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KOMPARATIVNA ANALIZA EKSPANZIJE KOSTI UPOTREBOM DENASH BORERA NASUPROT CEPANJA GREBENA EKSPANDERIMA PRI POSTAVLJANJU IMPLANTATA U USKIM GREBENIMA

A COMPARATIVE ANALYSIS OF BONE EXPANSION USING DENSAR BURS VERSUS RIDGE SPLIT WITH EXPANDERS FOR IMPLANT PLACEMENT IN NARROW RIDGES

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Sažetak

Uvod: Gubitak zuba dovodi do značajne resorpcije alveolarnog grebena, što otežava postavljanje zubnih implantata. Neposredna ugradnja implantata i tehnike kao što su vođena koštana regeneracija i tehnika cepanja grebena imaju za cilj da reše ove izazove, ali nose rizike.

Cilj istraživanja je bio da se proceni povećanje debljine kosti i opstanak implantata u uskim grebenima sa horizontalnom atrofijom tretiranim dvema različitim tehnikama: tehnikom cepanja alveolarnog grebena i oseodensifikacijom Densah® borerima, uz istovremenu ugradnju implantata.

Materijal i metode: U studiji je uključeno ukupno 30 uskih grebena sa rasponom širine između 3–6 mm i odgovarajućom vertikalnom visinom kosti tretiranih pomoću dve različite tehnike: tehnikom cepanja grebena (RST) i oseodensifikacijom (OD) Densah® borerima.

Rezultati: Razlika u bukolingvalnoj širini (mm) između dva vremenska intervala dve grupe pokazuje značajne razlike posle procedure sa p-vrednostima < 0,001, što ukazuje na bolje rezultate u grupi sa Densah® borerima.

Zaključak: Nalazi sugerišu da oseodensifikacija nudi superiorne rezultate, pokazujući značajnu ekspanziju kosti i primarnu stabilnost, što je čini obećavajućom tehnikom za dentalnu implantologiju u slučajevima uskih grebena.

Ključne reči: Densah boreri, greben split, uski greben

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Abstract

Introduction: Tooth loss leads to significant alveolar ridge resorption, complicating dental implant placement. Immediate implant placement and techniques like guided bone regeneration and ridge split technique aim to address these challenges but come with risks.

Aim of the study was to evaluate bone thickness augmentation and implant survival in narrow ridges with horizontal atrophy treated with two different techniques: the ridge split technique and osseodensification with Densah® burs, with simultaneous implant placement.

Material and methods: A total of 30 narrow ridges with a width range between 3–6 mm and adequate vertical bone height were considered for the study and divided into two groups for treatment by two different techniques: the ridge split technique (RST) and osseodensification (OD) with Densah® burs.

Results: The difference of buccolingual width (mm) between two time intervals of two groups show significant differences post-procedure with p-values < 0.001, suggesting better outcomes in group with Densah® burs.

Conclusion: Findings suggest osseodensification offers superior outcomes, demonstrating significant bone expansion and primary stability, making it a promising technique for dental implantology in cases of narrow ridges.

Key words: Densah burs, ridge split, narrow ridge

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Introduction

Bone resorption after tooth loss is an inevitable event that often results in inadequate bone dimensions for dental implant placement in an ideal position¹. After tooth extraction, the buccolingual alveolar ridge dimension decreases significantly, over 3–12 months, and the amount of resorption can reach approximately 50% of the original bone width².

Dental implantology has undergone transformative advancements in recent years, revolutionizing the restorative dentistry landscape. Dental implants can be placed into edentulous alveolar ridges where adequate buccolingual bone width is available to support a fixed-type dental prosthesis. A minimum of 1.0–1.5 mm of bone width thickness should be present on the buccal and lingual aspects of the implants. A regularly desired 4-mm diameter implant requires an average of 6 mm buccolingual ridge width. This creates a great challenge in implant dentistry for clinicians because alveolar ridge atrophy always occurs after tooth extraction, which restricts the use of dental implants to restore oral function.

Several surgical techniques have been described for augmentation of the atrophic mandibular alveolar ridge. The ridge split technique (RST) has been developed for the reconstruction of the buccolingually reduced bone width of the alveolar process. The ridge split procedure is a technique used to increase the width of a narrow ridge with simultaneous implant placement into the bone bed. The buccal cortical plate fracture is the main surgical concern associated with the RST³.

Osseodensification is an innovative biomechanical method for bone preparation that is designed to supplant traditional bone subtractive drilling, ultimately enhancing the quality of the implant site⁴. When compared with the conventional subtractive drilling technique, this method improves the primary and secondary stability of the implant and the percentage of bone-implant contact (BIC) by up to threefold.

The most commonly used devices for evaluating primary stability are removal torque and resonance frequency analysis (RFA)⁵. Ostell™ ISQ device, developed by Meredith in 1987, is a noninvasive method that can reproducibly assess bone-to-implant contact through direct attachment of a transducer to the implant body. ISQ values range from 1 to 100, with higher ISQ values denoting higher implant stability. ISQ values in the range of 40–80 indicate that the dental implant is clinically stable⁶.

