of the socket under profuse saline irrigation. A "bleeding bone bed" was considered an essential prerequisite to graft placement.

Defects were treated with 1 of 2 forms of bioactive glass (Fig 1b), Perioglas or Biogran, acquired on the open market and selected on a random basis. When bone could be collected during the intramarrow perforation of the sites, it was mixed with the graft. Gore-Tex (W. L. Gore, Flagstaff, AZ) barrier membranes were employed when sockets lacked a buccal/labial cortical plate (Fig 1c).

The time between augmentation and implantation ranged from 3 to 11 months, with a mean of 6.0 months (Table 1). Graft consolidation was subjectively assessed prior to implant surgery by comparing radiopacity of the graft and the trabecular pattern of the grafted area to intraoral radiographs obtained approximately 1 month after grafting surgery.

At the time of implantation, osteotomies were cut using a 2.5-mm trephine to harvest a core of bone. Biopsy sites were identified by their granular appearance and by using previous clinical photographs to confirm the original site of grafting. At least 1 core sample from each patient was then immediately fixed in 10% formalin. Osteotomies were completed according to normal protocol[18] followed by placement of the appropriate size titanium dental implant (Astra Tech AB, Mölndal, Sweden), so that the largest possible implant should be placed into the available bone volume. Typically osteotomies would pass apical to the zone of the graft, such that the apical portion of the implant would engage native bone.

Trephined cores were sent to the Department of Histopathology at King's College London Dental Institute, where they were processed and demineralized prior to routine histologic sectioning to 5 μm and staining with hematoxylin and eosin for light microscopic evaluation. In addition, 2 specimens

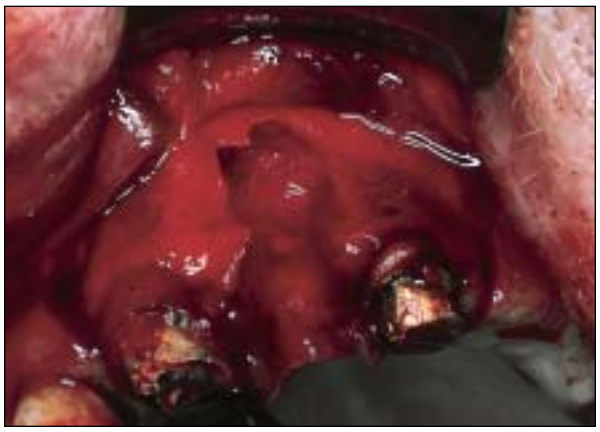

Fig 1a Patient 3 presented with a failing 7-unit fixed partial denture on 4 natural abutments. A large dentoalveolar defect is the result of an advanced perio-endo lesion, with loss of the labial cortical plate.

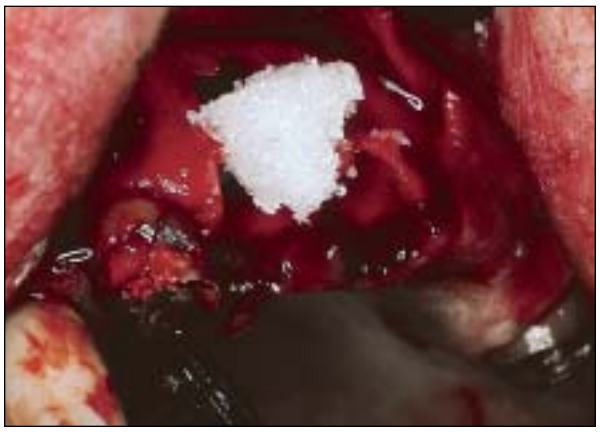

Fig 1b Defects such as those in Fig 1a were filled with bioactive glass soaked in saline or the patient's own blood.

Fig 1c *(Right)* For sockets without a labial/buccal cortical plate, the bioactive glass was localized by placement of a Gore-Tex barrier membrane.

