CLINICAL INVESTIGATIONS

Effectiveness of Lateral Bone Augmentation on the Alveolar Crest Dimension: A Systematic Review and Meta-analysis

I. Sanz-Sánchez[1], A. Ortiz-Vigón[1], I. Sanz-Martín[1], E. Figuero[1,2], and M. Sanz[1,2]*

Abstract: *Lateral ridge augmentation procedures are aimed to reconstruct deficient alveolar ridges or to build up peri-implant dehiscence and fenestrations. The objective of this systematic review was to assess the efficacy of these interventions by analyzing data from 40 clinical studies evaluating bone augmentation through either the staged or the simultaneous approach. The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) guideline for systematic reviews was used. The primary outcomes were the changes at reentry, in the ridge width, and in the vertical and horizontal dimensions of the peri-implant defect, measured in millimeters, in the staged and simultaneous approaches, respectively. The results of the meta-analysis showed, for the simultaneous approach, a statistically significant defect height reduction when all treatments were analyzed together (weighted mean difference [WMD] = –4.28 mm; 95% confidence interval: [CI] –4.88, –3.69; P < 0.01). The intervention combining bone replacement grafts with barrier membranes was associated with superior outcomes The most frequently used intervention was the combination of xenograft and bioabsorbable membrane. Similarly, for the staged approach, there was a statistically significant horizontal gain when all treatment groups were combined (WMD = 3.90 mm; 95% CI: 3.52, 4.28; P < 0.001). The most frequently used intervention was the use of autogenous bone blocks. Both treatment strategies led to high survival and success rates (>95%) for the implants placed on the regenerated sites. Nonexposed sites gained significantly more in the simultaneous and staged approaches (WMD = 1.1 and 3.1 mm).*

Key Words: dental implant, alveolar ridge augmentation, alveolar bone loss, bone regeneration, bone substitutes, bone transplantation.

Introduction

The use of dental implants to rehabilitate partially or fully edentulous patients is a highly predictable treatment with cumulative survival rates >90% at 10 y (Moraschini et al. 2015). However, in spite of the many technological advances in implant dentistry, bone availability is still the main prerequisite for safe and predictable implant placement as well as for attaining adequate aesthetic outcomes. An adequate alveolar ridge, however, is often lacking as a result not only from trauma, pathology, chronic/acute infections, or the consequence of severe periodontitis but also as the consequence of loss of mechanical function following tooth extraction or tooth loss. This physiologic bone loss after tooth extraction has been demonstrated in experimental studies reporting vertical and horizontal bone resorption (Araujo and Lindhe 2005; Vignoletti et al. 2012). In humans, approximately 50% of the bone volume is lost after tooth extraction during the first year (Schropp et al. 2003; Tan et al. 2012), and these resorptive changes may significantly alter the bone availability for placing dental implants (Ashman 2000); hence, bone augmentation procedures are frequently indicated, either concomitant with implant placement or as a staged intervention.

Residual alveolar ridges have been classified depending on their predominant bone-deficient component, as horizontal, vertical, or

DOI: 10.1177/0022034515594780. [1]Section of Graduate Periodontology, University Complutense, Madrid, Spain; [2]ETEP (Etiology and Therapy of Periodontal Diseases) Research Group, University Complutense, Madrid, Spain; *corresponding author, marsan@ucm.es

A supplemental appendix to this article is published electronically only at http://jdr.sagepub.com/supplemental

combined (Seibert 1983); following this classification, bone-regenerative interventions have also been divided depending on their main objective, in lateral or vertical bone augmentation procedures. Predominantly vertical ridge deficiencies are less frequent, and the probability of achieving predictable outcomes with existing vertical bone augmentation procedures is low. A recent systematic review reported that even though there is clinical and histologic evidence of the successful vertical ridge augmentation, there is a low degree of predictability and a high frequency of complications (Rocchietta et al. 2008).

Surgical interventions for lateral bone augmentation with the aim of placing a functional osseointegrated implant are highly predictable procedures, with reported implant survival rates of 87% to 95% for the simultaneous approach and 99% to 100% for the staged approach (Donos et al. 2008). A recent systematic review (Kuchler and von Arx 2014) assessing horizontal ridge augmentation procedures in the anterior maxilla also reported similarly high percentages of survival rate for the simultaneous and staged surgical approaches (100% and 96.8%, respectively). These reviews, however, did not assess the dimensional changes on the alveolar ridge as a consequence of the regenerated surgical procedure.

Most studies aiming for lateral bone augmentation have used the principles of guided bone regeneration by combining different bone replacement grafts and barrier membranes. There is, however, no clear evidence which is the ideal graft or membrane material. Some authors still consider the autogenous bone as the ideal bone replacement graft, but we lack clear information whether the use of bone substitutes—allogenic, xenogeneic, or alloplastic—can provide similar or better outcomes. Similarly, there is no clear evidence on the ideal composition or need of using a barrier membrane covering the bone replacement graft.

It is therefore the purpose of this systematic review 1) to evaluate the available evidence on the effectiveness of the interventions aimed for lateral ridge augmentation, either simultaneously with implant placement or as a staged procedure, and 2) to further identify which are the most suitable biomaterials, as bone replacement grafts as well as barrier membranes.

Material and Methods

A protocol was developed to answer the following PICO question (i.e., population, intervention, comparison, and outcome):

> In situations with horizontal alveolar ridge deficiencies (population), what is the effectiveness of different regenerative surgical interventions (either staged or simultaneous; intervention and comparison) to increase the width of the alveolar ridge and resolve the crest deficiency (outcome)?

Eligibility Criteria for Study Inclusion

Inclusion criteria

- Randomized controlled clinical trials (RCTs), controlled clinical trials (CCTs), and prospective case series with a minimum sample size of 10 patients and a minimum follow-up time of 6 mo
- Patients >18 y and in good general health requiring the placement of ≥1 implant in sites presenting ridge deficiencies
- Interventions aimed for lateral ridge augmentation (simultaneous or staged approach)
- Outcome variables evaluating the changes (baseline and final data) in the dimension of the peri-implant defect (simultaneous approach) and in the horizontal dimension of the ridge (staged approach)

Exclusion criteria

- Studies assessing the effectiveness of interventions aimed at vertical bone augmentation (distraction osteogenesis, orthognatic surgery, interpositional grafts, etc.)
- Studies aimed at regenerating extractions sockets with or without implant placement

Type of interventions and comparisons

Studies were selected when included interventions aimed for lateral ridge augmentation with 1 of these objectives:

- To locally augment the bone horizontally around an implant to cover exposed threads in dehiscence or fenestration-type defects (simultaneous approach)
- To locally augment the bone horizontally to enable the placement of a dental implant in a subsequent intervention (staged approach)

The following procedures were considered: guided bone regeneration, autogenous bone blocks, allogeneic or xenogeneic bone blocks, and ridge expansion techniques. Studies assessing the efficacy of interventions aimed at vertical bone augmentation (distraction osteogenesis, orthognatic surgery, interpositional grafts, etc.) or at regenerating extraction sockets with or without implant placement were not included in this systematic review.

The changes between baseline and the reentry, 3 to 9 mo later, were used for assessing the efficacy of all interventions, including all types of prospective studies, while only data from clinical trials were used for evaluating differences among specific interventions.

Types of outcomes

The primary outcomes were the changes between baseline and reentry in the dimension of the peri-implant defect (width and height) in the simultaneous approach (Appendix Fig. 1) and the horizontal dimension of the ridge in the staged approach. In addition, these changes were used for comparing among the different interventions.

The following secondary outcomes were studied:

- Success rates of the lateral augmentation, defined by complete coverage of the exposed implant (simultaneous) or by achieving the adequate ridge dimension for the placement of an implant with the

desired dimensions (staged; Donos et al. 2008)
- Percentage of cases in need of regrafting
- Implant survival rates (in percentages)
- Implant success rate (according to Albrektsson's criterion or other success criteria; in percentages)
- Occurrence of postoperative surgical complications (in percentages; flap dehiscence, graft or membrane exposure, loss of integration, fracture of the buccal plate, local infection, prolonged pain, paresthesia, etc.)
- Occurrence of technical and/or biological complications (in percentages)—defined as the occurrence of peri-implant diseases: bleeding on probing with or without increased probing pocket depth or radiographic bone loss
- Interproximal crestal bone–level changes assessed radiographically (in millimeters)
- Status of peri-implant soft tissues (probing pocket depth, gingival indexes, plaque indexes, mucosal recession, width of keratinized tissue)
- Aesthetic outcomes (white and pink esthetic scores, papilla index, or the displacement of the midfacial mucosal level)
- Patient-reported outcome measurements (pain, discomfort, satisfaction, etc.)