The rationale for undertaking this comparative evaluation stems from the

imperative to establish evidence-based practices in immediate implant placement, particularly in cases involving narrow ridges.

Aim

The study aimed to evaluate bone thickness augmentation and implant survival in narrow ridges with horizontal atrophy treated with two different techniques: the ridge split technique and osseodensification with Densab® burs, with simultaneous implant placement.

1. To evaluate the increase in bone thickness obtained by RST before implant placement and after 6 months based on CBCT.
2. To evaluate the increase in bone thickness obtained by ODT before implant placement and after 6 months, based on CBCT.
3. To evaluate the implant stability obtained by RST at the time of implant placement and after 3 months based on RFA.
4. To evaluate the implant stability obtained by ODT at the time of implant placement and after 3 months based on RFA.
5. To compare crestal bone levels radiographically around implants placed at the time of implant placement, 1 week after placement, and 3 months post implant placement with RST.
6. To compare crestal bone levels radiographically around implants placed at the time of implant placement, 1 week after placement, and 3 months post implant placement with ODT.

Materials and Methods

A randomized prospective study was conducted in the Department of Oral and Maxillofacial Surgery, Faculty of Dental Sciences, SGT University, Gurugram, following approval by the institutional ethical committee with clearance No. FODS/EC/OMS/2022/20

Patient Selection

A total of 30 narrow ridges with a width range between 3–6 mm and adequate vertical bone height were considered for the study. These sites were equally divided into two groups for treatment by two different techniques: the ridge split technique (RST) and osseodensification (OD) with Densab® burs.

Site selection for the two groups was done randomly by the chit system before surgery. Each patient provided informed consent before beginning the study and was free to discontinue it at any time. Patients were included in this study based on the following criteria:

Inclusion Criteria:

- 1) Patient's age ranging between 18 and 60 years.
- 2) Patients having narrow/atrophied ridges within a range of 3–6 mm buccolingual width irrespective of the anterior/posterior site in the maxilla/mandible.
- 3) Patients who were cooperative, motivated, and hygiene conscious and gave their consent to be included in the study understanding the risks involved.
- 4) ASA Classification Class 1 patients.

Exclusion Criteria:

- 1) According to ASA Classification Class 3 patients—uncontrolled diabetes with complications to vascular or other organs, i.e., retinopathy, neuropathy, etc.

- 2) Inadequate patient compliance.
- 3) Poorly motivated or patients unable to keep the follow-up are excluded.
- 4) Patient with heavy smoking and alcohol abuse.

Surgical procedure

In a comparative study of two surgical techniques for dental implant placement, patients were treated under strict aseptic conditions and local anesthesia. The first group underwent the RST, which involved a mid-crestal incision with papillary sparing, followed by vertical releasing incisions. A mucoperiosteal flap was raised to expose the ridge, and osteotomies were created using Piezo tips to minimize bone trauma. Sequential use of rotary expanders widened the bone to accommodate the implants. Postoperative care included suturing, antibiotics, and chlorhexidine rinses. Patients were monitored for bone loss and implant stability over several follow-up visits up to six months, including CBCT scans and ISQ measurements to assess bone thickness and implant stability (Figures 1–6).



Figure 1. Pre op view of narrow ridge irt 46, 47

Figure 2. Full thickness mucoperiosteal flap elevation



Figure 3. Intra op view of ridge split ***Figure 4.*** Implants insertion



Figure 5. Closure made without tension **Figure 6.** ITP X ray of implants placement

In contrast, the second group underwent implant placement using the ODT. This technique began with a mid-crestal incision and vertical incisions beyond the mucogingival line, followed by raising a mucoperiosteal flap. Initial osteotomies were made with a pilot drill, and osseodensification was performed using specially designed Densah® Burs in a counterclockwise motion to compact bone and expand the osteotomy gradually. Similar postoperative care and follow-up assessments were conducted as in the first group to evaluate bone changes, implant stability, and complications. (Figures 7–12)

Both groups were managed postoperatively with antibiotics, analgesics, and chlorhexidine rinses, with regular follow-

ups to monitor healing and assess implant success. Data analysis, using statistical methods like the Paired t Test, aimed to compare bone thickness, Implant Stability Quotient (ISQ), and crestal bone levels between the two techniques. The study's findings were evaluated for statistical significance to determine the efficacy and outcomes of each approach in implant dentistry.

Overall, the study highlighted the procedural differences, postoperative management, and rigorous follow-up required to evaluate the effectiveness of RST and ODT in enhancing bone volume and implant stability for successful prosthetic rehabilitation.



