Effect of lateral bone augmentation procedures in correcting peri-implant bone dehiscence: a systematic review and network meta-analysis

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ABSTRACT

Purpose: To evaluate the effect of different lateral bone augmentation (LBA) procedures on the complete correction of a peri-implant bone dehiscence (BD) or fenestration (BF).

Methods: A literature search was performed for studies including at least one treatment arm where any LBA had been applied to correct a BD/BF at implant placement. Studies where BD/BF was left untreated were also retrieved as negative control. Data from 24 selected articles were used to perform a network meta-analysis. Based on the proportion of non-resolved BD/BF at implant surgical uncovering, a hierarchy of LBA procedures was determined.

Results: The absence of treatment of BD/BF performed substantially worse compared to other treatments. Among the investigate treatments, no statistically significant differences were found among treatments for the proportion of non-resolved BD. However, treatments based on a combination of a graft material and membrane/periosteum showed the tendency to perform better than treatments using graft material or membrane alone.

Conclusion: Treatments including the use of graft alone, membrane alone, or combinations of grafts and either membrane or patient's own periosteum of a BD/BF at implant placement resulted in a similar proportion of cases with complete dehiscence correction.

Scopo: Valutare l'effetto di diverse procedure di aumento osseo orizzontale (LBA) per la correzione complete di una deiscenza (BD) o fenestrazione (BF) peri-implantare.

Materiali e metodi: È stata effettuata una ricercar bibliografica per studi che includessero almeno un braccio di trattamento dove una procedura di LBA era stata utilizzata per correggere una BD/BF al posizionamento implantare. Studi dove BD/BF non veniva trattata sono stati raccolti come controllo negativo. I dati di 24 articoli sono stati utilizzati per effettuare una network meta-analisi. È stata determinata una gerarchia di procedure di LBA, basata sulla proporzione di BD/BF non risolta alla scopertura implantare.

Risultati: Non sono state trovate differenze statisticamente significative tra i trattamenti in termini di proporzione di BD/BF non risolte. Il mancato trattamento di BD/BF ha funzionato sostanzialmente peggio degli altri trattamenti. I trattamenti basati sulla combinazione di un materiale da innesto e una membrana o il periostio del paziente sembravano funzionare meglio che il materiale da innesto o la membrana utilizzati singolarmente.

Conclusioni: I trattamenti basati sull'utilizzo di materiale da innesto utilizzato da solo, membrana utilizzata da sola, o la combinazione di un materiale da innesto sia con una membrana che col periostio del paziente di una BD/BF al momento del posizionamento implantare sono risultati in una proporzione simile di casi con correzione completa della deiscenza.

INTRODUCTION

At healed extraction sites, residual ridge dimensions are often inadequate for the prosthetically-driven placement of dental implants[1,2,3,4]. As a consequence, implant placement in native bone may often result in either a peri-implant bone dehiscence (BD), when loss of the marginal bone is observed, or fenestration (BF), when the marginal bone maintains its integrity.

Compared to sites with either intact peri-implant bone[5] or surgically treated peri-implant BD[6], untreated BD is associated with higher risk for mucosal recession[5] and interproximal bone loss[6]. Moreover, experimentally-induced peri-implantitis progressed more rapidly in presence of a BD[5].

Even though comparable data for untreated BF are still missing, the presence of exposed implant threads after implant placement, even with an integer marginal bone bridge, may have the same detrimental effect on peri-implant tissue conditions observed for untreated BD over time.

Collectively, these findings support the rationale for either preventing the formation of a peri-implant BD/BF by performing socket preservation / pre-implant lateral bone augmentation (LBA) or correcting the peri-implant BD/BF at implant placement with a LBA.

Several LBA procedures aimed at correcting a BD/BF simultaneously with implant placement were proposed in the literature. Among these, Guided Bone Regeneration (GBR) is based on the use of barrier membrane with or without an additional bone substitute, and is the most investigated and validated option. Other reconstructive approaches, mainly based on the use of a graft material covered either by a full thickness flap[7,8,9] or patient's own periosteum[10], have been also proposed and investigated. According to two recent systematic reviews, LBA results in a mean vertical reduction of 4.28 mm of BD/BF[11] and a percentage vertical reduction of 81.3% in BD/BF[12] when performed simultaneously to implant placement.