Search strategy

Electronic databases—the National Library of Medicine (MEDLINE via Pubmed) and Cochrane Central Register of Controlled Trials—were searched for human studies published until December 2014. A specific search strategy was developed for MEDLINE (Appendix) and revised for the other databases. No language restrictions were applied. All reference lists of the selected studies were checked for cross-references. A hand search of the most relevant journals between 2004 and 2014 was also performed (Appendix). Search for gray literature was not attempted.

Screening methods

Two reviewers (I.S.S. and I.S.M.) did the primary search by independently screening the titles and abstracts. The same reviewers evaluated the full manuscript of those studies meeting the inclusion criteria or those with insufficient data in the title and abstract to make a clear decision. Any disagreement was resolved by discussion with a third reviewer (E.F.). One independent reviewer (A.O.V.) performed the manual search. The inter-reviewer reliability (percentage of agreement and kappa correlation coefficient) of the screening method was calculated.

Data extraction

Three reviewers (I.S.S., I.S.M., A.O.V.) independently extracted the data. Any disagreement was discussed, and a fourth reviewer (E.F.) was consulted when necessary. Authors of studies were contacted for clarification when data were incomplete or missing. Data were excluded until further clarification could be available if agreement could not be reached. When the results of a study were published more than once or if the results were presented in a number of publications, the data with longest follow-up were included only once.

Assessment of risk of bias

Quality of the included RCTs and CCTs was assessed by 2 reviewers (I.S.S. and I.S.M.), independently and in duplicate, following the Cochrane Collaboration recommendations (Higgins and Green 2011). The following items were evaluated as low, high, or unclear risk of bias:

Selection bias—sequence generation and allocation concealment
Performance bias—blinding of participants/personnel
Detection bias—blinding of outcome assessment
Attrition bias—incomplete outcome data
Selective reporting bias—selective reporting outcomes
Other potential risk of bias

The Newcastle-Ottawa scale for cohort studies and a modification of the scale for cross-sectional studies were used for the assessment of risk of bias in individual observational studies (Wells et al. 2011). This scale includes 5 main categories: representativeness of the exposed cohort, ascertainment of exposure, assessment of outcome, follow-up long enough for the outcome of interest, and adequacy of follow-up.

Data synthesis

To summarize and compare the selected studies, the data on the primary and secondary outcomes were pooled and described with weighted mean differences (WMDs) and 95% confidence intervals (CIs). For comparing the changes in peri-implant defect and ridge dimension between baseline and reentry visits, all study designs were included, considering each arm of RCTs or CCTs as an independent study. When specific interventions were compared, only RCTs or CCTs were included.

The statistical heterogeneity among studies was assessed using the Q test according to Dersimonian and Laird and the I^2 index (heterogeneity: I^2 = 25%, low; 50%, moderate; 75%, high). When the heterogeneity values were high, a subgroup analysis was carried out using as explanatory variables either study design (RCT, CCT, or cases series) or type of procedure. The study-specific estimates were pooled with both the fixed effects model (Mantel-Haenzel-Peto test) and the random effects model (Dersimonian-Laird test). If a significant heterogeneity was found, the random effects model was chosen.

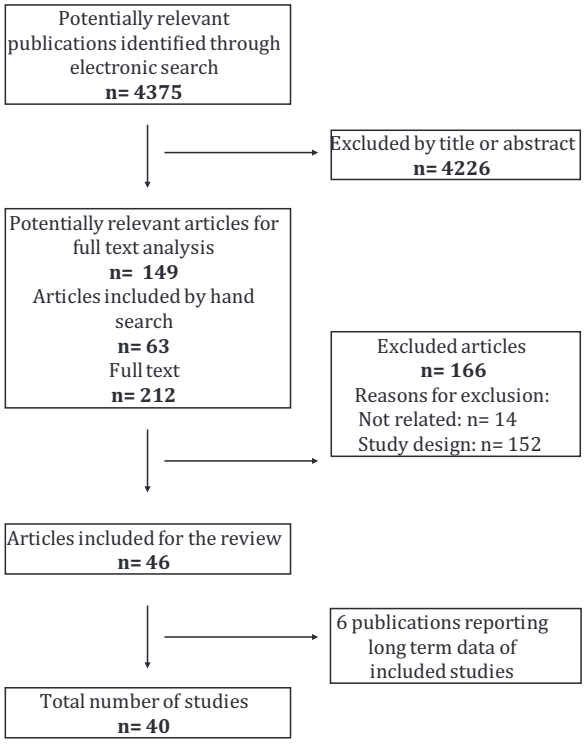
Forest plots were created to illustrate the effects of the different studies and the global estimation in the meta-analysis. STATA (StataCorp LP, College Station, TX, USA) intercooled software was used to perform all analyses. Statistical significance was defined as $P < 0.05$.

Results

Search

The Figure depicts the study flowchart: 4,375 titles were identified by the electronic search. Once the titles and abstracts were evaluated, 4,226 studies were discarded (agreement = 86.19%; 95% CI = 83.54%, 88.47%; kappa = 0.60; $P < 0.001$) resulting in 149 studies. After

Figure
Flowchart depicting the search strategy and selection process.



the addition of 63 articles found on the manual search, 212 studies were subjected to full-text analysis. After this analysis, 46 final publications were included reporting data from 40 studies, since 6 publications reported long-term data from already-included studies (agreement = 96.73%; 95% CI = 92.58%, 98.60%; kappa = 0.83; $P < 0.001$). The reasons for excluding the remaining studies are reported in Appendix Table 1, and the list of excluded references can be found in the Appendix.

Description of Studies

Table 1 depicts the methodological characteristics of the selected studies. From the 40 selected studies, 21 investigated the simultaneous approach (2 CCTs, 9 RCTs, and 10 case series); 17, the staged approach (3 CCTs, 3 RCTs, and 11 case series); and 2, the ridge expansion procedure (2 case series). When data from more than 1 experimental or control group was reported in RCTs or CCTs, each comparison was considered independently (represented in Table 3, Appendix Figs. 2 and 3, and Appendix Tables 4 and 5 as Lorenzoni et al. 1998a, 1998b; Moses et al. 2005a, 2005b; Park et al. 2008a, 2008b). Similarly, in case series where data from more than 1 group were reported (Nemcovsky et al. 2000; represented in Appendix Figs. 2 and 3 and Appendix Table 4 as Nemcovsky et al. 2000a, 2000b) or when further patients were subsequently added (Zitzmann et al. 2001; Jung et al. 2013), each comparison was also considered independently.

This systematic review pooled data of 1,242 patients at baseline, with a total of 1,881 implants placed. The mean follow-up period was of 21.48 mo, with a minimum of 4 mo (De Stavola and Tunkel 2013) and a maximum of 150 (Jung et al. 2013). When stratified by treatment group, 783 patients were treated with the simultaneous approach (755 completed the follow-up), 373 patients with the staged approach (364 completed the follow-up), and 86 patients with the ridge expansion approach (80 completed the follow-up).

Assessment of Risk of Bias

Appendix Table 2 depicts the risk of bias for RCTs and CCTs. Only 2 studies showed a low risk of bias in all the fields (Becker et al. 2009; Ramel et al. 2012). In general, most RCTs showed a low risk of bias in the majority of the categories.

The quality of reporting in case series is depicted in Appendix Table 3. None of the studies met the 5 quality categories.

Effects of Interventions: Primary Outcome

Simultaneous approach

Table 2 depicts the meta-analysis evaluating the changes in defect height. For all studies, there was a statistically significant defect height reduction (WMD = −4.28 mm; 95% CI, −4.88, −3.69; $P < 0.01$). The maximum defect height reduction was reported for the combination of particulate xenograft + bone morphogenic protein (BMP) + bioabsorbable membrane (WMD = −6.80 mm; 95% CI, −8.48, −5.11; $P < 0.001$), whereas the minimum was for the combination of particulate autologous bone + bioabsorbable membrane (WMD = −3.38 mm; 95% CI, −5.79, −0.96; $P < 0.006$). The guided bone regeneration procedure using a particulate xenograft + bioabsorbable membrane was the most frequently used combination (n = 10), demonstrating a significant reduction in the defect height (WMD = −4.42 mm; 95% CI, −5.48, −3.36; $P < 0.001$; Appendix Fig. 2).