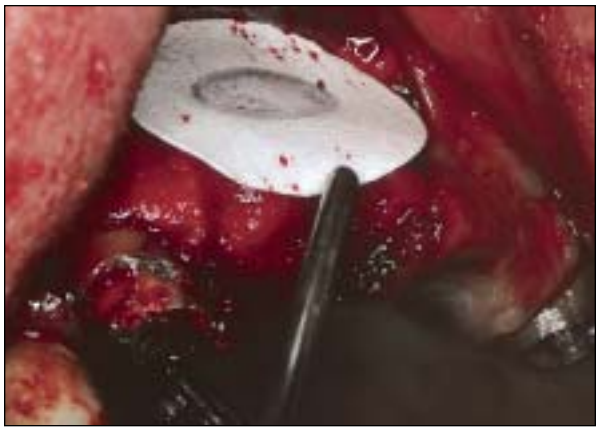

Table 1 Individual Patient Data in Chronologic Order of Biopsy Date

Patient	Age	Sex	Graft material	Interval (mo)	No. of implants	In function (mo)	Restoration type
1	44	M	BG	7	9	44	Fixed prosthesis
2	65	M	BG	3	5	18*	Overdenture
3	55	F	PG	9	4	43	Fixed prosthesis
4	27	F	PG	3	1	24	Single tooth
5	35	F	BG	4.5	1	27	Single tooth
6	42	M	PG/BG	7.5	4†	40	Single tooth
7	64	F	PG + Gtx	5.5	2‡	27	Single tooth
8	45	M	PG + Gtx	7	2	35	Fixed prosthesis
9	45	M	PG + Gtx	5	1	38	Single tooth
10	41	M	PG + Gtx	6	2	22	Single tooth
11	75	F	PG	3	3	30	Overdenture
12	27	F	BG	4	1	29	Single tooth
13	49	F	BG + Gtx	5	1	23	Single tooth
14	50	F	PG	7	1	26	Single tooth
15	49	F	PG	7	1	23	Single tooth
16	40	F	PG	8.5	1	25	Single tooth
17	56	M	PG + Gtx	11	1	23	Single tooth
Mean	47.6	—	—	6.0	2.4	29.2	Fixed prosthesis

PG = Perioglas; BG = Biogran; Gtx = Gore-Tex.
*Patient died during study period.
†3 failed.
‡1 failed.

were embedded in resin to produce sawn sections, which were stained with Sanderson's bone stain and Paragon stain.

After a 3- to 6-month osseointegration phase, all implants were exposed according to recognized protocol[18] and restored with ceramometal prostheses. Baseline radiographs were taken at the time of prosthesis placement, 6 months postloading, and then annually thereafter.

Implant success was defined by the absence of implant mobility, the absence of adverse soft tissue reactions, the absence of pain or infection, and a marginal bone loss of less than one-third the length of the implant over the entire period of function. The removal of a mobile implant or bone loss measuring greater than one-third the length of the implant, even if still immobile, was used to define implant failure.

The occlusion was checked using 8-µm foil (Shimstock, Hanel, Germany), which was to resist withdrawal only under maximal clenching. Soft tissue health was evaluated visually and via light probing with a PDT Sensor-probe Type C (Rota-Dent, Cambridgeshire, United Kingdom) to determine the presence or absence of bleeding on probing. Marginal bone levels were assessed radiographically using a long cone technique with a Rinn film holder (Rinn Corp, Elgin, IL). Bone levels were measured at 8× magnification using a template based on the microthreads of an Astra Tech ST implant, which are 0.185 mm apart and commence 0.7 mm from the standard implant reference point at the head of the implant just below the most coronal bevel. Measurements were rounded up to within 1 decimal place, since it was not possible to determine bone loss to a higher degree of accuracy.

RESULTS

All grafting procedures were successfully carried out according to the individual patient treatment plans, without unforeseen complications. It was not clinically possible to determine any difference in the handling properties of the 2 glasses, which were wetted and packed in an identical manner.

Table 1 provides information for each patient. In total, 6 patients received Biogran and 12 received Perioglas in 18 sites and 21 sites, respectively. One patient was treated with paired defects. Six patients required the use of a Gore-Tex barrier membrane because of the lack of a buccal/labial cortical plate.

In 4 patients, the graft material/tissue mass appeared to take on an intense reddish color and could be described as having a rubbery consistency. In 2 of these patients (6 and 7), severe pain was associated with osteotomy preparation, which remained unremitting and uncharacteristic after placement of the implants. The pain was not easily controlled by analgesics. In both of these patients the only relief was achieved by removal of the 4 offending implants after only 2 to 3 weeks. Their removal resolved the pain, and healing was subsequently uneventful. For 1 of these patients, who lost 3 of 4 implants, a subsequent diagnosis of carcinoma of the colon was made, and it is proposed that this patient may have been immunocompromised at the time of grafting and implant placement. The remaining implant has been retained in function without further compromise.

