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Clinical and radiographical performance of implants placed with simultaneous guided bone regeneration using resorbable and nonresorbable membranes after 22–24 years, a prospective, controlled clinical trial

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Abstract

Aim: The aim was to evaluate the performance of implants placed with simultaneous guided bone regeneration (GBR) using resorbable or nonresorbable membranes compared to implants placed in pristine bone without bone regeneration after an observation period of 22–24 years.

Material and Methods: The patient cohort of this clinical trial was treated from 1994 to 1996. Dehiscence defects were treated with GBR by either using resorbable collagen membranes (BG) or nonresorbable ePTFE membranes (GT). Implants placed in pristine bone served as a control (CT). Clinical parameters, marginal bone levels, and technical outcomes were evaluated following restoration placement and at the present follow-up. A 3D radiographic analysis was conducted in order to assess buccal and oral bone dimensions. Implant survival was assessed with Kaplan–Meier analysis and a frailty model (level of significance 5%).

Results: Out of the originally 72 patients (mean age 75.4 ± 15.70 years) with 265 implants, 39 patients with 147 implants were included in the study after a median period of 23.5 years. Implant survival was 89.3% in group BG (n = 100), 90.2% in group GT (n = 37), and 93.8% in group CT (n = 105), without significant differences (Frailty proportional hazard model p = .79). Smoking had a negative effect on survival (p = .0122). Mean vertical marginal bone levels were −2.3 ± 1.4 mm (BG, n = 59), −3.0 ± 1.5 mm (GT, n = 21), and −2.3 ± 1.6 mm (CT, n = 52). The vertical buccal bone levels were −3.0 ± 1.9 mm (BG, n = 57), −3.5 ± 2.2 mm (GT, n = 21), and −2.6 ± 1.8 mm (CT, n = 49), without significant differences.

Conclusion: Implant placement with GBR procedures provides treatment outcomes with favorable implant survival rates (89.3%–93.8%) after 23.5 years. Smoking, however, affected implant survival negatively.

Ronald E. Jung and Lily V. Brügger contributed equally to the study.

KEYWORDS
bone regeneration, bone substitute, CBCT, dental implants, guided bone regeneration, long-term outcomes

1 | INTRODUCTION

Systematic reviews reported survival rates for titanium dental implants of over 95% after an observation period of 5 years (Jung et al., 2012; Pjetursson et al., 2012). In addition, there are several studies with adequate design and number of patients reporting outcomes of up to 10 years (Gotfredsen, 2012; Lekholm et al., 1999; Matarasso et al., 2010; Windael et al., 2018) or even 20 years (Bergenblock et al., 2012; Chappuis et al., 2013; Misje et al., 2013). Still, the large majority of prospective studies are limited to 5 years of follow-up or less. Since the 1980s, dental implants are used on a regular base in order to replace missing teeth and restore patient's function and esthetics (Branemark et al., 1995). In the light of this background, it is assumed that most implants remain in function for a period exceeding the currently well-documented 5 years. Long-term follow-up studies are required to better understand survival rates, and factors influencing success from complications after the first 5 years in service.

A frequent condition at implant placement is the occurrence of bony dehiscence or fenestration defects (Dahlin et al., 1995; Merli et al., 2016). Various techniques have been described to reconstruct bony deficiencies, with guided bone regeneration (GBR) being most frequently applied (Benic & Hammerle, 2014; Dahlin et al., 1988, 1989). The technique was originally based on the use of form-stable, nonresorbable membranes, without a substitute material (Dahlin et al., 1989). The technique was then modified by adding a bone substitute material underneath the membrane (Mattout et al., 1995). In the following years, resorbable membranes offered an additional advantage, as there is no need for membrane removal in a second surgical intervention. At this stage, the present study was initiated to compare the use of established nonresorbable membranes (e-PTFE membrane) with resorbable collagen membrane, both in combination with xenogeneic particulated grafting material in a split-mouth design (Zitzmann et al., 1997, 2001). Ever since, a large number of membranes and bone substitute materials were introduced. Until today, the use of a resorbable collagen membrane combined with a xenogenic-particulated grafting material with or without autogenous bone particles is frequently applied (Thoma et al., 2019).

Currently, the majority of long-term follow-up studies on implants placed with simultaneous GBR procedures primarily evaluated the success of GBR procedures through the analysis of two-dimensional peri-apical radiographs (Bergenblock et al., 2012; Jemt & Johansson, 2006; Misje et al., 2013). The use of cone beam computer tomography (CBCT) analyzing the peri-implant tissues three-dimensionally has been documented in more recent studies (Benic et al., 2017; Buser et al., 2013; Chappuis et al., 2013; Thoma, Bienz, Payer, et al., 2019). Limited clinical and 3D data are available about the bone volume on the buccal aspect of implants treated with regenerative procedures.

Therefore, the aim of the present clinical study was to evaluate the performance of implants placed with simultaneous guided bone regeneration (GBR) using resorbable or nonresorbable membranes compared to implants placed in pristine bone without bone regeneration after an overall observation period of 22–24 years in function.

2 | MATERIALS AND METHODS

2.1 | Study design and original population

The present study reports on a patient cohort treated at the Clinic of Fixed and Removable Prosthodontics and Dental Material Science at the University of Zurich, Switzerland (today Clinic of Reconstructive Dentistry). The study was designed as a prospective, randomized controlled clinical trial and patients were recruited from 1994 to 1996 (Zitzmann et al., 2001). At that time, 72 patients were included, of which 54 were women. The outcomes after 12–14 years have been reported previously (Jung et al., 2013). Patients were invited to attend yearly recalls at the clinic for the first 5 years following implant placement and were subsequently referred back to private offices for regular maintenance.