Since the persistence of exposed implant threads following LBA is may favor the occurrence of a biological complication compared to an implant with an intact or fully restored peri-implant bone plate[5,13], the complete correction of a BD/BF should be preferred to other outcome measures (e.g., mean changes in BD/BF dimensions) when evaluating the clinical effectiveness of a LBA procedure. The rate of complete BD/BF correction following LBA, however, has never been evaluated as the primary outcome measure in a systematic review. The aim of the present systematic review was to evaluate the effect of different LBA procedures on the complete correction of a BD/BF from implant placement to uncovering.

MATERIALS AND METHODS

Protocol development and focused question

The manuscript was prepared according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations[14]. Ethical approval was not required for this systematic review.

The following focused question was addressed: "*What is the rate of complete correction of a BD/BF following a LBA procedure performed at implant placement?*".

A protocol was developed a priori to collect and summarize the evidence from prospective (i.e., randomized controlled trials; RCTs; controlled clinical trials, CCTs; and case series/reports) and retrospective studies including at least one arm evaluating any intervention for LBA (simultaneous to implant placement) to correct a BD/BF. When available, data derived from the study arm where the BD/BF was left untreated were also retrieved as negative control.

Study selection criteria

Inclusion criteria (PICOS)

1. **P (Population)**: adults (≥18 y-o) presenting a BD or a BF, with no restrictions in terms of defect dimensions, immediately after type III or IV implant placement[15];
2. **I (Intervention)**: any procedure for LBA to correct a BD/BF, performed concomitantly to implant placement (T0);
3. **C (Comparison)**: any of the aforementioned interventions, or no treatment of BD/BF.
4. **(Outcomes)**: studies were included if the proportion of implants showing complete defect resolution (i.e. residual defect height = 0 mm) at surgical re-entry (T1) was reported or could be either extracted or derived. The changes in BD/BF height (DH), width (DW) (in mm and/or %), and buccal bone thickness (BBT) (in mm and/or %) between T0 and T1, implant survival rate (ISR), radiographic bone level (RBL), probing depth (PD) and bleeding on probing (BoP) were the secondary outcome variables. The implant was set as statistical unit. For studies where a patient-level analysis was performed, implant-level data were derived or requested to the Authors;

5. **S (Study design)**: prospective (i.e., randomized controlled trials; RCTs; controlled clinical trials, CCTs; and case series/reports) and retrospective studies including at least one arm evaluating the Intervention or Comparison. Only study arms including at least 5 patients were considered eligible for this systematic review.

Search strategy

Electronic search

A literature search was conducted on the *Medline (Pubmed)* database up to and including September 2021. Also, Elsevier Scopus© (www.scopus.com), and the Cochrane Oral Health Group Specialty Trials' Register (www.thecochranelibrary.com) were consulted. Only full-text articles written in English were considered. Also, the reference lists of previous systematic reviews on LBA simultaneous to implant placement were hand-searched to identify additional potentially relevant articles. Titles and abstracts from the electronic searches were managed by EndNote® v.X7 software. No attempt to identify possible grey literature was performed.

Screening methods

Two investigators (M.S. and A.S.) independently evaluated the titles and abstracts of all identified studies. After this phase, full-text versions were obtained for the studies that appeared to meet the inclusion criteria or for which the title and abstract provided insufficient information to make a clear decision. Disagreements concerning eligibility were resolved by consensus or, if disagreement persisted, by arbitration through a third reviewer (R.F.). Articles that fulfilled all inclusion criteria were processed for data extraction.

Data extraction: characterization of the intervention

Data extraction was performed in duplicate by 2 reviewers (M.S. and A.S.). Extracted data included details of the population, intervention, comparison outcome, and study characteristics. In particular, the following information were retrieved: study design, population (statistical unit, number of implants), type of LBA procedure (if any) and treatment outcomes. Disagreement between the reviewers was resolved by discussion with a third

reviewer (R.F.). If data were missing, the authors of the original article were contacted and asked to provide further details.