Table 3 depicts the meta-analysis comparing defect height reductions among interventions (RCTs or CCTs). The highest WMD was found when particulate xenograft + nonbioabsorbable membrane were compared with the same bone substitute + bioabsorbable membrane (WMD = −1.80 mm; 95% CI, −3.22, −0.37; $P < 0.014$] or when particulate xenograft + autologous graft + nonbioabsorbable membrane were compared with autologous graft + bioabsorbable membrane (WMD = −1.45 mm; 95% CI, −1.91, −0.99; $P < 0.001$).

Appendix Table 4 depicts the meta-analysis evaluating defect width

Table 1.
Methodological Characteristics of the Selected Studies, the Regenerative Objective (Simultaneous, Staged, or Ridge Expansion), the Types of Interventions, and the Outcomes Measured

Reference	Study Design	Mean Follow-up, mo	Test / Control, *n*		Interventions		Study Outcomes Measured
			Patients[a]	Implants	Test	Control	
Simultaneous							
Moses et al. 2005	CCT	NR	41 (41) / 17 (17)	73 / 34	Xenograft + tricalcium-phosphate + collagen membrane (Ossix or Bio-Gide)	Xenograft (Bio-Oss) + tricalcium-phosphate (Cerasorb) + Gore Tex membrane	IS, WR, HR, EX
Lorenzoni et al. 1998	CCT	6	38 (38) / 45 (45)	38 / 45	Xenograft + autologous chips + polyglycolid bioabsorbable membrane	Xenograft + autologous chips + ePTFE or Ti-PTFE membrane	IS, HR, EX, EXH
Zitzmann et al. 1997; Zitzmann et al. 2001; Jung et al. 2013	RCT (split)	150	75 (58) / 25 (22)	112 / 41	Xenograft + collagen membrane	Xenograft + ePTFE	IS, WR, EX, EXW, IS, MBL, PPD, PI, ML
Carpio et al. 2000	RCT (parallel)	6	23 (23) / 25 (25)	23 / 25	Xenograft + collagen membrane	Xenograft + ePTFE membrane	IS, SP, WR, HR, EX
Jung, Halg, et al. 2009; Ramel et al. 2012	RCT (parallel)	36	19 (18) / 18 (18)	19 / 18	Xenograft + polyethylen glycol bioabsorbable membrane	Xenograft + collagen membrane	IS, WR, HR, EX ISC, MBL
Jung et al. 2003; Jung, Windisch, et al. 2009	RCT (split)	60	11 (10) / 11 (10)	18 / 16	Xenograft + rh-BMP2 + collagen membrane	Xenograft + collagen membrane	IS, SP, WR, HR, EX, PPD
Van Assche et al. 2013	RCT (split)	12	14 (14) / 14 (14)	14 / 14	HA-60% TCP-40% + collagen membrane	Xenograft + collagen membrane	IS, WR, HR, EX, PPD, CAL, BOP
Schneider et al. 2014	RCT (parallel)	6	19 (19) / 21 (21)	19 / 21	Xenograft + polylactide / polyglycolide acid bioabsorbable membrane	Xenograft + Ti-PTFE membrane	IS, SP, WR, HR, EX
Friedmann et al. 2011	RCT (parallel)	6	17 (17) / 20 (20)	37 / 36	HA-60% TCF-40% + collagen membrane	HA-60% TCF-40% + cross-linked collagen membrane	IS, SP, WR, HR, RG, EX
Park et al. 2008	RCT (3-arm)	6	9 (9) / 9 (8)	9 / 8	Cancellous allograft + collagen membrane or acellular dermal matrix	Cancellous allograft	IS, SP, WR, HR, RG, EX,EXW
Becker et al. 2009; Schwarz et al. 2012	RCT (parallel)	4	27 (23) / 27 (26)	41 / 37	Xenograft + cross-link collagen membrane	Xenograft + collagen membrane	IS, SP, WR, HR, RG, EX, PPD, CAL, BOP, PI, ML
Blanco et al. 2005	Case series	60	19 (19)	26	Particulate autologous bone or allograft + e-PTFE membrane		IS, ISC, SP, HR, RG, EX, EXH, MBL
De Boever and De Boever 2005	Case series	46.6	13 (13)	16	Xenograft + ePTFE membrane		IS, SP, HR, RG, RG, PPD, BOP, PI
Dahlin et al. 1995	Case series	24	45 (44)	55	ePTFE membrane alone		IS, HR, EX, EXH
Jovanovic et al. 1992	Case series		11 (11)	19	ePTFE membrane alone or with autologous bone chips		IS, WR, HR, RG, EX, EXW, EXH, MBL
von Arx and Kurt. 1999	Case series	6.6	15 (15)	20	Autologous bone chips		IS, SP, HR, RG, EX, EXH
Nemcovsky et al. 2000	Case series	7	14 (14)	14	Xenograft + collagen membrane		IS, WR, HR, EX
Hammerle and Lang 2001	Case series	6.7	10 (10)	10	Xenograft + collagen membrane		IS, SP, WR, HR
Tawil et al. 2001	Case series	NR	17 (17)	17	Autologous bone chips + collagen membrane		IS, WR, HR, EX, EXW, EXH
Nemcovsky et al. 2002	Case series	NR	24 (24)	31	Xenograft + collagen membrane		IS, WR, HR, EX

continued)

Table 1.
(continued)

Reference	Study Design	Mean Follow-up, mo	Test / Control, *n*		Interventions		Study Outcomes Measured
			Patients[a]	Implants	Test	Control	
Widmark and Ivanoff 2000	Case series	6	21 (21)	21	Autologous bone chips		IS, HR
Staged							
Chiapasco et al. 1999	CCT	22.4	15 (15) / 15 (15)	30 / 44	Autologous bone chips + ePTFE membrane	Autologous blocks	IS, ISC, SP, WG, RG, EX, EXW
Maiorana et al. 2005	CCT	5.3	12 (12) / 14 (12)	19 / 24	Autologous ramus / calvaria blocks + xenograft	Autologous ramus / calvaria blocks	SP, WG
Beitlitum et al. 2010	CCT	NR	12 (12) / 15 (15)	NR	Particulate allograft + particulate autologous chips + bioabsorbable cross-linked membrabe	Particulate allograft + bioabsorbable cross-linked membrabe	SP, WG, RG, EX, EXW
Antoun et al. 2001	RCT (parallel)	6	5 (5) / 8 (8)	NR	Autologous chin block grafts + ePTFE membrane	Autologous chin blocks	SP, WG, EX, BLCT, PPD, PPD
Cordaro et al. 2011	RCT (parallel)	24	11 (11) / 11 (11)	28 / 27	Autologous ramus blocks + collagen membranes	Autologous ramus blocks	IS, ISC, SP, WG, EX, BOP
de Freitas et al. 2013	RCT (parallel)	6	12 (12) / 12 (12)	32 / 30	rh-BMP2 and Ti-Mesh	Autologous bone chips + Ti-Mesh	IS, SP, WG, EX, BLCT
Buser et al. 1996; Buser et al. 2002	Case series	60	40 (37)	60	Autologous ramus / chin blocks + ePTFE membrane		IS, SP, WG, RG, EX, PPD, CAL, BOP, PI, MBL, PPD, CAL, PI
Hämmerle et al. 2008	Case series	NR	12 (12)	17	Collagen membrane + xenograft		IS, SP, WG, RG, EX
Parodi et al. 1998	Case series	NR	16 (16)	27	Collagen sponges + collagen membrane		IS, WG, RG
Knapp et al. 2003	Case series	6	12 (12)	NR	Biactive glass + ePTFE membrane		SP, WG, RG, EX
von Arx and Buser 2006	Case series	5.8	58 (58)	NR	Autologous ramus / symphysis blocks + xenograft + collagen membranes		WG, RG, EX
Urban et al. 2011	Case series	22.8	25 (25)	76	Xenograft + autologous bone chips + collagen membrane		IS, SP, WG, RG
Acocella et al. 2010	Case series	5.2	15 (15)	30	Autologous ramus blocks		IS, ISC, SP, WG
Acocella et al. 2012	Case series	5.68	16 (16)	34	Fresh frozen blocks		IS, ISC, SP, WG, EX
Verdugo et al. 2011	Case series	40	15 (15)	15	Autologous ramus / symphysis blocks + autologouss bone chips		IS, SP, WG, RG, BLCT
De Stavola and Tunkel 2013	Case series	4	10 (10)	0	Autologous ramus blocks		WG, EX
Feuille et al. 2003	Case series	6	12 (10)	NR	Particulate allograft + Ti-PTFE membrane		WG
Ridge expansion							
Kolerman et al. 2014	Case series	52.4	41 (35)	116	Ridege expansion + particulate allograft + collagen membran		IS, ISC, SP, WR, EX, PPD, BOP, PI
Chiapasco et al. 2006	Case series	20.4	45 (45)	110	Ridge expansion without regenerative materials		IS, ISC, SP, WG, BLCT, PPD, BOP, PI