For the present follow-up investigation, a protocol was developed and approval was obtained by the local ethics committee (BASEC-Nr. 2018–00804). All patients were invited for clinical and radiographical examination with a letter explaining the rationale of the study. Patients who did not reply were contacted by phone and/or additionally in writing. Prior to the follow-up visit, each participant gave written consent for the examination.

2.2 | Dental implants and regeneration procedures

From 1994 to 1996, 72 patients received 265 implants. Of these, 256 were Brånemark implants (Nobel Biocare Services AG, Göteborg, Sweden), followed by 8 Biomed 3i (Biomet 3i, Palm Beach Gardens, FL, USA) and one single IMZ implant (Friatec® AG). Out of 265 implants, 112 implants were treated with a resorbable membrane (BG) and 41 with a nonresorbable (GT). The remaining 112 implants were placed in pristine bone and did not require further regenerative therapies. These are considered as the control group (CT).

Group BG: Sites with a dehiscence defect following implant placement, treated with GBR using deproteinized bovine bone mineral (Geistlich Bio-Oss®, Geistlich Pharma AG, Wolhusen, Switzerland) and a resorbable, native collagen membrane (Geistlich Bio-Gide®, Geistlich Pharma AG, Wolhusen, Switzerland).

Group GT: Sites with a dehiscence defect following implant placement, treated with GBR using deproteinized bovine bone mineral (Geistlich Bio-Oss®, Geistlich Pharma AG) and a nonresorbable membrane made of expanded polytetrafluorethylene (e-PTFE; Gore-Tex®, W.L. Gore/Implant Innovations, West Palm Beach, FL, USA).

Group CT: Implants placed in pristine bone without regenerative therapy.

Further details on the original procedures and randomization processes were reported earlier (Zitzmann et al., 1997, 2001).

2.3 | Follow-up examination

From 2018 to 2019, the follow-up examination was conducted at the Clinic of Reconstructive Dentistry, University of Zurich, Switzerland. Patients were asked to fill out a health questionnaire assessing systemic diseases, allergies, and medications. Age, gender, and smoking habits were recorded. Additional questions were related to experienced pain or the occurrence of suppuration at a specific implant site during the entire follow-up period. Furthermore, patients were asked about their satisfaction with the implant prosthesis, based on a visual analogue scale with scores from 0 to 100.

2.4 | Clinical examination

The type of implant prosthesis (fixed, removable, or unloaded) was recorded. In case of fixed restorations, the reconstruction material (porcelain-fused-to-metal (PFM) or all-ceramic reconstructions) was assessed based on the report in patients' charts. The clinical examination comprised plaque control record at each implant site (PI, Plaque Index, O'Leary et al., 1972), probing pocket depth (PPD), bleeding on probing (BOP) at six sites, and the buccal height of the keratinized mucosa (KM) (O'Leary et al., 1972) (Ainamo & Bay, 1975). The 6 values around each implant for PPD were averaged to one value per implant. The percentage out of the 6 values, measured per implant, was evaluated for PI and BOP (6 values being 100%). The buccal marginal soft tissue level (MSTL) was measured by using the implant/abutment junction as reference, with negative values representing an exposure of the implant. Peri-implant mucosal condition (PC) was classified according to the definition: 0 = healthy, 1 = slightly red, 2 = very red/swollen, 3 = pus, and 4 = hyperplastic.

Technical parameters comprised abutment survival, crown survival, framework fractures, chipping of crown, and abutment screw loosening. Furthermore, color match (exceeding one full shade) as compared to the neighboring tooth was evaluated. Differences exceeding 1 full shade were recorded as a mismatch. The following outcomes were rated with the Modified United States Public Health Service (USPHS) criteria, ranging from alpha to delta: surface texture of the crown, anatomical form, and marginal integrity (with a dental probe).

2.5 | Radiographic analysis

Digital intraoral radiographs were captured using the long-cone paralleling technique with a film holder (Kerrhawe SA, Bioggio, Switzerland). Vertical marginal bone levels (BoneL) were measured with an image analysis software (imageJ, National Institutes of Health, Bethesda, MD, United States). The thread pitch of the implant was used to scale for the measurements and the implant-shoulder (IS) was used as a reference point. Both mesial and distal levels were measured and the measurement with the lower bone level was used for evaluation, similar to earlier reports (Jung et al., 2013; Zitzmann et al., 1997, 2001) (Figure 1).

In addition, a cone beam computed tomography (CBCT) scan was taken for the analysis of the buccal bone (Morita accuitomo, J. Morita Corp., Tokyo, Japan). The settings for the field of view ranged between 40 mm × 40 mm and 100 mm × 100 mm, depending on the number of implants of interest. The voxel size ranged between 0.125 mm (for the small field) and 0.250 mm. Dicom files were saved as a set of single frames and imported into an image analysis software (OsiriX Lite, Pixmeo SARL, Bernex, Switzerland). A cross section was adjusted in accordance to the implant axis for each implant eligible for evaluation. The marginal bone levels at the buccal (BoneLbucc)