Quality Assessment (risk of bias in individual studies)

For included RCTs, methodological quality assessment was performed according to the revised Cochrane risk-of-bias tool for randomized trials (RoB version2.0, updated October 2018)[16]. Five main domains for risk of bias were assessed: randomization process, deviations from the intended interventions, missing outcomes, measurement of the outcomes, and selection of the reported result. A risk-of-bias judgment (among "low risk of bias," "high risk of bias," or "some concerns") was assigned to each domain (depending on the descriptions given for each field) or to the entire study. For non-randomized studies, methodological quality assessment was performed according to the Risk of Bias in Non-randomized Studies of Interventions (ROBINS-I)[17]. Seven main domains for risk of bias were assessed: bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, bias in selection of the reported result. A risk-of-bias judgment (among "low risk of bias," "moderate risk of bias," "serious risk of bias," "critical risk of bias," or "no information") was assigned to each domain (depending on the descriptions given for each field) or to the entire study.

Statistical methods

Since many studies reported results related to a single treatment arm without a comparator, data could not be analyzed according to the standard network meta-analysis[18]. An alternative analysis of baseline model to include data from single-arm studies was therefore undertaken[19].

Treatment arms were grouped as follows:

- spontaneous healing (i.e., exposed implant surface covered by a full thickness flap) (SELF);
- graft material (bone substitute, autogenous bone, or combination) covered by a mucoperiosteal flap (BG);

- resorbable membrane alone (RM);
- resorbable membrane combined with a graft material (RM+BG);
- non-resorbable membrane alone (NRM);
- non-resorbable membrane combined with a graft material (NRM+BG);
- patient's own periosteum combined with a graft material (PERI + BG).

A Bayesian approach with the statistical software OpenBUGS was used to undertake all the analyses. Bayesian analysis used Markov Chain Monte Carlo (MCMC) method to obtain posterior distributions of parameters in the model, and 3 sets of non-informative priors were used to initiate 3 chains of simulations, where each chain iterated for 100,000 times and the first 50,000 iterations were burn-ins and discarded. Therefore, 150,000 times in total were used for the calculations of posterior distributions of parameters in the present analysis.

Study outcomes

Primary outcome

The proportion of non-resolved BD/BF at T1 was considered the primary outcome. Among the included studies, RM+BG was the most frequently reported treatment, and was therefore considered as the reference group. The effect size was expressed as odds ratio (OR). If one treatment had an odds ratio greater than 1, this implied a worse treatment effect than RM+BG in resolving BD/BF. Treatments were ranked by the surface under the cumulative ranking curve (SUCRA). SUCRA is a numeric presentation of the overall ranking and is presented as a single number associated with each treatment. The higher the SUCRA value, the better is the treatment position in the ranking.

Secondary outcomes

Absolute and percentage changes in DH, DW, BBT between T0 and T1, ISR, RBL, PD and BoP were the secondary outcomes. For both absolute and percentage change, mean and standard deviation (SD) were used to perform the analysis. For studies not reporting mean and SD, the mean difference between T0 and T1 was

calculated and the SD was obtained by assuming the correlation coefficient between T0 and T1 being 0.5. Data were expressed as mean and standard error (SE), while SUCRA was used for treatment ranking.

RESULTS

Summary of the literature search and description of the included studies

After the removal of 402 duplicates and the exclusion of 14.748 records out of 14.822 records identified through database search, full text papers were evaluated for eligibility for 74 records.

The screening and selection process resulted in the inclusion of 24 studies (9 RCTs, 6 CCTs and 9 case series). Details of the included studies are reported in Table 1. Quality assessment of the included studies is reported in Appendix 3 and 4.

Mean changes in DH, DW and BBT were reported or could be retrieved/derived from 18, 10 and 7 studies, respectively, whereas percentage change in DH, DW and BBT could be retrieved from 19, 6 and 1 studies, respectively. ISR was reported or could be retrieved/derived in 23 studies. RBL, PD and BoP were reported in 7, 3 and 2 studies, respectively.