In addition, 3 membranes became exposed, necessitating their early removal in 2 patients because of infection. All the above patients were instructed to continue with the chlorhexidine mouthwash and were prescribed 400 mg metronidazole 3 times a day for 5 days.

Another patient (#2) died 18 months after completion of his treatment. However, at the time of his death, 5 successful and functioning implants remained in grafted sites.

Histology

Microscopy revealed a mixed response. For the 8 grafts harvested prior to 6 months, glass was seen to be intimately related to an adherent connective tissue (Fig 2).

There was evidence of an inflammatory infiltrate in specimens harvested from patient 1, but this was considered to be more likely associated with remnants of inflamed periodontal tissue and not as a reaction to the glass, since there was an absence of macrophages. For patients 6 and 7 and all other specimens, there was no evidence of an inflammatory infiltrate and the overall appearance was indicative of a biocompatible material.

There was an absence of any new bone for all cores harvested within 6 months. A consistent appearance of bone was seen only in the cores harvested after a 6-month healing period. For the majority of these cores, minimal bone growth was noted at the periphery, and this was invariably described as mixed woven and lamellar in character.

In the 8 specimens harvested 7 months or more after grafting, bone appeared to lie close to the surface of glass particles, suggesting growth by apposition. It was also possible to identify bone growth within cavities in the glass particles (Fig 3).

The characteristic fissuring (Figs 2 and 3) of the glass particles was routinely seen in all specimens, but it was not possible for the histopathologist to

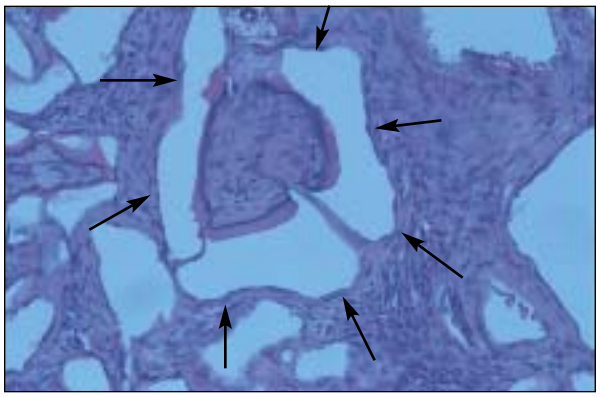

Fig 2 Section from a trephine harvested 5 months after grafting from patient 9 (H&E; magnification ×200). One complete glass particle can be seen in the center of the frame along with other glass fragments completely surrounded by an adherent connective tissue, in close apposition with the amorphous silica gel layer. Fissuring of the glass particle is clearly evident.

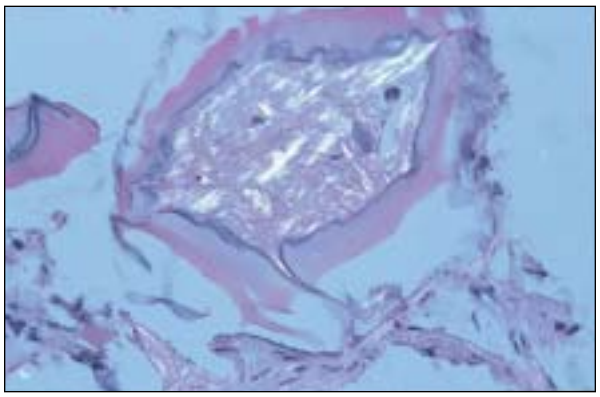

Fig 3 Section from a trephine harvested 7 months after grafting from patient 14 (H&E; polarized light; magnification ×400). One complete but fissured glass particle is in view, with lamellar bone filling the central cavity.

determine the difference between the 2 materials under light microscope.

Clinical Outcome

Apart from the 4 implants removed just 2 to 3 weeks after placement, all other implants were immobile at the time of abutment connection.