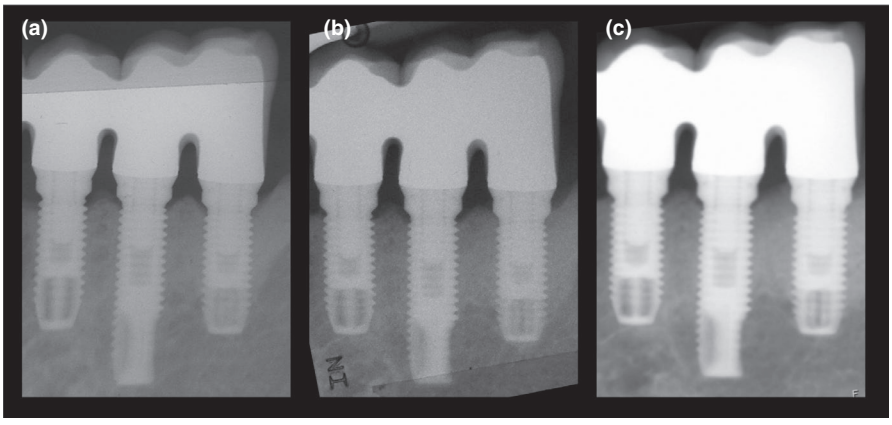

FIGURE 1 Periapical X-rays at baseline (a), at 13 years (b), and at 23 years (c)

and oral (BoneLoral) aspect were measured, using the IS as a reference point. Furthermore, the buccal bone thickness was measured horizontally at IS-1 mm, IS-3 mm, IS-5 mm, and IS-7 mm (Figure 2).

2.6 | Statistical analysis

Data were collected in a spreadsheet (Excel, Microsoft Corporation, Redmond, United States) and statistical analysis was conducted with a statistical analysis program (SAS 9.4, SAS Corp.). Mean, median, standard deviation (±*SD*), and interquartile range were used to describe continuous variables, whereas counts and percentages were used for categorical variables. Intergroup and intragroup comparisons were performed with appropriate mixed models because of the clustered data. Patient was always the random factor in these models. Implant survival was assessed with a Kaplan–Meier analysis. The study population was considered a heterogenous sample including individuals with different hazards. To account for this heterogeneity, due to unmeasured covariates, a frailty proportional hazard Cox model was applied with clustered data to evaluate factors potentially affecting implant survival. Spearman correlations were used to analyze associations of the parameters KM, MSTL, and BoneLbucc. The level of significance was set at $\alpha = 0.05$. No correction was applied for multiple testing.

3 | RESULTS

3.1 | Study population

Out of 72 patients with 265 implants, 39 patients (54.2%) with 147 implants (55.5%) have completed the follow-up examination after a median period of 23.5 years, ranging from 22.2 years to 24.6 years. Their mean age at the follow-up examination was 75.8 ± 10.5 years and 4 out of 39 patients were smokers. Twenty-three patients died (31.9%) over the course of the follow-up period and 10 patients (13.9%) were lost to follow-up due to geographic reasons or severe illness. For the patients available at the follow-up, 24 reported one or more systemic diseases in the health questionnaire. Mean satisfaction with the implant prosthesis was 97.5 ± 5.4%, whereas twenty-four out of 33 patients reported 100% satisfaction. Implant characteristics are summarized in Table 1 for all 39 patients who have completed the follow-up.

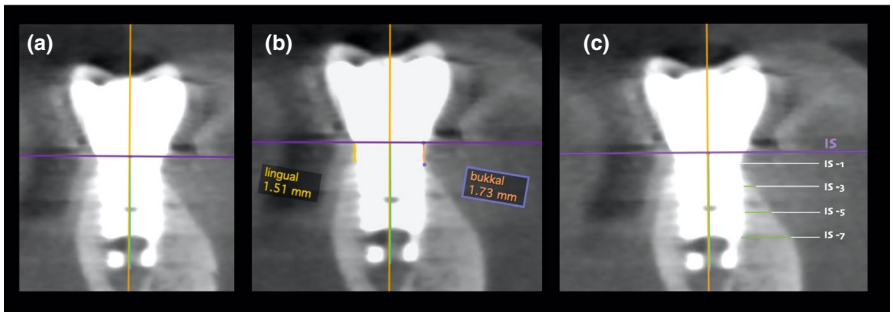

FIGURE 2 Bucco-oral cross section as selected for evaluation (a). Vertical measurements from implant shoulder to first (buccal or oral) bone to implant contact (b). Horizontal measurements at the level of 1, 3, 5, and 7 mm below the implant shoulder (c). IS, implant shoulder; −1 = buccal bone thickness at 1 mm below IS; −3 = buccal bone thickness at 3 mm below IS; −5 = buccal bone thickness at 5 mm below IS; −7 = buccal bone thickness at 7 mm below IS

TABLE 1 Population characteristics at a median observation period of 23.5 years

Group		BG	GT	CT
Number (Implants)		**68**	**23**	**56**
Jaw	Maxilla	28 (19.1%)	15 (10.2%)	22 (15.0%)
	Mandible	40 (27.2%)	8 (5.4%)	34 (23.1%)
Location	Front	20 (13.6%)	10 (6.8%)	13 (8.8%)
	Premolar	27 (18.4%)	10 (6.8%)	19 (12.9%)
	Molar	21 (14.3%)	3 (2.0%)	24 (16.3%)
Reconstruction	Fixed	59 (41.3%)	21 (14.7%)	46 (32.2%)
	Removable	6 (4.2%)	2 (1.4%)	9 (6.3%)
Material for fixed reconstructions	Porcelain-fused-to-metal	55 (44.6%)	21 (17.0%)	43 (34.8%)
	All-ceramic	2 (1.6%)	0 (0.0%)	3 (2.4%)

Note: BG = guided bone regeneration with resorbable membrane; GT = guided bone regeneration with nonresorbable membrane; CT = implant is placed in pristine bone.