Primary outcome

The results from the baseline model are reported in Table 2. Among the treatment groups, SELF showed a substantial difference in the rate of non-correction of BD/BF compared to RM+BG (OR: 5.78×10^{38}; CI: 4.83×10^{5} – 1.32×10^{86}), whereas none of the other treatments comparisons showed any significant difference.

The probabilities of treatment ranking and the SUCRA are reported in Table 3. Treatments based on a combination of a graft material and membrane/periosteum (i.e. RM+BG, NRM+BG, and PERI+BG) appeared to perform better than treatments using graft material alone or membrane alone (i.e. BG, RM, and NRM), but the differences were not statistically significant. SELF had the worst effect amongst all treatments.

Secondary Outcomes

DH

The results for absolute change in DH are reported in Table 4. RM+BG and NRM+BG showed 4.03 mm and 4.66 mm reductions in DH, respectively, while smaller treatment effects were reported for NRM, PERI+BG and SELF. NRM+BG showed a non-significant better effect while NRM and PERI+BG showed a non-significant worse effect compared to RM+BG. Only the 2.4 mm difference between SELF and RM+BG was statistically significant (Table 4).

The results of percentage change are reported in Table 5. For percentage change, BG, RM, and NRM+BG, showed a smaller reduction than RM+BG

Treatments based on a combination of a graft material and membrane/periosteum (i.e. RM+BG, NRM+BG, and PERI+BG) appeared to perform better than treatments using graft material or membrane alone (i.e. BG, RM, and NRM), even though differences were not statistically significant. SELF had the worst effect amongst all treatments.

DW

Table 6 shows the results related to the absolute change in DW. PERI+BG showed 1.5 mm greater reduction in defect width than RM+BG, while other treatments showed small, non-significant differences.

Treatments based on a combination of a graft material and membrane/periosteum (i.e. RM+BG, NRM+BG, and PERI+BG) appeared to perform better than treatments using graft material or membrane alone (i.e. BG, RM, and NRM), even though differences were not statistically significant. SELF had the worst effect amongst all treatments.

Since only 3 studies (Mattout 1995, Trombelli et al. 2019, 2020) reported the mean and SD of the percentage change in DW, no network meta-analysis could be performed for the latter.

BBT

Results for absolute change in BBT are reported in Table 7. NRM+BG and PERI+BG showed greater increases in BBT than RM+BG.

Since only 1 study (Temmerman et al. 2019) reported the percentage change in BBT, without SD, no network meta-analysis could be performed for the latter.

Implant Survival Rate (ISR)

ISR ranged between 80% and 100%. Since ISR was 100% in most study arms, the differences amongst various treatments could not be reliably estimated (the credible interval would have been extremely wide and not interpretable).

RBL, PD and BoP

Due to the paucity of studies reporting data on RBL, PD and BoP, and the high heterogeneity in observation interval, these parameters were not included in the network meta-analysis.

Heterogeneity and Risk of Bias in Included Studies

Among the included RCTs, 1 resulted at high risk of bias[30], 7 presented some concerns[25,30,34,35,37,38,40] and 1 was at low risk of bias[39]. Among non-randomized studies, 1 study presented a critical risk of bias[31] whereas 6 studies presented a serious [23,27,36,] and moderate[20,26,42] risk of bias.

As the number of studies included in the analysis of each outcome was too few, it was not possible to obtain a robust estimate of heterogeneity. Especially in the Bayesian meta-analysis, the estimate is prone to the influence of prior distribution.

CONCLUSIONS

Within the limitations of the present review, the results indicate that the reconstructive treatment (including use of graft alone, membrane alone, or combinations of grafts and either membrane or patient's own periosteum) of a BD/BF at implant placement favorably and significantly impacts on the probability to obtain complete correction of the BD/BF at implant uncovering when compared to full-thickness flap repositioning on the BD/BF. Encouraging data were reported for the combination of membrane/periosteum and graft, which showed a tendency to perform better than other treatments, but confirmatory studies are needed for this finding.