BLCT, bone levels measured by 3-dimensional methods; BOP, bleeding on probing; CAL, peri-implant clinical attachment level; CCT, controlled clinical trial; ePTFE, expanded polytetrafluoroethylene; EX, exposure; EXH, exposed site height; EXW, exposed site width; HA, hydroxyapatite; HR, height reduction; IS, implant survival; ISC, implant success; MBL, marginal bone levels assessed radiographically; ML, mucosal level; NR, not reported; PI, peri-implant plaque index; PPD, peri-implant probing depth; rh-BMP2, recombinant human bone morphogenic protein 2; RCT, randomized controlled trial; RG, regrafting necessity; SP, success rate procedure; TCP, tricalcium phosphate; Ti, titanium; WG, width gain; WR, width reduction.
[a]Baseline (final).

Table 2.
Meta-analysis for Defect Height Reduction in Simultaneous Procedures: Baseline vs. Final (mm)

Group: Subgroup	*n*	Weighted Mean Difference					Heterogeneity	
		IV	DL	95% CI		*P* Value	^{2}	*P* Value
All	32		−4.287	−4.882	−3.692	<0.001	95.3	<0.001
Study design								
RCT	15		−4.198	−5.068	−3.327	<0.001	94.2	<0.001
CCT	6		−3.598	−4.149	−3.047	<0.001	81.8	<0.001
Case series	11		−4.811	−5.632	−3.989	<0.001	90.5	<0.001
Intervention								
Nonbioabsorbable membrane	2	−3.617		−4.332	−2.902	<0.001	0.0	0.968
Particulate allograft	1	−3.600		−5.472	−1.728	<0.001	—	—
Particulate allograft + bioabsorbable membrane	2	−4.992		−6.534	−3.449	<0.001	0.0	0.852
Particulate autologous bone	1	−4.140		−5.206	−3.074	<0.001	—	—
Particulate autologous bone + nonbioabsorbable membrane	1	−5.750		−6.922	−4.578	<0.001	—	—
Particulate autologous bone + bioabsorbable membrane	2		−3.380	−5.798	−0.962	0.006	92.1	<0.001
Particulate autologous bone + xenograft + nonbioabsorbable membrane	3	−3.726		−4.057	−3.394	<0.001	0.0	0.902
Particulate autologous bone + xenograft + bioabsorbable membrane	4		−3.491	−2.002	−2.002	<0.001	96.9	<0.001
Particulate autologous bone + synthetic graft + bioabsorbable membrane	1	−4.000		−5.226	−2.774	<0.001	—	—
Particulate xenograft + bone morphogenic protein + bioabsorbable membrane	1	−6.800		−8.484	−5.116	<0.001	—	—
Particulate xenograft + nonbioabsorbable membrane	3		−4.868	−8.077	−1.659	<0.001	99.2	<0.001
Particulate xenograft + bioabsorbable membrane	10		−4.422	−5.484	−3.361	<0.001	93.0	<0.001
Particulate xenograft or allograft + nonbioabsorbable membrane	1	−6.130		−7.236	−5.024	<0.001	—	—

CCT, clincial controlled trial; CI, confidence interval; DL, DerSimonian and Laird (random effect) model; IV, inverse-variance weighted (fixed effect) model; RCT, randomized controlled trial.

reductions (final vs. baseline; Jovanovic et al. 1992; Carpio et al. 2000; Tawil et al. 2001; Nemcovsky et al. 2002). For all studies combined, there was a statistically significant defect width reduction (WMD = −2.69 mm; 95% CI, −3.04, −2.33; $P <$ 0.001; Jung et al. 2003). The maximum defect width reduction was obtained for the combination of particulate xenograft + BMP + bioabsorbable membrane (WMD = −5.69 mm; 95% CI, −6.68, −4.69; $P < 0.001$), whereas the minimum was for the particulate allograft alone (WMD = −1.38 mm; 95% CI, −2.36, −0.39; $P < 0.006$; Park et al. 2008). The guided bone regeneration procedure combining particulate xenograft+ bioabsorbable membrane was the most frequently used procedure ($n = 7$), demonstrating a significant reduction in the defect width (WMD = −3.28 mm; 95% CI, −3.72, −2.82; $P < 0.001$; Appendix Fig. 3).

Appendix Table 5 depicts the meta-analysis comparing defect width reductions between procedures (RCTs or CCTs). Eight comparisons were possible, but only 1 found statistical significant

Table 3.
Meta-analysis for Differences in Defect Height Reduction for Comparative Studies in Simultaneous Procedures: Test vs. Control (mm)

Control	Test		Weighted Mean Difference				Heterogeneity	
		n	IV	95% CI		*P* Value	^{2}	*P* Value
Particulate autologous bone + xenograft + nonbioabsorbable membrane	Particulate autologous bone + xenograft + bioabsorbable membrane	2[a,b]	0.310	–0.082	0.701	0.121	0.5	0.316
Particulate autologous bone + xenograft + nonbioabsorbable membrane	Particulate autologous bone + bioabsorbable membrane	2[c,d]	–1.456	–1.915	–0.998	<0.001	0.0	0.832
Particulate xenograft + nonbioabsorbable membrane	Particulate xenograft + bioabsorbable membrane	1[e]	–1.800	–3.229	–0.371	0.014	—	—
Particulate xenograft + nonbioabsorbable membrane	Particulate autologous bone + xenograft + bioabsorbable membrane	1[f]	–0.180	–0.501	0.141	0.272	—	—
Particulate xenograft + bioabsorbable membrane	Particulate xenograft + bioabsorbable membrane	2[g,h]	1.250	0.462	2.037	0.002	0.0	0.667
Particulate xenograft + bioabsorbable membrane	Particulate xenograft + bone morphogenic protein + bioabsorbable membrane	1[i]	1.400	–0.759	3.559	0.204	—	—
Particulate autologous bone + xenograft + bioabsorbable membrane	Particulate autologous bone +synthetic graft + bioabsorbable membrane	1[j]	–0.100	–1.333	1.133	0.874	—	—
Particulate synthetic graft + bioabsorbable membrane	Particulate synthetic graft + bioabsorbable membrane	1[k]	0.350	0.991	0.991	0.285	—	—
Particulate allograft	Particulate allograft + bioabsorbable membrane	2[l,m]	1.375	0.002	2.748	0.050	0.0	0.831

CI, confidence interval; DL, DerSimonian and Laird (random effect) model; IV, inverse-variance weighted (fixed effect) model.
[a]Moses et al. (2005a)
[b]Moses et al. (2005b).
[c]Lorenzoni et al. (1998a).
[d]Lorenzoni et al. (1998b).
[e]Schneider et al. (2014).
[f]Carpio et al. (2000).
[g]Jung, Halg, et al. (2009).
[h]Becker et al. (2009).
[i]Jung et al. (2003).
[j]Van Assche et al. (2013).
[k]Friedmann et al. (2011).
[l]Park et al. (2008a).
[m]Park et al. (2008b).

differences between test and control, showing a higher reduction when using a particulate synthetic graft with a collagen bioabsorbable membrane as compared with the use of the same graft with a cross-link bioabsorbable collagen membrane (WMD = 1.00 mm; 95% CI, 0.58, 1.41; $P < 0.001$; Friedmann et al. 2011).

Staged approach

Table 4 depicts the meta-analysis evaluating bone width gains. For all studies, there was a statistically significant bone width gain (WMD = 3.90 mm; 95% CI, 3.52, 4.28; $P < 0.001$). The maximum bone width gain was reported for the combination of particulate xenograft + autologous bone + bioabsorbable membrane (WMD = 5.68 mm; 95% CI, 5.00, 6.35; $P < 0.001$), whereas the minimum was for the combination of particulate synthetic graft + nonbioabsorbable membrane (WMD = 1.10 mm; 95% CI, –0.33, 2.53; $P = 0.131$. The lateral bone augmentation procedure using an autologous bone block alone was the most frequently used ($n = 6$), demonstrating a significant width gain (WMD = 4.25 mm; 95% CI, 4.04, 4.47; $P < 0.001$; Appendix Fig. 4).