3.2 | Implant survival

Implant survival was 89.3% in group BG, 90.2% in group GT, and 93.8% in group CT at the follow-up examination (Figure 3). The survival time did not differ significantly between the treatments (Frailty model, $p = .79$). Further factors were tested with this model. Smoking was a significant factor affecting survival negatively ($p = .012$), without interaction with treatment. Age, length of follow-up, location (front/premolar/molar), and jaw did not have a significant influence on survival. Treatment was never significant in combination with these factors.

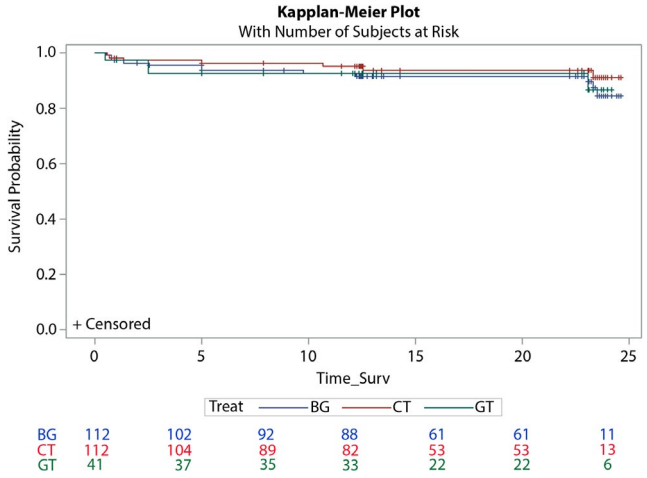

FIGURE 3 Kaplan–Meier Plot depicting the survival probability for each treatment group. BG = guided bone regeneration with resorbable membrane; GT = guided bone regeneration with nonresorbable membrane; CT = implant is placed in pristine bone; Time_Surv = Follow-up in years

3.3 | Clinical parameters

The descriptive data of all clinical parameters are summarized in Table 2. At baseline, the width of the keratinized mucosa (KM) measured 3.6 ± 1.9 mm on average (BG), 3.0 ± 1.8 mm (GT), and 2.7 ± 1.9 (CT). At the 23.5-year follow-up, KM was 3.6 ± 2.9 mm (BG), 3.7 ± 3.3 mm (GT), and 2.9 ± 3.1 (CT). At baseline, the buccal marginal soft tissue level (MSTL) measured −0.1 ± 0.9 mm (BG), 0.1 ± 1.3 mm (GT), and −0.2 ± 0.9 mm (CT). At the 23.5-year follow-up, MSTL was −0.4 ± 2.0 mm (BG), −0.4 ± 2.3 mm (GT), and −0.3 ± 1.7 mm (CT). The number of sites with 1 mm or more recession amounted to 16.3% ($N = 21$) for BG, 5.4% ($N = 7$) for GT, and 14.1% ($N = 18$) for CT. The occurrence of pain was reported by 1.5% (BG), 0.0% (GT), and 15% (CT) of the patients in the respective groups. The occurrence of suppuration was reported by 11.8% (BG), 34.8% (GT), and 14.3% (CT) at a specific implant site over the entire study period. All technical parameters are reported in Table 3.

TABLE 2 Clinical parameters

Variable	Group	*N*	Mean	*SD*	Min	Q1	Median	Q3	Max
PI (%)	BG	58	18.0	30.0	0.0	0.0	0.0	33.0	100.0
	GT	21	6.0	12.0	0.0	0.0	0.0	0.0	33.0
	CT	50	21.0	34.0	0.0	0.0	0.0	33.0	100.0
PPD (mm)	BG	58	2.9	1.1	1.0	2.0	3.0	4.0	6.0
	GT	21	3.3	1.1	1.0	3.0	3.0	4.0	6.0
	CT	50	3.1	1.1	1.0	2.0	3.0	4.0	6.0
BOP (%)	BG	58	34.0	35.0	0.0	0.0	17.0	50.0	100.0
	GT	21	38.0	35.0	0.0	0.0	33.0	50.0	100.0
	CT	50	41.0	37.0	0.0	0.0	33.0	67.0	100.0
PC (score 0–4)	BG	56	1.0	1.3	0.0	0.0	0.0	1.0	4.0
	GT	21	2.2	1.6	0.0	0.0	3.0	3.0	4.0
	CT	50	0.9	1.2	0.0	0.0	0.5	1.0	4.0
KM (mm)	BG	58	3.6	2.9	0.0	1.0	3.0	5.0	10.0
	GT	21	3.7	3.3	0.0	0.0	4.0	6.0	10.0
	CT	51	2.9	3.1	0.0	0.0	2.0	5.0	12.0
MSTL (mm)	BG	58	−0.4	2.0	−8.0	−1.0	0.0	1.0	2.0
	GT	21	−0.4	2.3	−6.0	−1.0	0.0	1.0	3.0
	CT	50	−0.3	1.7	−4.0	−1.0	0.0	1.0	2.0

Note: Q1 = first quartile; Q3 = third quartile.

Abbreviations: BOP, bleeding on probing; KM, keratinized mucosa; Max, maximum; Min, minimum; MSTL, midfacial soft tissue level; N, number of sites; PC, peri-implant mucosal condition; PI, plaque index; PPD, probing pocket depth; *SD*, standard deviation.