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Reference	Publication date	Study design	Test implants (after dropout)	Test implants 2 (after dropout)	Control implants (after dropout)	Intervention test	Intervention test 2	Intervention control	Study outcomes
Dahlin[20]	1991a	CCT (split)	7	X	7	ePTFE membrane	X	SH	CDC (%), ΔVDH (%), ISR (%)
Dahlin[21]	1991b	Case Series	8	X	X	ePTFE membrane	X	X	CDC (%)
Jovanovic[22]	1992	Case series	14	X	X	ePTFE membrane	X	X	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%), RBL
Mattout[23]	1995	CCT (parallel)	11	X	9	ePTFE membrane + DFDBA	X	ePTFE membrane	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%)
Mayfield[24]	1997	Case series	12	X	X	PLA/PGA membrane	X	X	CDC (%), ISR (%), RBL
Zitzmann[25]	1997	RCT (split)	43	X	39	Collagen membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (%), ISR (%)
Schlegel[26]	1998	CCT (parallel)	14	X	15	PDS membrane + ACBP	X	ACBP	CDC (%), ΔVDH (%), ISR (%)
Majzoub[27]	1999	CCT (parallel)	12	X	10	Laminar bone sheet	X	ePTFE membrane	CDC (%), ΔVDH (%), ISR (%)
Widmark[28]	2000	Case series	9	X	X	ACBP	X	X	CDC (%), ΔVDH (%), ISR (%)
Rosen[29]	2001	Case series	8	X	X	Poly-(DL-lactide) membrane + FDBA/DFDBA	X	x	CDC (%), ISR (%)
Jung[30]	2003	RCT (split)	10	X	10	Collagen membrane + DBBM	X	Collagen membrane +	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)

								DBBM + rhBMP-2	
Veis[31]	2004	CCT (parallel)	16	16	14	ePTFE membrane + ACBP (Ramus)	ePTFE membrane + ACBP (Tuberosity)	ePTFE membrane + ACBP (Symphysis)	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
Wang[32]	2004	Case series	6	X	X	Collagen membrane + ACBP + DFDBA + HA	x	X	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)
De Boever[33]	2005	Case series	15	X	X	ePTFE membrane + DBBM	X	x	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%), PD, RBL
Van Assche[34]	2013	RCT (split)	14	X	14	Collagen membrane + DBBM	X	Collagen membrane + HA/β-TCP	CDC (%), ΔVDH (%), ISR (%), PD, BoP, RBL
Schneider[35]	2014	RCT	19	X	21	PA/PGA membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔBBT (mm), ISR (%)
Konstantinidis[36]	2015	CCT	9	X	26	Collagen membrane + CPS	X	Titanium mesh + CPS	CDC (%), ΔVDH (mm), ISR (%)
Lee[37]	2015	RCT (parallel)	14	X	14	Collagen membrane + DBBM	X	Pericardium membrane + DBBM	CDC (%), ΔVDH (mm), ΔDW (mm), ISR (%)
Jung[6]	2017	RCT (parallel)	15	X	13	Collagen membrane + DBBM	X	SH	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ISR (%), RBL
Naenni[38]	2017	RCT	13	X	13	Collagen membrane + DBBM	X	ePTFE membrane + DBBM	CDC (%), ΔVDH (mm), ΔVDH (%), ISR (%)

Benic[39]	2019	RCT (parallel)	12	X	12	Collagen membrane + DBBM Block	X	Collagen membrane + DBBM	CDC (%), ΔVDH (%), ISR (%)
Temmerman[40]	2019	RCT (parallel)	14	X	14	Collagen membrane + DBBM + ACBP	X	Collagen membrane + DBBM	CDC (%), ΔVDH (%), ΔDW (%), ΔBBT (%), ISR (%), RBL
Trombelli[41]	2019	Case series	15	X	X	Patient's periosteum + DBBM	X	X	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%)
Trombelli[42]	2020	Case series	11	X	x	Patient's periosteum + DBBM	X	x	CDC (%), ΔVDH (mm), ΔVDH (%), ΔDW (mm), ΔDW (%), ISR (%), PD, BoP, RBL