Eight patients were treated by their referring restorative dentist; the remainder were restored by the first author. All prosthetic restorations utilized recommended components and the manufacturer's protocol (Astra Tech). Eleven patients received 1 or more single-tooth restorations, 4 patients had their implants linked (sometimes to other implants placed at the same time, but in non-grafted sites) for fixed prostheses, and 2 patients were restored with nonresilient overdentures using a milled bar protocol[19] (Table 1).

All patients were followed up 3 to 6 months after placement of the definitive prosthesis, and annually thereafter regardless of whether they had been restored by the referring dentist. Only 1 patient (#5) was lost to follow-up, in addition to the patient who died. For all remaining patients, implants remained immobile, and their prostheses were found to be stable. Bleeding on probing was noted occasionally, but it was questionable whether this was associated with any disease, since at no time was there evidence of a true peri-implant mucositis. Visually, all soft tissues appeared pink and healthy. No patients complained of pain and there was no evidence of infection associated with any implants.

With regard to marginal bone levels, only the most current radiographs were evaluated, regardless of baseline values. No follow-up radiographs were available for patients 5 and 15, and patient 2 was unable to have intraoral radiographs because of the lack of vestibular depth. His orthopantomograph was considered unsuitable for measuring bone levels. Of the remaining implants, 16 (48%) demonstrated no marginal bone loss (Fig 4a), while for the other 52%, bone loss ranged from 0.7 to 2.2 mm (Fig 4b). These data yielded a mean bone loss of 0.5 mm mesially and 0.4 mm distally. No implants had bone levels even remotely approaching the one-third mark, which would have classified them as a failure.

When considering the total data at the 1-year follow-up, the cumulative success rate was 90%. As a result of the death of patient 2, the cumulative success for implants in function for greater than 18 months dropped to 88.6%. However, if the patient with carcinoma (#6) is excluded from the data, the cumulative success rate rises to 96.8%.

DISCUSSION

With increasing awareness of dental implants, more patients are demanding this type of treatment over conventional alternatives. As a result, many less-than-ideal sites require preliminary augmentation procedures prior to implant placement.

While autogenous bone remains the optimal graft material, many clinicians prefer to recommend alternatives, since this can help to avoid a second

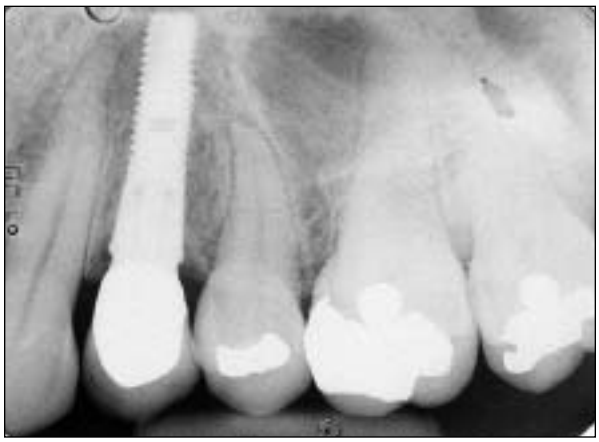

Fig 4a Radiographtaken after 2 years of function for the implant in patient 14. There is an increase in the radiopacity of the surrounding tissue. The radiograph also demonstrates excellent maintenance of marginal bone.

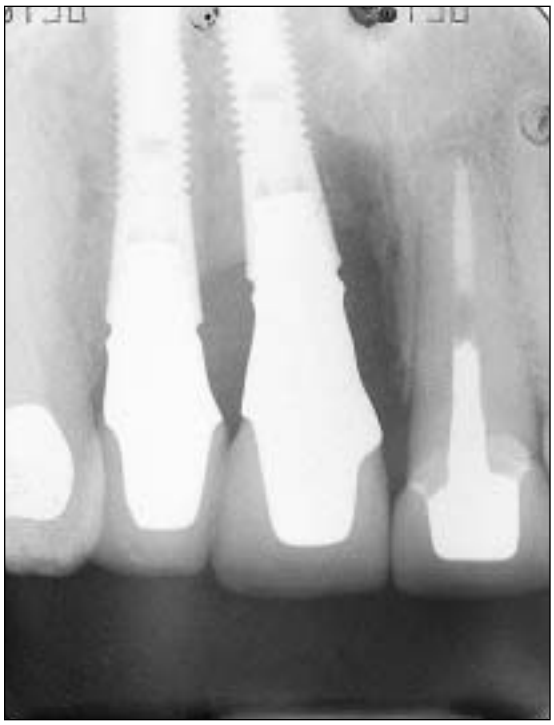

Fig 4b *(Right)* Radiograph taken after 1 year of function for the implant placed into grafted tissue (maxillary right central incisor) in patient 13. There has been a clear loss of bone on both mesial and distal surfaces, which has stabilized. In this case, bone loss was likely the result of an unfavorable crown-to-implant ratio.