TABLE 3 Summary of all technical outcomes as counts and percentages

Technical parameters		Frequency (Percentage)
Abutment survival	Yes	108 (76.1%)
	No	34 (23.9%)
Crown survival	Yes	110 (84.0%)
	No	21 (16.0%)
Framework fracture	No fracture	109 (97.3%)
	Fracture	3 (2.7%)
Chipping of crown	No	80 (79.2%)
	Yes	21 (20.8%)
Abutment screw loosening	No	106 (98.2%)
	Yes	2 (1.9%)
Color match (compared to the neighboring, exceeding one full shade)	Yes	76 (69.7%)
	No	33 (30.3%)
Anatomical form (USPHS)	Alpha	81 (76.4%)
	Bravo	18 (17.1%)
	Charlie	6 (5.7%)
	Delta	1 (0.9%)
Surface texture crown (USPHS)	Alpha	47 (42.7%)
	Bravo	63 (57.3%)
	Charlie	0 (0.0%)
	Delta	0 (0.0%)
Marginal integrity (USPHS) (with a dental probe)	Alpha	91 (93.8%)
	Bravo	5 (5.2%)
	Charlie	0 (0.0%)
	Delta	1 (1.0%)

3.4 | Radiographic analysis

The conventional analysis obtained baseline values at 6 months following crown insertion. At baseline, the bone levels (BoneL) amounted to −0.3 ± 0.7 mm (BG), −0.4 ± 0.8 mm (GT), and −0.3 ± 0.5 mm (CT). After a median observation period of 23.5 years, BoneL was −2.3 ± 1.4 mm (BG, loss from baseline to 23.5 y:2.1 ± 1.4), −3.0 ± 1.5 mm (GT, loss from baseline to 23.5 y:2.5 ± 1.5), and −2.3 ± 1.5 mm (CT, loss from baseline to 23.5 y:2.0 ± 1.4) (Figure 4). Intragroup comparisons showed significant changes over the entire observation period (all $p < .0001$). The changes were not significantly different among the three groups (intergroup: $p = .768$).

The 3D analysis based on bucco-oral sections of the CBCTs revealed mean vertical buccal bone levels (BoneLbucc) of −3.0 ± 1.9 mm (BG), −3.5 ± 2.2 mm (GT), and −2.6 ± 1.8 mm (CT) after 23.5 years (intergroup $p = .7554$) (Figure 4). The corresponding oral vertical bone levels amounted to −2.3 ± 1.6 mm (BG), −2.9 ± 1.5 mm (GT), and −2.2 ± 2.1 mm (CT) (intergroup, $p = .3186$). The buccal bone thickness at different levels is presented in Figure 5.

3.5 | Further analyses

A correlation analysis was performed with KM, MSTL in regard to BoneLbucc. Considering the data of the follow-up for all parameters, the correlations (positive or negative) were very weak with <0.2 (Spearman correlation coefficient) for group BG and GT, but also for group CT with <0.25. With the initial values for KM (obtained 6 months following prosthesis placement) as compared to BoneLbucc (only available at 23.5 years), correlations amounted to 0.1 (BG), −0.4 (GT), and 0.3 (CT). Similarly for MSTL, the values were 0.3 (BG), −0.3 (GT), and 0.0 (CT). Finally, considering the change of KM over the entire observation period in regard to BoneLbucc, Spearman correlations were 0.1 (BG), −0.4 (GT), and −0.1 (CT). Similarly for MSTL, the values were 0.3 (BG), −0.0 (GT), and 0.3 (CT).

Representative cases with stable soft and hard peri-implant tissues for each group are shown in Figure 6. The most severe cases with peri-implant bone loss and soft tissue recession of all three groups are shown in Figure 7.

4 | DISCUSSION

The present clinical trial investigated long-term outcomes of GBR treatment and documented (i) favorable survival rates ranging from 89.3% to 93.8% for augmented and nonaugmented sites after the mean follow-up of 23.5 years; (ii) a negative impact of smoking on implant survival; (iii) stable marginal bone levels; (iv) comparable buccal and oral bone levels between sites with or without bone

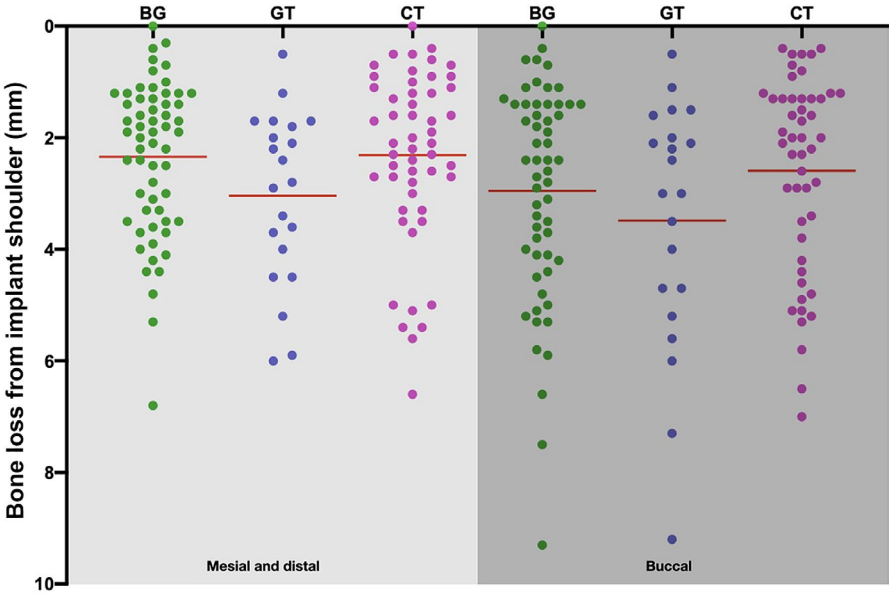

FIGURE 4 Scatterplots depicting the marginal bone levels at mesial and distal sites (BoneL, left side) and buccal sites (BoneLbucc, right side) at 23.5 years. The red line represents the mean. BG = guided bone regeneration with resorbable membrane; GT = guided bone regeneration with nonresorbable membrane; CT = implant is placed in pristine bone