In RCTs and CCTs, 4 studies used autologous bone blocks as control group and were compared with different test treatments (autologous particulate + nonbioabsorbable membrane; autologous block + particulate xenograft; autologous

Table 4.
Meta-analysis for Bone Width Gain in Staged Procedures: Baseline vs. Final (mm)

Group: Subgroup	*n*	Weighted Mean Difference					Heterogeneity	
		IV	DL	95% CI		*P* Value	^{2}	*P* Value
All	17		3.906	3.527	4.284	<0.001	84.6	<0.001
Study design								
RCT	2		3.902	3.167	4.636	<0.001	0.0	0.680
CCT	4	3.792		3.150	4.434	<0.001	90.5	<0.001
Case series	11		3.904	3.366	4.441	<0.001	84.6	<0.001
Intervention								
Allograft blocks	1	4.120		3.317	4.923	<0.001	—	—
Autologous bone blocks	6	4.257		4.039	4.476	<0.001	0.0	0.501
Autologous bone blocks + nonbioabsorbable membrane	1	3.550		3.104	3.996	<0.001	—	—
Autologous bone block + particulate xenograft + nonbioabsorbable membrane	1	3.930		3.012	4.848	<0.001	—	—
Autologous bone block + particulate xenograft + bioabsorbable membrane	1	4.600		4.266	4.934	<0.001	—	
Autologous bone block + xenograft	1	4.460		4.018	4.902	<0.001	—	—
Collagen sponge + bioabsorbable membrane	1	2.500		1.679	3.321	<0.001	—	—
Particulate allograft + bioabsorbable membrane	1	3.500		1.657	5.343	<0.001	—	—
Particulate autologous bone + nonbioabsorbable membrane	1	2.670		2.128	3.212	<0.001	—	—
Particulate synthetic graft + nonbioabsorbable membrane	1	1.100		–0.328	2.528	0.131	—	—
Particulate xenograft + bioabsorbable membrane	1	3.700		2.758	4.642	<0.001	—	—
Particulate xenograft + autologous bone + bioabsorbable membrane	1	5.680		5.001	6.359	<0.001	—	—

CCT, clincial controlled trial; CI, confidence interval; DL, DerSimonian and Laird (random effect) model; IV, inverse-variance weighted (fixed effect) model; RCT, randomized controlled trial.

block + nonbioabsorbable membrane; autologous block + particulate xenograft + bioabsorbable membrane). The meta-analysis demonstrated better results, although nonsignificant, for the use of autologous bone blocks (WMD = –0.27 mm; 95% CI, –1.16, 0.61; $P < 0.545$).

Ridge expansion

Only 2 studies measured the amount of horizontal bone gain after a ridge expansion procedure (Chiapasco et al. 2006; Kolerman et al. 2014). The initial bone width varied between 3.73 mm (SD = 0.67; Kolerman et al. 2014) and 4.2 mm (SD = 1.2; Chiapasco et al. 2006); at reentry surgery, the bone width gain was 3.5 mm (SD = 0.93) and 3.9 mm (SD = 0.8), respectively. These procedures have high implant survival and success rates (>95%). With computer tomography, the reported bone width reabsorption at 36 mo was scarce (loss of 0.8 mm; SD = 0.3 mm; Chiapasco et al. 2006).

Effects of Interventions: Secondary Outcomes

Table 5 depicts the results on the secondary outcomes for the simultaneous and staged approaches. All studies reported high implant survival rates (97.82%; range, 78.2% to 100%). Implant

Table 5.
Percentages in Implant Survival, Success Rate of the Procedure, Exposure of the Regenerative Material, and Need of Regrafting

References	Test[a]			
	Implant Survival	Success Procedure	Exposure	Need of Regrafting
Chiapasco et al. 1999	100 (100)	93 (100)	13.3 (0)	6.6 (0)
Maiorana et al. 2005	NR	91.6 (85.7)	NR	NR
Beitlitum et al. 2010	NR	73.3 (91.6)	20 (16.6)	20 (8.3)
Antoun et al. 2001	NR	100 (100)	20/0	NR
Cordaro et al. 2011	100 (100)	100 (100)	27.2 (9.09)	NR
de Freitas et al. 2013	100 (100)	100 (100)	8.33 (16.6)	NR
Buser et al. 1996	100	100	5	5
Buser et al. 2002	98	100	5	5
Hämmerle et al. 2008	100	92	0	NR
Parodi et al. 1998	100	100	NR	0
Knapp et al. 2003	100	100	50	66.6
von Arx and Buser 2006	NR	100	5.17	3.44
Urban et al. 2011	100	96	NR	4
Acocella et al. 2010	100	100	NR	NR
Acocella et al. 2012	100	100	6.25	NR
Verdugo et al. 2011	100	100	NR	0
De Stavola and Tunkel 2013	100	NR	0	NR
Feuille et al. 2003	100	NR	NR	NR
Moses et al. 2005	99 (100)	NR	35.5 (41.2)	NR
Lorenzoni et al. 1998	100 (100)	NR	50 (34.2)	NR
Zitzmann et al. 1997	98 (95)	NR	9.3 (43.9)	NR
Zitzmann et al. 2001	98 (95)	NR	NR	NR
Jung et al. 2013	91 (92)	NR	NR	NR
Carpio et al. 2000	78.2 (84)	NR	13.04 (8)	NR
Jung, Halg, et al. 2009	100 (100)	NR	31.5 (16.6)	NR
Ramel et al. 2012	100 (100)	NR	NR	NR
Jung et al. 2003	100 (100)	90.9 (100)	9.1 (0)	NR
Jung, Windisch, et al. 2009	100 (100)	NR	NR	NR
Van Assche et al. 2013	100 (100)	NR	7.14 (14.2)	NR
Schneider et al. 2014	100 (100)	79 (95.2)	26.3 (9.5)	NR
Friedmann et al. 2011	100 (100)	76.4 (75)	23.5 (25)	23.5
Park et al. 2008	100 (100)	100 (100)	38.9 (25)	0 (0)
Becker et al. 2009	100 (100)	100 (100)	17.4 (7.7)	0 (0)
Schwarz et al. 2012	NR	NR	NR	NR
Blanco et al. 2005	96	96.1	11.53	0
De Boever and De Boever 2005	94	94	NR	0
Dahlin et al. 1995	100	NR	11.8	NR
Jovanovic et al. 1992	100	NR	15.8	0
Von Arx and Kurt 1999	100	95	5.26	0
Nemcovsky et al. 2000	100	NR	0	NR

continued)

Table 5.
(continued)

References	Test[a]			
	Implant Survival	Success Procedure	Exposure	Need of Regrafting
Hämmerle and Lang 2001	100	90	NR	NR
Tawil et al. 2001	100	NR	11.8	NR
Nemcovsky et al. 2002	100	NR	0	NR
Widmark and Ivanoff 2000	95	NR	NR	NR
Kolerman et al. 2014	100	95	4.31	NR
Chiapasco et al. 2006	97	98	NR	NR

NR, not reported.
[a]Values presented in percentages. Control in parentheses.

success rate from 12 to 60 mo varied between 91% and 100% when the criterion by Albrektsson et al. (1986) was used (Chiapasco et al. 1999; Blanco et al. 2005; Chiapasco et al. 2006; Acoccella et al. 2010; Acoccella et al. 2012; Ramel et al. 2012; Kolerman et al. 2014). One study used the criteria by Buser et al. (1997), with a success rate of 100% after 24 mo, for both the test and the control (Cordaro et al. 2011). The need of regrafting was reported in 7 studies and ranged from 0% to 23.5%. All the studies reported the advent of adverse events, with the most frequent being membrane and/or graft exposure.