surgical donor site, thus reducing morbidity. However, many patients have expressed concern for perceived risks of cross-infection with allogeneic grafts or xenografts. Consequently, there has been an active market for the research and development of synthetic graft materials.

Many studies have been carried out to demonstrate the efficacy of one graft material versus another, and within the group of synthetic graft materials the bioactive glasses have been the subject of considerable investigation. These have shown the material to undergo a sequential reaction to encourage bonding of hard and soft tissues[10–14] and to be both non-toxic and biocompatible.[20] However, little has been published to date to give any insight as to whether such grafts can support functioning dental implants.

This study set out to record the success over a 2- to 3-year period of titanium dental implants placed into sites grafted with bioactive glass. In addition, histology of the graft/host tissue was evaluated from cores harvested at the time of implant placement, to determine whether new bone formation was present.

It is currently known from in vitro studies that low levels of dissolution of the bioactive glass particles in the physiologic environment exert a genetic control over osteoblast cell cycle and rapid expression of genes that regulate osteogenesis.[21–24] Xynos and coworkers[23] have shown that within 48 hours, a group of genes was activated—including genes encoding nuclear transcription factors and potent growth factors—using cultures of human osteoblasts, obtained from excised femoral heads of patients (aged 50 to 70 years) undergoing total hip arthroplasty.

In particular, insulin-like growth factor-II (IGF-II), IGF-binding proteins, and proteases that cleave IGF-II from their binding proteins were indentified.[21–24] The activation of numerous early response genes and synthesis of growth factors was shown to modulate the cell cycle response of osteoblasts to the bioactive glasses and their ionic dissolution products. These results indicate that bioactive glasses can enhance osteogenesis through direct control over genes that regulate cell cycle induction and progression. However, these molecular biology results also confirm that osteoprogenitor cells must be in a chemical environment suitable for passing checkpoints in the cell cycle towards the synthesis and mitosis phases. Only a select number of cells from a population are capable of dividing and becoming mature osteoblasts.

The above studies that demonstrated rapid osteogenesis in the presence of bioactive glasses were performed in culture environments. In addition, only animal experiments have consistently demonstrated predictable results, with the formation of new bone over relatively short healing times,[8,13–15, 25,26] which contrast with the findings in this human study, which indicate that new bone

formation within the graft cannot be demonstrated histologically after less than 6 months of healing.

Until now it has been difficult to demonstrate these findings in the human, since the majority of studies using bioactive glass have expounded its success by clinical rather than histologic means.[4,5,9,16] In particular, the demonstration of reduced pocket probing depths and graft appearance on radiographs have been cited to extrapolate histologic findings from animals and conclude, perhaps erroneously, that the graft has been osseoincorporated.

Histology has been available for only a few cases. A recent study by Nevins and associates[17] was the first to provide a series of cases with histology for 5 patients treated with Perioglas for the repair of periodontal defects. While the demands for regeneration of bone, periodontal ligament, and cementum are unquestionably greater than for bone augmentation, 3 of the 5 biopsies were harvested at 7 months without evidence of tissue regeneration. However, the authors rightly drew attention to the contradictory appearance of the radiographs when compared to the histology, which showed little bone even for those harvested at 12 months.

In the current study, human histology was evaluated for 17 patients consecutively treated with 2 forms of bioactive glass, Biogran and Perioglas, for the repair of a total of 40 extraction sockets. The staged technique of grafting first and subsequently placing implants provided a unique opportunity to gain reentry and harvest bone cores at a variety of healing times.