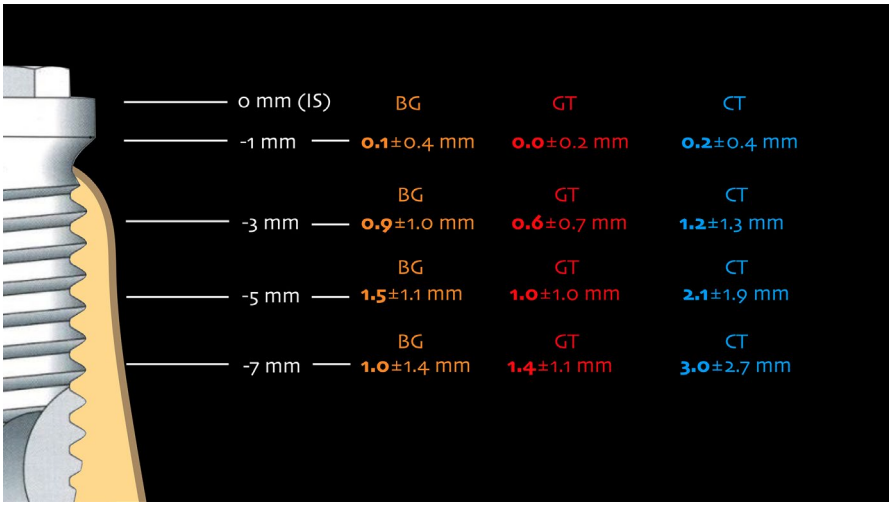

FIGURE 5 Buccal bone thickness at a median observation period of 23.5 years. Means and standard deviations. BG = guided bone regeneration with resorbable membrane; GT = guided bone regeneration with nonresorbable membrane; CT = implant is placed in pristine bone; IS, implant shoulder, reference point

regeneration; and (v) a weak correlation of the amount of buccal KM, change in MSTL, and BoneLbucc.

Implant survival rates are of utmost importance in longitudinal studies, especially as the number of studies reporting long-term data is limited to date. In the present study, implant survival rates amounted to 89.3% in group BG, 90.2% in group GT, and 93.8% in group CT at 22–24 years of follow-up. Based on the present results, the outcome of implants placed with simultaneous GBR was comparable to implants placed in pristine bone. The survival rates were slightly higher at the time-point of the 5-year follow-up, amounting to 95.4% (BG), 92.6% (GT), and 97.3% (CT) (Zitzmann et al., 2001). In summary, the number of implants lost between implant placement and 5 years was comparable with the number of implants lost from year 5 to 22–24. Another long-term study had a follow-up time of 18 years and presented an overall implant survival of 96.8% (Bergenblock et al., 2012). One further study presented an 89.5% cumulative implant survival rate at 20 years (Chappuis et al., 2013). Despite the differences in the aim and design of these studies, the survival rates can be considered comparable and in line with the present results.

Smoking as a risk factor for implant loss was already identified in the 1990s (Bain, 1996; De Bruyn & Collaert, 1994; Haas et al., 1996; Zitzmann et al., 1999). Cigarette smoking was also associated with reduced healing after guided tissue regeneration with nonresorbable membranes (Tonetti et al., 1995). One longitudinal study with a follow-up of 20 years evaluated smoking as being a significant risk factor for marginal bone loss (Jansson et al., 2002b). The results of these studies are in line with the present findings. Smoking proved to be a significant risk factor, impairing implant survival.

Technical outcomes rendered 84.0% implant prosthesis survival, 20.8% of ceramic chippings, and 1.9% of abutment screw loosening. A recent systematic review on longitudinal studies with 5 years of follow-up revealed higher crown survival rates (98.3%), as well as less chipping (2.8% metal ceramic vs. 2.9% zirconia ceramic), but more abutment (or occlusal) screw loosening (3.6% metal ceramic vs. 1% zirconia ceramic) (Pjetursson et al., 2018). Chipping is a frequent