For the simultaneous approach, a meta-analysis evaluating the differences in defect height reduction between the exposed and nonexposed membrane cases demonstrated a significant higher reduction in the nonexposed cases (WMD = 1.01 mm; 95% CI, –0.38, 1.64; $P < 0.002$; Appendix Fig. 5). Mean radiographic bone-level changes ranging from 1.21 mm (SD = 0.46) to 2.41 mm (SD = 0.89) were reported in studies following the implants placed in regenerated sites for at least 1 y (Jung, Halg, et al. 2009; Ramel et al. 2012). Technical complications (Jung, Windisch, et al. 2009) or biological complications (Zitzmann et al. 2001; De Boever and De Boever 2005; Ramel et al. 2012; Schwarz et al. 2012; Van Assche et al. 2013; Schneider et al. 2014) were seldom reported, with only 1 study reporting a higher risk of mucositis and peri-implantitis during a period of 4 y, when a residual dehiscence was present at reentry surgery (Becker et al. 2009). Similarly patient-reported outcome measurements and aesthetic outcomes were seldom reported. In 1 study (Jung et al. 2013), there was a mean recession of the gingival margin of 0.98 mm (SD = 1.2) in the bioabsorbable membrane group versus 0.12 mm (SD = 1.1) in the nonbioabsorbable membrane group after 150 mo of implant loading. Similarly, Schwarz et al. (2012) reported a mean recession after 4 y of 0.2 mm (SD = 0.3) in the group of patients that did not have residual dehiscence, as opposed to 0.5 mm (SD = 0.7) in the presence of a residual dehiscence.

In comparative studies, no significant differences were reported for changes in probing pocket depth, clinical attachment level, or bleeding on probing. It was remarkable that in the study by Schwarz et al. (2012), the group with no residual dehiscence had significantly less bleeding than the ones with residual dehiscence ≤1 or >1 mm (29.1% vs. 45.8% vs. 54.1%).

In the stage approach, all the studies except 1 (Feuille et al. 2003) reported adverse events, with the most frequent being membrane and/or graft exposure, pain, hemorrhage, infection, temporal paresthesia, or hematoma. The meta-analysis showed a significant higher gain in the nonexposed cases (WMD = 3.10 mm; 95% CI, 2.58, 3.61; $P < 0.001$; Appendix Fig. 6). With computer tomography, 1 study (Antoun et al. 2001) reported a mean radiologic gain of 4.2 mm (SD = 1.9) when the autologous onlay graft was covered with a nonbioabsorbable membrane versus 2.5 mm (SD = 2.1) when the membrane was not used. In another study (de Freitas et al. 2013), application of recombinant human BMP-2 with a collagen sponge carrier achieved a mean radiologic gain of 1.5 mm (SD = 0.7) versus 0.5 mm (SD = 0.9) with particulate autologous bone covered by a titanium mesh. Few studies reported on the status of peri-implant soft tissues (probing pocket depth, clinical attachment level, or bleeding on probing), and none evaluated the advent of technical or biological complications, patient-reported outcome measurements, or aesthetic outcomes.

Discussion

Main Findings

The results from this systematic review—based on 46 publications reporting data from 40 investigations—indicate that a high variability in terms of the interventions aimed for lateral bone augmentation and the different combinations of bone replacement grafts and barrier membranes used. This variability resulted in a low number of studies within each subgroup, which in many cases did not allow for adequate statistical analysis. The main findings of the meta-analysis show that these interventions significantly reduced the defect height in the simultaneous approach and achieved significant horizontal bone gain in the staged

approach, hence supporting with scientific evidence the use of these regenerative procedures. Moreover, both treatment approaches demonstrated high survival and success rates (>95%) when implants were placed in these regenerated sites.

These results agree with a previous systematic review reporting that dental implants placed in regenerated bone had survival rates similar to those of implants placed in pristine bone (Donos et al. 2008). The most distinctive outcome of this systematic review, however, was the evaluation of the relative effectiveness of the different regenerative interventions on the dimensional changes assessed in the alveolar ridge, which had not been evaluated before.

Subgroup Analysis

In the simultaneous treatment approach, the use of particulate autologous bone chips was historically considered the gold standard as bone replacement graft; however, the results from this systematic review show that particulated xenograft was the most frequently used bone replacement graft, demonstrating a significant vertical defect reduction (WMD: –4.42 mm). The highest defect reduction was reported when BMP was combined with a xenograft and a bioabsorbable membrane, although these results were based on a single study with 10 patients (Jung et al. 2003).

In this simultaneous approach, the use of a barrier membrane covering the bone replacement graft demonstrated beneficial outomes when compared with the use of graft alone (WMD = –4.99 vs. –3.6 mm). Moreover, the highest WMD in defect reduction favoring a test group was found when particulate allograft plus a bioabsorbable membrane was compared with the same graft alone (Park et al. 2008). These findings therefore support the use of a barrier membrane and the biologic principles of guided bone regeneration (Kostopoulos et al. 1994; Schenk et al. 1994). However, the use of a membrane alone does not have a rationale in this indication (lateral bone augmentation) since there is a need for space maintenance under the membrane to avoid its collapse and this scaffolding effect must be provided by the use of bone replacement grafts (Hämmerle et al. 1997; Okazaki et al. 2005).

The use of a barrier membrane, however, may lead to more postoperative complications, mainly exposure, that may jeopardize the regenerative outcomes. In fact, data from this systematic review demonstrated that when the outcomes between exposed and nonexposed sites were compared, the latter had greater vertical defect resolution (WMD = 1.01 mm). These results are in agreement with those published by Machtei (2001), who found significantly better results (6-fold greater) for the nonexposed sites.

In the staged approach, this systematic review showed that the use of bone blocks is the most frequently used procedure, although when the block is combined with a particulated xenograft, the results were superior than when a bone block was used alone. In comparative studies, the bone block was frequently used as the standard control treatment, and it was compared with different combinations of bone blocks, particulated replacement grafts, and barrier membranes. These studies, however, showed that the bone block alone attained increased ridge widths (WMD = –0.27 mm). It is well documented that using autogenous bone blocks has important drawbacks, mainly its morbidity when the graft is harvested and the different degree of graft resorption during healing (Benic and Hämmerle 2014). It has been hypothesized that the use of barrier membranes and particulate bone graft substitutes may limit these resorptive changes (Antoun et al. 2001; Cordaro et al. 2011). In fact, the findings of this systematic review support the use of particulate bone grafting over the bone blocks.

Similarly to what was reported in the simultaneous approach, the ocurrence of membrane exposure in the staged approach had a significant negative impact on the regenerated outcomes. In fact, the results showed that in staged procedures, nonexposed sites had significantly greater gain when compared with exposed sites (WMD = 3.1 mm).

When the outcomes between the staged and simultaneous treatments were compared, the meta-analysis showed that the average width gains were slightly higher for the simultaneous (WMD = 4.28 vs. 3.90 mm). These differences are, however, difficult to interpret since the main outcome for the simultaneous approach is defect reduction in millimeters, while for the staged approach, the main outcome is bone width gain in millimeters.

Limitations

When evaluating these results, one must take into consideration that the different measurement methods employed in the studies were not standardized and there were clear inherent differences in the clinical scenarios evaluated. The healing periods varied significantly among the studies, which depended mainly on the treatment approach and biomaterials selected.

Despite the comprehensive strategy used to identify all publications available for answering the selected PICO question, it is possible that some gray literature was not included, since the databases utilized did not search for this particular literature.

It is important to remark that the study design had a clear influence on the magnitude of the outcome, mainly in the simultaneous approach, since the results from case series were superior when compared with RCTs. The relevance of appropriate study design in implant dentistry has been stressed—particularly, the importance of carrying out well-designed clinical trials to minimize overestimation of the clinical results and reduce the risk of bias (Tonetti and Palmer 2012). In this systematic review, we included not only RCTs and CCTs but also prospective case series, which may be considered a limitation, but we chose to broaden the inclusion criteria since there was a limited number of high-quality RCTs (in fact, only 2 of the reported RCTs were considered as low risk of bias).

Conclusions

The results from this systematic review and meta-analysis showed that lateral

ridge augmentation procedures are effective in treating deficient alveolar ridges prior or simultaneously to the placement of dental implants. Results from the meta-analysis showed, for the simultaneous approach, that the combination of bone replacement grafts and barrier membranes was associated with superior outcomes. For the staged approach, the combination of bone blocks, particulated grafts, and barrier membranes provided the best outcomes, although the morbidity and advent of postoperative complications with this procedure should not be underestimated.

Implication for Clinical Practice

The results from this systematic review indicate that whenever possible, priority should be given to those procedures that are less invasive, involve less risk of surgical complications, and achieve the treatment goal in the shortest period.

Implications for Research

From this review, it can be concluded that there is a clear need for well-designed RCTs with long-term follow-up to establish clear clinical guidelines. Similarly, there is a need for standarized meassurement methods that can evaluate the dimensional changes in the residual alveolar ridge in a reproducible and reliable manner. In this aspect, the advent of new digital technologies able to analyze the changes in soft and hard tissues could be promising.