Histology revealed a mixed response, with grafts harvested up to 6 months showing no apparent new bone formation. In these specimens the glass particles could clearly be seen in association with adherent connective tissue, as described by Nevins and colleagues.[17] However, after 7 months, there was sparse new bone formation present. The bone was of a mixed woven and lamellar nature and could be seen both at the periphery and centrally within the specimens, underscoring the idea that this material is both osteoconductive and osteoproductive.[14] It was also possible to demonstrate bone forming within the central cavities of individual glass particles. The amount of bone seen in any one specimen was minimal, although with increasing duration more bone was apparent, often embedding the glass particles within it. In only 1 specimen was there any evidence of an inflammatory infiltrate; however, this was not thought to be related to the presence of the glass, which consistently demonstrated a high degree of histologic biocompatibility.

No obvious histologic differentiation could be made between the 2 forms of bioactive glass, although the data size and lack of histomorphometry do not allow any real conclusions to be drawn in this regard.

Clinical parameters, such as the clinical appearance of the healed graft sites as well as the radiographic appearance, influenced the healing time frames for each patient, which varied from 3 to 11 months.

In 4 patients, the grafts were found to have an unusual consistency; they were rubbery and intensely red in color. This tissue was hypersensitive to instrumentation and in 2 patients necessitated the removal of 4 implants, which resulted in resolution of the pain. When evaluating the histology, there was nothing untoward about the appearance of the tissue from these specimens, which showed an adherent connective tissue surrounding the glass particles. There was no evidence of an inflammatory infiltrate. It was a source of concern that all of these patients had been treated with material (Perioglas) that had the same batch number. However, after thorough investigation by the manufacturer, no batch-related problems could be ascertained. Other patients in the current study had received material from the same batch without complication.

Of the 2 patients who required implant removal, 1 patient (#6) had 3 of 4 implants removed. However, he had also been diagnosed with carcinoma of the colon and this may have had a contributory effect, although this would not explain how 1 implant managed to survive.

In addition to these unforeseen events, 2 of the 6 Gore-Tex membranes used became infected because of early exposure, which necessitated their early removal. It is probable that such infections may have had a negative impact on the outcome of the graft. In 1 of these patients (#7), membrane infection was followed by the loss of 1 implant placed into the grafted site, which was of this unusual rubbery consistency.

For all other sites in all other patients, implants appeared to successfully osseointegrate, based on their clinical immobility and an absence of pain or infection. No further implant losses were recorded.

The cumulative survival rate of 90% at the 1-year follow-up is comparable to other studies of implants in grafted bone[27,28] and is comparable to studies for implants in general.[29–31] The death of 1 patient who had 5 successfully functioning implants adversely affected the cumulative success rate, as did the patient who lost 3 of 4 implants. Exclusion of these 2 patients yielded a cumulative success rate of 96.8% for implants in function from 22 to 44 months. Again, these results are comparable with other 3-year data.[29–31]

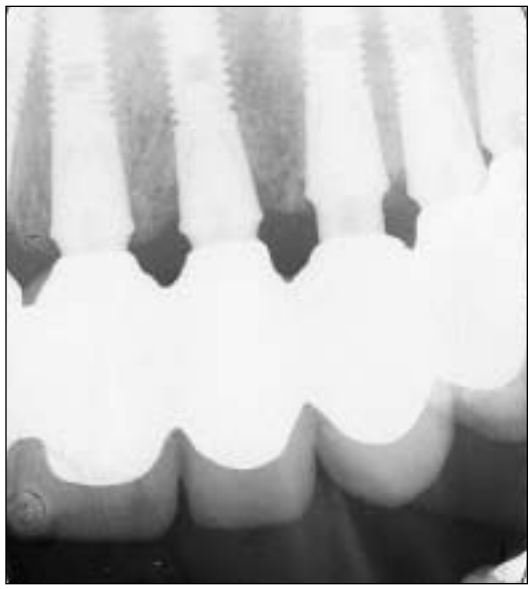

Fig 5 Radiograph from patient 1 demonstrates the close relationship between the marginal bone and the reference level, just below the bevel at the most coronal aspect of these Astra Tech implants.