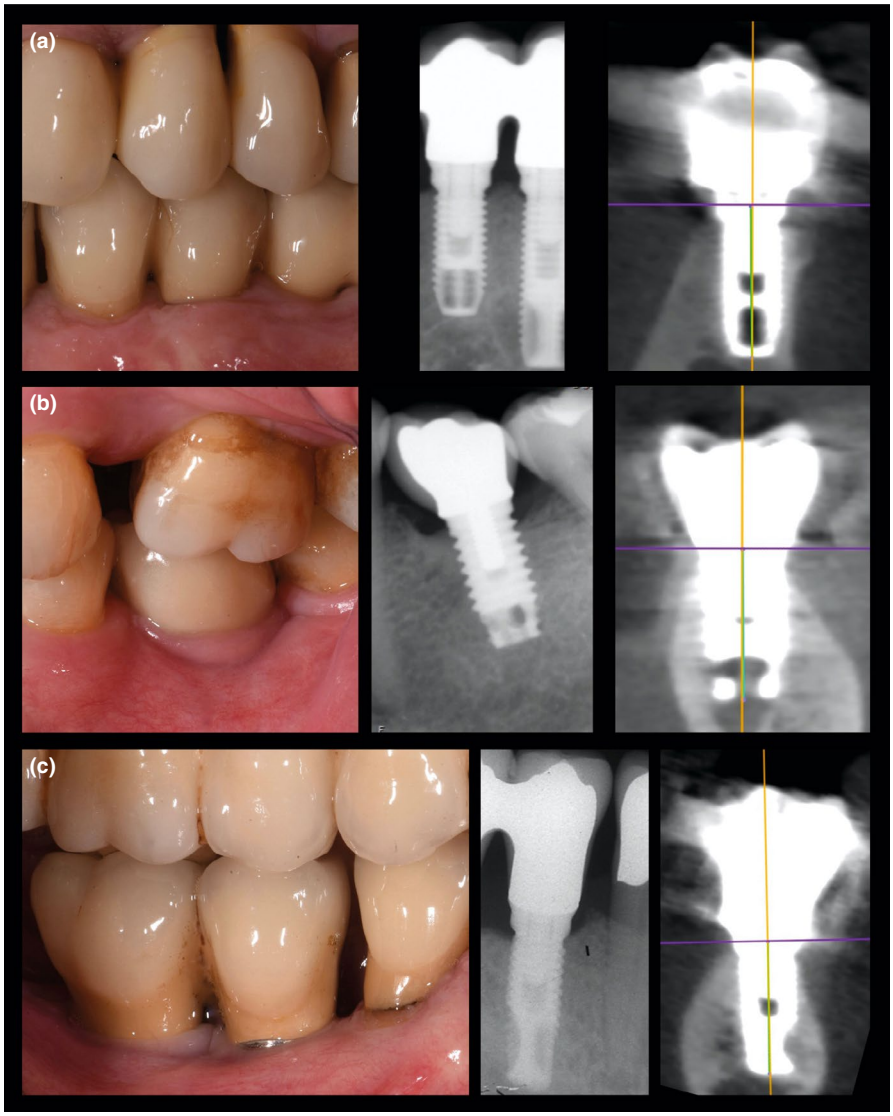

FIGURE 6 Representative cases with stable soft and hard peri-implant tissues for group BG = guided bone regeneration with resorbable membrane (a), GT guided bone regeneration with nonresorbable membrane (b), and CT = implant is placed in pristine bone (c)

technical complication, rendering, for example, 6.5% (Tey et al., 2017), 9.2% (Walton, 2015), and 11.0% (Karlsson et al., 2018) after 5 years and 20.3% after 10 years (Wittneben et al., 2014). A longitudinal clinical study of 20 years was reported on single crowns and fixed-partial dentures revealing a survival rate of 84% (Chappuis et al., 2013), which is comparable to the results of the present study after a mean observation period of 23.5 years. Ceramic chipping and screw loosening were reported as slightly higher with 28% and 3%, respectively (Chappuis et al., 2013).

Intragroup comparisons revealed a significant marginal bone loss over the entire observation period. Group GT showed the highest bone loss (2.6 mm) over the observation period. However, marginal bone levels remained highly stable in comparison to the 12- to 14-year follow-up (Jung et al., 2013). Even in cases with limited or no bone regeneration, implant survival was not affected by application of GBR techniques. In comparison with other studies, it has to be taken into account that usually the mean marginal bone loss is reported. However, the present study and all earlier reports on the patient cohort have considered the implant aspect with the higher loss (mesial or distal). Another study with 513 subjects found a mean bone loss of 10% after 20 years, which corresponds to an annual marginal bone loss of around 0.1 mm (Jansson et al., 2002a). This is comparable with the present results. Another 15-year follow-up study, not distinguishing whether or not GBR was used, described a mean bone loss of 0.5 mm after 5 years and thereafter only minimal changes up to 10 years (0.0 mm) and up to 15 years (0.1 mm), respectively. 1.3% of the implants showed a bone loss of more than 3.0 mm after 15 years in function (Jemt & Johansson, 2006). Moreover, several studies with varying lengths of follow-up have reported similar marginal bone levels for augmented and nonaugmented sites, being in line with the present data (Benic et al., 2009, 2017; Zumstein et al., 2012).

The buccal bone levels after 22–24 years amounted between −2.6 mm and −3.5 mm. Long-term outcomes of GBR investigated by 3D computed tomography are still rare. In a recent study, implants with machined surfaces placed in pristine bone were compared with implants having received GBR using DBBM and a collagen membrane. The buccal bone levels were −1.98 ± 0.98 mm for pristine