Author Contributions

I. Sanz-Sánchez, I. Sanz-Martín, contributed to conception, design, data acquisition, analysis, and interpretation, drafted and critically revised manuscript; A. Ortiz-Vigón, contributed to conception, design, and data acquisition, drafted and critically revised manuscript; E. Figuero, contributed to conception, design, and data analysis, drafted and critically revised manuscript; M. Sanz, contributed to conception, design, and data interpretation, drafted and critically revised manuscript. All authors gave final approval and agree to be accountable for all aspects of the work.

Acknowledgments

The authors received no financial support and declare no potential conflicts of interest with respect to the authorship and/or publication of this article.

References

Acocella A, Bertolai R, Colafranceschi M, Sacco R. 2010. Clinical, histological and histomorphometric evaluation of the healing of mandibular ramus bone block grafts for alveolar ridge augmentation before implant placement. J Craniomaxillofac Surg. 38(3):222–230.

Acocella A, Bertolai R, Ellis E, Nissan J, Sacco R. 2012. Maxillary alveolar ridge reconstruction with monocortical fresh-frozen bone blocks: a clinical, histological and histomorphometric study. J Craniomaxillofac Surg. 40(6):525–533.

Albrektsson T, Zarb G, Worthington P, Eriksson AR. 1986. The long-term efficacy of currently used dental implants: a review and proposed criteria of success. Int J Oral Maxillofac Implants. 1(1):11–25.

Antoun H, Sitbon JM, Martinez H, Missika P. 2001. A prospective randomized study comparing two techniques of bone augmentation: onlay graft alone or associated with a membrane. Clin Oral Implants Res. 12(6):632–639.

Araujo MG, Lindhe J. 2005. Dimensional ridge alterations following tooth extraction: an experimental study in the dog. J Clin Periodontol. 32(2):212–218.

Ashman A. 2000. Postextraction ridge preservation using a synthetic alloplast. Implant Dent. 9(2):168–176.

Becker J, Al-Nawas B, Klein MO, Schliephake H, Terheyden H, Schwarz F. 2009. Use of a new cross-linked collagen membrane for the treatment of dehiscence-type defects at titanium implants: a prospective, randomized-controlled double-blinded clinical multicenter study. Clin Oral Implants Res. 20(7):742–749.

Beitlitum I, Artzi Z, Nemcovsky CE. 2010. Clinical evaluation of particulate allogeneic with and without autogenous bone grafts and resorbable collagen membranes for bone augmentation of atrophic alveolar ridges. Clin Oral Implants Res. 21(11):1242–1250.

Benic GI, Hämmerle CH. 2014. Horizontal bone augmentation by means of guided bone regeneration. Periodontol 2000. 66(1):13–40.

Blanco J, Alonso A, Sanz M. 2005 . Long-term results and survival rate of implants treated with guided bone regeneration: a 5-year case series prospective study. Clin Oral Implants Res. 16(3):294–301.

Buser D, Dula K, Hirt HP, Schenk RK. 1996. Lateral ridge augmentation using autografts and barrier membranes: a clinical study with 40 partially edentulous patients. J Oral Maxillofac Surg. 54(4):420–432.

Buser D, Mericske-Stern R, Bernard JP, Behneke A, Behneke N, Hirt HP, Belser UC, Lang NP. 1997. Long-term evaluation of non-submerged ITI implants. Part 1: 8-year life table analysis of a prospective multi-center study with 2359 implants. Clin Oral Implants Res. 8(3):161–172.

Buser D, Ingimarsson S, Dula K, Lussi A, Hirt HP, Belser UC. 2002. Long-term stability of osseointegrated implants in augmented bone: a 5-year prospective study in partially edentulous patients. Int J Periodontics Restorative Dent. 22(2):109–117.

Carpio L, Loza J, Lynch S, Genco R. 2000. Guided bone regeneration around endosseous implants with anorganic bovine bone mineral: a randomized controlled trial comparing bioabsorbable versus non-resorbable barriers. J Periodontol. 71(11):1743–1749.

Chiapasco M, Abati S, Romeo E, Vogel G. 1999. Clinical outcome of autogenous bone blocks or guided bone regeneration with e-PTFE membranes for the reconstruction of narrow edentulous ridges. Clin Oral Implants Res. 10(4):278–288.

Chiapasco M, Ferrini F, Casentini P, Accardi S, Zaniboni M. 2006. Dental implants placed in expanded narrow edentulous ridges with the Extension Crest device: a 1-3-year multicenter follow-up study. Clin Oral Implants Res. 17(3):265–272.

Cordaro L, Torsello F, Morcavallo S, di Torresanto VM. 2011. Effect of bovine bone and collagen membranes on healing of mandibular bone blocks: a prospective randomized controlled study. Clin Oral Implants Res. 22(10):1145–1150.

Dahlin C, Lekholm U, Becker W, Becker B, Higuchi K, Callens, Van Steenbergue D. 1995. Treatment of fenestration and dehiscence bone defects around oral implants using the guided tissue regeneration technique: a prospective multicenter study. Int J Oral Maxillofac Implants. 10(3):312–318.

De Boever AL, De Boever JA. 2005. Guided bone regeneration around non-submerged implants in narrow alveolar ridges: a prospective long-term clinical study. Clin Oral Implants Res. 16(5):549–556.

de Freitas RM, Susin C, Spin-Neto R, Marcantonio C, Wikesjo UM, Pereira LA, Marcantonio E Jr. 2013. Horizontal ridge augmentation of

the atrophic anterior maxilla using rhBMP-2/ACS or autogenous bone grafts: a proof-of-concept randomized clinical trial. J Clin Periodontol. 40(10):968–975.

De Stavola L, Tunkel J. 2013. A new approach to maintenance of regenerated autogenous bone volume: delayed relining with xenograft and resorbable membrane. Int J Oral Maxillofac Implants. 28(4):1062–1067.

Donos N, Mardas N, Chadha V. 2008. Clinical outcomes of implants following lateral bone augmentation: systematic assessment of available options (barrier membranes, bone grafts, split osteotomy). J Clin Periodontol. 35 (Suppl 8):173–202.

Feuille F, Knapp CI, Brunsvold MA, Mellonig JT. 2003. Clinical and histologic evaluation of bone-replacement grafts in the treatment of localized alveolar ridge defects: part 1. Mineralized freeze-dried bone allograft. Int J Periodontics Restorative Dent. 23(1):29–35.

Friedmann A, Gissel K, Soudan M, Kleber BM, Pitaru S, Dietrich T. 2011. Randomized controlled trial on lateral augmentation using two collagen membranes: morphometric results on mineralized tissue compound. J Clin Periodontol. 38(7):677–685.

Hämmerle CH, Jung RE, Yaman D, Lang NP. 2008. Ridge augmentation by applying bioresorbable membranes and deproteinized bovine bone mineral: a report of twelve consecutive cases. Clin Oral Implants Res. 19(1):19–25.

Hämmerle CH, Lang NP. 2001. Single stage surgery combining transmucosal implant placement with guided bone regeneration and bioresorbable materials. Clin Oral Implants Res. 12(1):9–18.

Hämmerle CH, Olah AJ, Schmid J, Fluckiger L, Gogolewski S, Winkler JR, Lang NP. 1997. The biological effect of natural bone mineral on bone neoformation on the rabbit skull. Clin Oral Implants Res. 8(3):198–207.

Higgins JP, Green S. 2011. Cochrane handbook for systematic reviews of interventions version 5.1.0. Oxford (UK): Cochrane Collaboration.

Jovanovic SA, Spiekermann H, Richter EJ. 1992. Bone regeneration around titanium dental implants in dehisced defect sites: a clinical study. Int J Oral Maxillofac Implants. 7(2):233–245.

Jung RE, Glauser R, Scharer P, Hämmerle CH, Sailer HF, Weber FE. 2003. Effect of rhBMP-2 on guided bone regeneration in humans. Clin Oral Implants Res. 14(5):556–568.

Jung RE, Fenner N, Hämmerle CH, Zitzmann NU. 2013. Long-term outcome of implants placed with guided bone regeneration (GBR) using resorbable and non-resorbable membranes after 12–14 years. Clin Oral Implants Res. 24(10):1065–1073.

Jung RE, Halg GA, Thoma DS, Hämmerle CH. 2009. A randomized, controlled clinical trial to evaluate a new membrane for guided bone regeneration around dental implants. Clin Oral Implants Res. 20(2):162–168.