All but 4 implants were associated with an absence of pain or infection, and soft tissues were generally healthy. The marginal bone data revealed a frequency of bone loss of 52%. For this group of implants, bone loss ranged from 0.7 to 2.2 mm. The total group data revealed a mean bone loss of 0.5 mm mesially and 0.4 mm distally. These figures are consistent with, although marginally higher than, other data quoted for Astra Tech implants placed into non-grafted sites.[32,33]

The values for marginal bone in this study were obtained by measuring from a fixed reference point on the implant, ie, the margin just below the bevel at the most coronal aspect of the implant (Fig 5), and was not compared to baseline data. Thus, in contrast to other data published in the literature,[27,34] which quote bone loss relative to baseline values, these current data could be considered the equivalent of a total bone loss.

While it is clear from the current study that bioactive glass cannot be relied upon to produce a graft/tissue mass incorporating vital bone for at least 7 months, it can nonetheless be stated that the use of these materials did not compromise implant success.

It is reasonable to postulate that the initial implant integration is likely to have derived only from those areas where implants came into contact with native bone. However, it is also probable that within the grafted area, increasing amounts of bone will have grown during the osseointegration process and subsequent functional loading periods. It would be desirable to have harvested graft perhaps en bloc surrounding an implant to assess further the histology, and to ascertain if the newly formed bone comes into contact with the implant surface. This could be recommended as the basis for future investigation.

CONCLUSION

The use of bioactive glass allowed slow incorporation of new bone into the grafted site after 7 months in this investigation. While it might be considered impractical from a time perspective to wait for bone incorporation prior to placing implants, it can be shown that the earlier placement of implants into the graft/tissue mass does not negatively impact upon the clinical outcome with respect to implant success.

ACKNOWLEDGMENTS

The authors thank Dr E. W. Odell, BDS, MSc, PhD, FDSRCS, MRCPath, of King's College London Dental Institute (Guy's Hospital) for processing the specimens and for reviewing the slides.

REFERENCES

1. Adell R, Lekholm U, Rockler B, Brånemark P-I. A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. Int J Oral Surg 1981;10:387–416.
2. Buser D, Weber HP, Brägger U, Balsiger C. Tissue integration of one-stage ITI implants: 3-year results of a longitudinal study with hollow-cylinder and hollow-screw implants. Int J Oral Maxillofac Implants 1991;6:405–412.
3. Arvidson K, Bystedt H, Frykholm A, von Konow L, Lothigius E. A 3-year clinical study of Astra dental implants in the treatment of edentulous mandibles. Int J Oral Maxillofac Implants 1992;7:321–329.
4. Schepers E, Ducheyne P, Barbier L, Schepers S. Bioactive glass particles of narrow size range: A new material for the repair of bone defects. Implant Dent 1993;2:151–156.
5. Shapoff CA, Alexander DC, Clark AE. Clinical use of a bioactive glass particulate in the treatment of human osseous defects. Compendium 1997;18:352–363.
6. Skogland A, Hising P, Young C. A clinical and histologic examination in humans of the osseous response to implanted natural bone mineral. Clin Oral Implants Res 1997;12:194–199.
7. Szabo G, Suba Z, Barabas J. Use of Bioplant HTR synthetic bone to eliminate major jawbone defects: Long-term human histological examinations. J Craniomaxillofac Surg 1997;25:63–68.
8. Turunen T, Peltola J, Helenius H, Yli-Urpo A, Happonen R-P. Bioactive glass and calcium carbonate granules as filler material around titanium and bioactive glass implants in the medullar space of the rabbit tibia. Clin Oral Implants Res 1997;8:96–102.