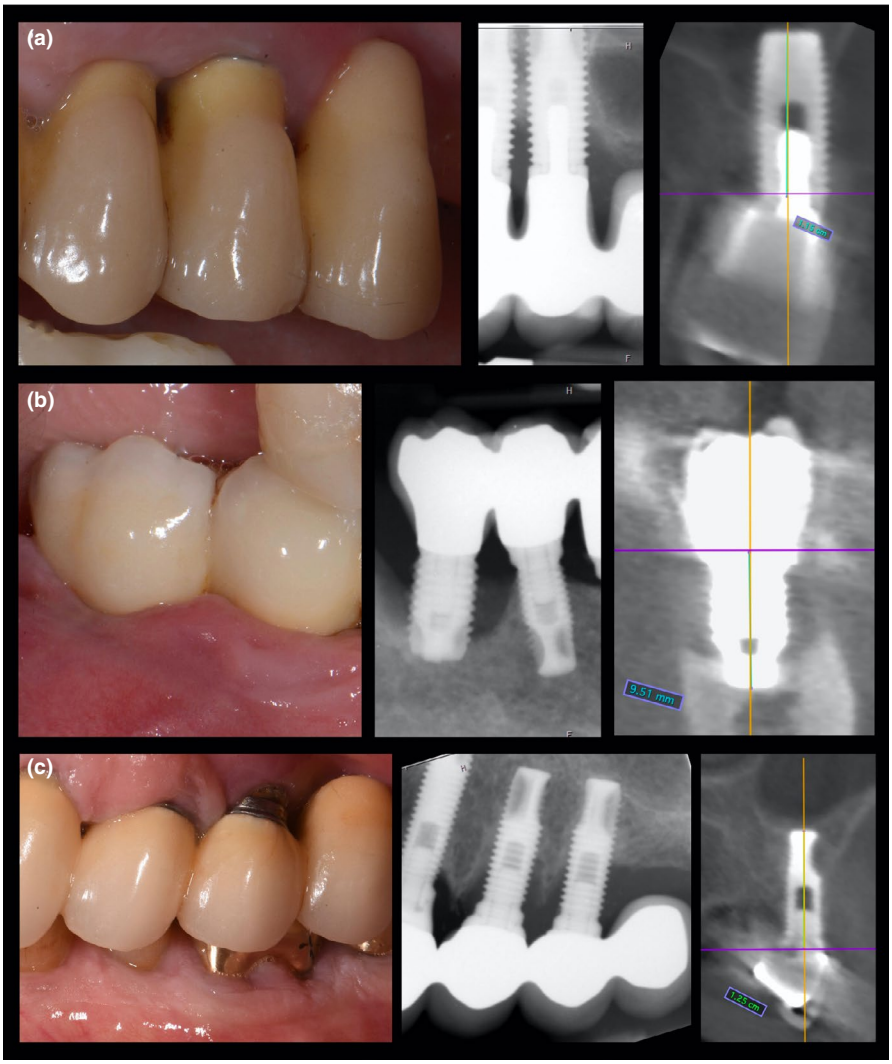

FIGURE 7 Most severe cases with peri-implant bone loss and soft tissue recession of group BG = guided bone regeneration with resorbable membrane (a), GT guided bone regeneration with nonresorbable membrane (b), and CT = implant is placed in pristine bone (c)

bone and −2.03 ± 0.99 mm for the GBR group after 15-years (Benic et al., 2017). Considering the longer follow-up in the present study, the results for the nonaugmented groups were similar, whereas the groups with GBR had slightly inferior results.

When analyzing statistically nonsignificant trends, group GT presented with slightly inferior results for several outcomes: BoneL, BoneLbucc, buccal bone thickness, occurrence of suppuration, higher PPD (mm), and PC. Limited amounts of bone regeneration in the GT group were particularly observed in immediate implant placement (Zitzmann et al., 1999), an indication which is no longer recommended for nonresorbable membranes. One of the limitations of this study is the heterogeneity of the size of the study groups, no power analysis, and the implant-based analysis. Patients presented with up to 8 (study) implants. Limiting is also the fact that the intraoral radiographs were not standardized. The evaluation of thin buccal bone plates in CBCT is subject to artifacts caused by the implants (Vanderstuyft et al., 2019). Radio-opaque structures such as titanium cause artifacts and appear bigger than they are. It can be assumed that bone plates of less than 0.5 mm thickness cannot be detected and will therefore be recorded as missing bone. An additional limitation is the missing information about the size and shape of the bony defects at the time of implant installation.

Despite these limitations, a 22- to 24-year follow-up of a prospective clinical trial remains an exception in the literature. Moreover, the study investigated on two material combinations for GBR, which have remained the two most often reported combinations over three decades, since this trial was initiated.

5 | CONCLUSIONS

Within the limitation of the present study, it can be concluded that implant treatment with and without GBR led to favorable survival rates ranging from 89.3% to 93.8% after 23.5 years in function. Smoking affected implant survival negatively, whereas early complications with GBR application did not affect implant survival. The mean satisfaction was 97.5 ± 5.4%. Stable bone levels were reported for the proximal, buccal, and oral aspects of the implants. Weak correlations without statistical significance were detected between the amount of keratinized mucosa, buccal marginal mucosa level, and buccal bone level.

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CONFLICT OF INTEREST

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AUTHOR CONTRIBUTIONS

Ronald Ernst Jung: Conceptualization (equal); Funding acquisition (equal); Methodology (equal); Project administration (equal); Supervision (equal); Validation (equal); Writing-original draft (equal). **Lily V Bruegger:** Conceptualization; Data curation; Funding acquisition; Investigation; Methodology; Visualization; Writing-original draft. **Stefan Bienz:** Data curation (equal); Project administration (equal); Supervision (equal); Validation (equal); Writing-original draft (equal). **Juerg Huesler:** Formal analysis (equal); Validation (equal); Visualization (equal); Writing-review & editing (equal). **Christoph H.F. Hämmerle:** Conceptualization (equal); Funding acquisition (equal); Writing-review & editing (equal). **Nicola Zitzmann:** Conceptualization (equal); Methodology (equal); Writing-review & editing (equal).

DATA AVAILABILITY STATEMENT

Data available on request from the authors.

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