TABLE 1 Methodological characteristics of the selected studies, the types of interventions and the outcomes measured
RCT: randomized controlled trial; CCT: controlled clinical trial; ePTFE: expanded polytetrafluorethylene; SH: spontaneous healing; PA/PGA: polyglycolide and polylactide; DBBM: deproteinized bovine bone mineral; rhBMP-2: recombinant human bone morphogenetic protein 2; FDBA: freeze-dried bone allograft; DFDBA: demineralized freeze-dried bone allograft; HA: hydroxyapatite; β-TCP: beta tri-calcium phosphate; CPS: calcium phosphosilicate; CDC (%): rate of complete dehiscence coverage; ΔVDH (mm): absolute change in vertical dehiscence depth; ΔVDH (%): percentage change in vertical dehiscence depth; ΔDW (mm): absolute change in dehiscence width; ΔDW (%): percentage change in dehiscence width; ISR: implant survival rate; PD: probing depth; BoP: bleeding upon probing; RBL: radiographic bone level.

Table 2 The Non-Resolved Dehiscence Odds Ratio (Reference Group=RM+BG)

Item	OR	SE	90% Credible Interval	
RM - RM+BG	1.17	3.28	0.16	7.67
NRM - RM+BG	0.67	2.20	0.19	2.40
NRM+BG - RM+BG	0.56	1.94	0.19	1.65
PERI+BG - RM+BG	0.17	3.73	0.02	1.39
GRAFT - RM+BG	1.67	3.13	0.26	10.40
SELF - RM+BG	5.78×10^{38}	4.06×10^{25}	4.83×10^{5}	1.32×10^{86}
	Estimate	SE	90% Credible Interval	
RM+BG (Absolute mean)	0.79	2.66	0.16	3.95
sd of RM+BG	2.54	1.06	2.25	2.71
tau	17.13			

Table 3 The Probability of Rank and SUCRA of the Non-Resolved Dehiscence

	Rank1	Rank2	Rank3	Rank4	Rank5	Rank6	Rank7	SUCRA
NRM	0.00	0.05	0.19	0.36	0.31	0.09	0.00	0.47
RM	0.06	0.13	0.13	0.14	0.23	0.32	0.00	0.45
RM+BG	0.08	0.26	0.27	0.20	0.14	0.06	0.00	0.63
NRM+BG	0.11	0.36	0.26	0.15	0.08	0.03	0.00	0.69
PERI+BG	0.71	0.13	0.07	0.04	0.03	0.02	0.00	0.89
GRAFT	0.04	0.08	0.09	0.11	0.21	0.48	0.00	0.37
SELF	0.00	0.00	0.00	0.00	0.00	0.00	1.00	0.00

Table 4 The Absolute Mean Difference of Vertical Dehiscence

Item	Mean	SE	90% Credible Interval	
RM+BG	4.03	0.99	2.40	5.65
NRM	2.78	1.74	-0.08	5.63
NRM+BG	4.66	1.52	2.15	7.15
PERI+BG	3.07	1.92	-0.09	6.23
SELF	1.65	2.00	-1.65	4.94

Table 5 The Absolute Percentage Change of Vertical Dehiscence

Item	Mean	SE	90% Credible Interval	
RM+BG	93.40	1.67	90.64	96.08
RM	74.88	9.42	59.63	90.61
NRM	86.69	7.30	74.72	98.69
NRM+BG	68.99	4.20	61.97	75.79
PERI+BG	94.30	5.01	86.16	100.00
BG	80.04	8.51	65.91	93.85

Table 6 The Absolute Mean Difference of Defect Width

Item	Mean	SE	90% Credible Interval	
RM+BG	1.95	0.69	0.81	3.05
NRM	1.58	1.24	-0.48	3.57
NRM+BG	2.43	1.03	0.68	4.04
PERI+BG	3.47	1.35	1.25	5.65
SELF	0.91	1.47	-1.51	3.29

Table 7 The Absolute Mean Difference of Buccal Bone Thickness

Item	Mean	SE	90% Credible Interval	
RM+BG	-1.47	0.70	-2.63	-0.33
NRM+BG	-0.11	1.19	-2.06	1.85
PERI+BG	-0.20	1.40	-2.48	2.09