9. Zamet JS, Darbar UR, Griffiths GS, Bulman JS, Brägger U, Bürgin W, Newman HN. Particulate Bioglass as a grafting material in the treatment of periodontal intrabony defects. J Clin Periodontol 1997;24:410–418.
10. Hench LL, Splinter RJ, Greenlee TK, Allen WC. Bonding mechanisms at the interface of ceramic prosthetic materials. J Biomed Mater Res 1971;5:117–141.
11. Hench LL, West JK. Biological applications of bioactive glasses. Life Chem Rep 1996;13:187–241.
12. Shimizu Y, Sugawara H, Furusawa T, Mizunuma K, Inada K, Yamashita S. Bone remodeling with resorbable bioactive glass and hydroxyapatite. Implant Dent 1997;6:269–274.
13. Johnson M, Sullivan S, Rohrer M, Collier M. Regeneration of peri-implant defects using Perioglas: A pilot study in rabbits. Int J Oral Maxillofac Implants 1997;12:835–839.
14. Wilson J, Low SB. Bioactive ceramics for periodontal treatment: Comparative studies in the Patus monkey. J Appl Biomater 1992;3:123–129.
15. Wilson J, Clark AE, Hall M, Hench LL. Tissue response to Bioglass endosseous ridge maintenance implants. J Oral Implantol 1993;19:295–302.
16. Low SB, King C, Krieger J. An evaluation of bioactive ceramic in the treatment of periodontal osseous defects. Int J Periodontics Restorative Dent 1997;17:359–361.
17. Nevins ML, Camelo M, Nevins M, et al. Human histologic evaluation of bioactive ceramic in the treatment of periodontal osseous defects. Int J Periodontics Restorative Dent 2000;20:459–467.
18. Norton MR (ed). Dental Implants. A Guide for the General Practitioner. London: Quintessence, 1995.
19. Norton MR, Ferber C. The nonresilient hybrid removable prosthesis: Treatment of choice for the atrophic maxilla. Int J Periodontics Restorative Dent 1999;19:189–197.
20. Wilson J, Pigott GH, Schoen FJ, Hench LL. Toxicology and biocompatibility of bioglasses. J Biomed Mater Res 1981;15:805–817.
21. Xynos ID, Hukkanen MVJ, Batten JJ, Buttery LD, Hench LL, Polak JM. Bioglass 45S5 stimulates osteoblast turnover and enhances bone formation in vitro: Implications and applications for bone tissue engineering. Calcif Tiss Int 2000;67:321–329.
22. Hench LL. Bioactive materials: The potential for tissue regeneration. J Biomed Mater Res 1998;41:511–518.
23. Xynos ID, Edgar AJ, Buttery LDK, Hench LL, Polack JM. Ionic dissolution products of bioactive glass increase proliferation of human osteoblasts and induce insulin-like growth factor II mRNA expression protein synthesis. Biochem Biophys Res Commun 2000;276:461–465.
24. Xynos ID, Edgar AJ, Buttery LDK, Hench LL, Polak JM. Gene expression profiling of human osteoblasts following treatment with ionic products of Bioglass 45S5 dissolution. J Biomed Mater Res 2001;55:151–157.
25. Oonishi H, Kushitani S, Yasukawa E, et al. Particulate Bioglass compared with hydroxyapatite as a bone graft substitute. Clin Orthop Rel Res 1997;334:316–325.
26. Schepers EJG, Ducheyne P. Bioactive glass particles of narrow size range for the treatment of oral bone defects: A 1-24 month experiment with several materials and particle sizes and size ranges. J Oral Rehabil 1997;24:171–181.
27. Nevins M, Mellonig JT, Clem DS III, Resier GM, Buser DA. Implants in regenerated bone: Long-term survival. Int J Periodontics Restorative Dent 1998;18:35–45.
28. Fugazzotto PA. Success and failure rates of osseointegrated implants in function in regenerated bone for 6 to 51 months: A preliminary report. Int J Oral Maxillofac Implants 1997;12:17–24.
29. Cox JF, Zarb GA. The longitudinal clinical efficacy of osseointegrated dental implants: A 3-year report. Int J Oral Maxillofac Implants 1987;2:91–100.
30. Buser D, Weber HP, Brägger U, Balsiger C. Tissue integration of one-stage ITI implants: 3-year results of a longitudinal study with hollow-cylinder and hollow-screw implants. Int J Oral Maxillofac Implants 1991;6:405–412.
31. Arvidson K, Bystedt H, Frykholm A, von Konow L, Lothigius E. A 3-year clinical study of Astra dental implants in the treatment of edentulous mandibles. Int J Oral Maxillofac Implants 1992;7:321–329.
32. Norton MR. Marginal bone levels at single tooth implants with a conical fixture design. The influence of surface macro- and microstructure. Clin Oral Implants Res 1998;9:91–99.
33. Palmer RM, Palmer PJ, Smith BJ. A 5-year prospective study of Astra single tooth implants. Clin Oral Implants Res 2000;11:179–182.
34. Buser D, Dula K, Lang NP, Nyman S. Long-term stability of osseointegrated implants in bone regenerated with the membrane technique. 5-year results of a prospective study with 12 implants. Clin Oral Implants Res 1996;7:175–183.