Jung RE, Windisch SI, Eggenschwiler AM, Thoma DS, Weber FE, Hämmerle CH. 2009. A randomized-controlled clinical trial evaluating clinical and radiological outcomes after 3 and 5 years of dental implants placed in bone regenerated by means of GBR techniques with or without the addition of BMP-2. Clin Oral Implants Res. 20(7):660–666.

Knapp CI, Feuille F, Cochran DL, Mellonig JT. 2003. Clinical and histologic evaluation of bone-replacement grafts in the treatment of localized alveolar ridge defects: part 2. Bioactive glass particulate. Int J Periodontics Restorative Dent. 23(2):129–137.

Kolerman R, Nissan J, Tal H. 2014. Combined osteotome-induced ridge expansion and guided bone regeneration simultaneous with implant placement: a biometric study. Clin Implant Dent Relat Res. 16(5):691–704.

Kostopoulos L, Karring T, Uraguchi R. 1994. Formation of jawbone tuberosities by guided tissue regeneration: an experimental study in the rat. Clin Oral Implants Res. 5(4):245–253.

Kuchler U, von Arx T. 2014. Horizontal ridge augmentation in conjunction with or prior to implant placement in the anterior maxilla: a systematic review. Int J Oral Maxillofac Implants. 29(Suppl):14–24.

Lorenzoni M, Pertl C, Keil C, Wegscheider WA. 1998. Treatment of peri-implant defects with guided bone regeneration: a comparative clinical study with various membranes and bone grafts. Int J Oral Maxillofac Implants. 13(5):639–646.

Machtei EE. 2001. The effect of membrane exposure on the outcome of regenerative procedures in humans: a meta-analysis. J Periodontol. 72(4):512–516.

Maiorana C, Beretta M, Salina S, Santoro F. 2005. Reduction of autogenous bone graft resorption by means of bio-oss coverage: a prospective study. Int J Periodontics Restorative Dent. 25(1):19–25.

Moraschini V, Poubel LA, Ferreira VF, Barboza Edos S. 2015. Evaluation of survival and success rates of dental implants reported in longitudinal studies with a follow-up period of at least 10 years: a systematic review. Int J Oral Maxillofac Surg. 44(3):377–388.

Moses O, Pitaru S, Artzi Z, Nemcovsky CE. 2005. Healing of dehiscence-type defects in implants placed together with different barrier membranes: a comparative clinical study. Clin Oral Implants Res. 16(2):210–219.

Nemcovsky CE, Artzi Z, Moses O, Gelernter I. 2000. Healing of dehiscence defects at delayed-immediate implant sites primarily closed by a rotated palatal flap following extraction. Int J Oral Maxillofac Implants. 15(4):550–558.

Nemcovsky CE, Artzi Z, Moses O, Gelernter I. 2002. Healing of marginal defects at implants placed in fresh extraction sockets or after 4–6 weeks of healing: a comparative study. Clin Oral Implants Res. 13(4):410–419.

Okazaki K, Shimizu Y, Xu H, Ooya K. 2005. Blood-filled spaces with and without deproteinized bone grafts in guided bone regeneration: a histomorphometric study of the rabbit skull using non-resorbable membrane. Clin Oral Implants Res. 16(2):236–243.

Park SH, Lee KW, Oh TJ, Misch CE, Shotwell J, Wang HL. 2008. Effect of absorbable membranes on sandwich bone augmentation. Clin Oral Implants Res. 19(1):32–41.

Parodi R, Carusi G, Santarelli G, Nanni F. 1998. Implant placement in large edentulous ridges expanded by GBR using a bioresorbable collagen membrane. Int J Periodontics Restorative Dent. 18(3):266–275.

Ramel CF, Wismeijer DA, Hämmerle CH, Jung RE. 2012. A randomized, controlled clinical evaluation of a synthetic gel membrane for guided bone regeneration around dental implants: clinical and radiologic 1- and 3-year results. Int J Oral Maxillofac Implants. 27(2):435–441.

Rocchietta I, Fontana F, Simion M. 2008. Clinical outcomes of vertical bone augmentation to enable dental implant placement: a systematic review. J Clin Periodontol. 35(Suppl 8):203–215.

Schenk RK, Buser D, Hardwick WR, Dahlin C. 1994. Healing pattern of bone regeneration in membrane-protected defects: a histologic study in the canine mandible. Int J Oral Maxillofac Implants. 9(1):13–29.

Schneider D, Weber FE, Grunder U, Andreoni C, Burkhardt R, Jung RE. 2014. A randomized controlled clinical multicenter trial comparing the clinical and histological performance of a new, modified polylactide-co-glycolide acid membrane to an expanded polytetrafluorethylene membrane in guided bone regeneration procedures. Clin Oral Implants Res. 25(2):150–158.

Schropp L, Wenzel A, Kostopoulos L, Karring T. 2003. Bone healing and soft tissue contour changes following single-tooth extraction: a clinical and radiographic 12-month prospective study. Int J Periodontics Restorative Dent. 23(4):313–323.

Schwarz F, Sahm N, Becker J. 2012. Impact of the outcome of guided bone regeneration in dehiscence-type defects on the long-term stability of peri-implant health: clinical observations at 4 years. Clin Oral Implants Res. 23(2):191–196.

Seibert JS. 1983. Reconstruction of deformed, partially edentulous ridges, using full thickness onlay grafts: part I. Technique and wound healing. Compend Contin Educ Dent. 4(5):437–453.

Tan WL, Wong TL, Wong MC, Lang NP. 2012. A systematic review of post-extractional alveolar hard and soft tissue dimensional changes in humans. Clin Oral Implants Res. 23(Suppl 5):1–21.

Tawil G, El-Ghoule G, Mawla M. 2001. Clinical evaluation of a bilayered collagen membrane (Bio-Gide) supported by autografts in the treatment of bone defects around implants. Int J Oral Maxillofac Implants. 16(6):857–863.

Tonetti M, Palmer R; Working Group 2 of the VIII European Workshop on Periodontology. 2012. Clinical research in implant dentistry: study design, reporting and outcome measurements: consensus report of Working Group 2 of the VIII European Workshop on Periodontology. J Clin Periodontol. 39(Suppl 12):73–80.

Urban IA, Nagursky H, Lozada JL. 2011. Horizontal ridge augmentation with a resorbable membrane and particulated autogenous bone with or without anorganic bovine bone-derived mineral: a prospective case series in 22 patients. Int J Oral Maxillofac Implants. 26(2):404–414.

Van Assche N, Michels S, Naert I, Quirynen M. 2013. Randomized controlled trial to compare two bone substitutes in the treatment of bony dehiscences. Clin Implant Dent Relat Res. 15(4):558–568.

Verdugo F, Simonian K, Frydman A, D'Addona A, Ponton J. 2011. Long-term block graft stability in thin periodontal biotype patients: a clinical and tomographic study. Int J Oral Maxillofac Implants. 26(2):325–332.

Vignoletti F, Discepoli N, Muller A, de Sanctis M, Munoz F, Sanz M. 2012. Bone modelling at fresh extraction sockets: immediate implant placement versus spontaneous healing: an experimental study in the beagle dog. J Clin Periodontol. 39(1):91–97.

von Arx T, Buser D. 2006. Horizontal ridge augmentation using autogenous block grafts and the guided bone regeneration technique with collagen membranes: a clinical study with 42 patients. Clin Oral Implants Res. 17(4):359–366.

von Arx T, Kurt B. 1999. Implant placement and simultaneous ridge augmentation using autogenous bone and a micro titanium mesh: a prospective clinical study with 20 implants. Clin Oral Implants Res. 10(1):24–33.

Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. 2011. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in metaanalyses. Ottawa Hospital Research Institute [accessed on 2015 Jun 16]. http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp.

Widmark G, Ivanoff CJ. 2000. Augmentation of exposed implant threads with autogenous bone chips: prospective clinical study. Clin Implant Dent Relat Res. 2(4):178–183.

Zitzmann NU, Naef R, Scharer P. 1997. Resorbable versus nonresorbable membranes in combination with Bio-Oss for guided bone regeneration. Int J Oral Maxillofac Implants. 12(6):844–852.

Zitzmann NU, Scharer P, Marinello CP. 2001. Long-term results of implants treated with guided bone regeneration: a 5-year prospective study. Int J Oral Maxillofac Implants. 16(3):355–366.