Figure 7. Pre-op view of narrow ridge irt 24 **Figure 8.** Densah bur expanding the osteotomy



Figure 9. Prepared osteotomy site **Figure 10.** Implant insertion

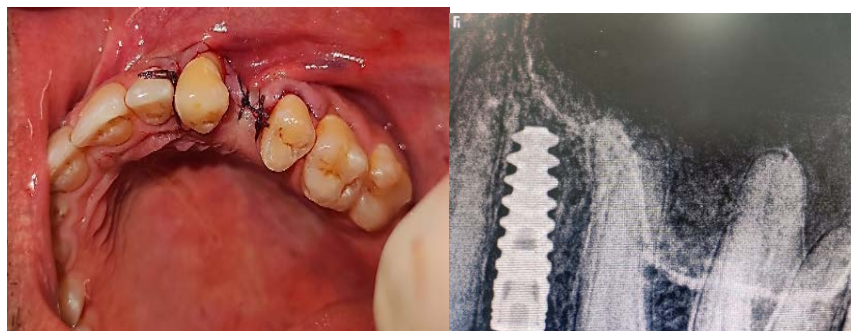


Figure 11. Closure made without tension **Figure 12.** Iopa showing implants placement

Results

The study compared two groups of patients undergoing dental implant procedures, focusing on various parameters such as patient demographics, site distribution, buccolingual width, ISQ, and crestal bone levels. Group 1 consisted of older patients (mean age 53.14 years), predominantly females (3 out of 5 patients), while Group 2 had younger patients (mean age 40.06 years) with an equal distribution of males and females (3 each). This demographic distribution was reflected in the frequency distribution graphs (Graph 1 and Graph 2) and the detailed tabular data (Table 1 and Table 2).

Table 1 shows the frequency N distribution of male and female patients along with their mean and SD of age among the two groups. In Group 1, 5 of 11 patients were included in the study, with a mean age of 53, of which 2 were males and 3 were females. In Group 2, 6 of 11 patients were included with a mean age of 40, of which 3 were males and 3 were females (Ref. Graph 1)

Graph 1, which pertains to Table 1, shows gender distribution along the X-axis and frequency distribution of patients along the Y-axis among the two groups.

Table 2 shows the Frequency N distribution of sites by region among two groups. It depicts in Group 1, of 15 sites, 5 in the mandibular anterior region, 8 in the maxillary anterior region, 0 in the mandibular

anterior region and 2 in the maxillary posterior region. In Group 2, of 15 sites, 9 in the mandibular anterior region, 3 in the maxillary anterior region, 2 in the mandibular anterior region and 1 in the maxillary posterior region (Figure 2)

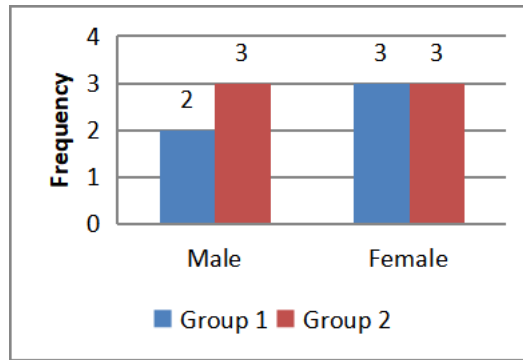
Graph 2, which pertains to Table 2, shows region distribution along the X-axis and frequency distribution of sites along the Y-axis among the two groups

Buccolingual width changes were measured before (T0) and after 6 months (T1) of implant placement using the Paired t Tests (Table 3), indicating significant reductions in both groups (Group 1: -2.44 mm, Group 2: -3.68 mm) with p-values < 0.001, highlighting effective bone expansion techniques. The Independent t Tests further compared buccolingual widths between groups at different time intervals (Table 4), showing significant differences post-procedure (T1) with p-values < 0.001, suggesting better outcomes in Group 2.

Table 3 shows the intra-group comparison of the mean difference of buccolingual width (mm) between two time intervals, T0 (buccolingual width before the procedure) and T1 (buccolingual width after 6 months of procedure), of two groups by the Paired t Test. The mean difference of buccolingual width (mm) between T0 and T1 of Group 1, -2.43667 ± 0.15045 , and of Group 2, -3.67533 ± 0.11592 , is $p < 0.001$

Table 1. Frequency N distribution of males and females and mean, SD of age of patients among two groups

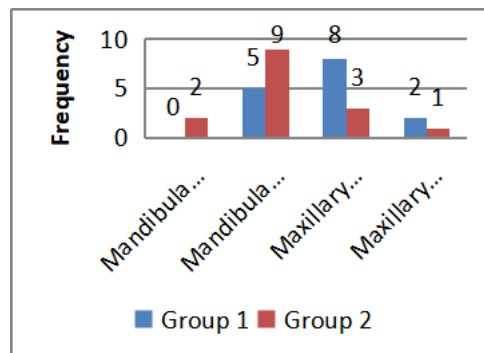
Group	Sex		Age
	Male	Female	Mean $\pm$ S.D.
Group 1	2	3	53.14 $\pm$ 5.414
Group 2	3	3	40.06 $\pm$ 13.225



Graph 1. Frequency distribution of male and female patients among two groups

Table 2. Frequency N distribution of sites by region among two groups

	Region			
	Mandibular anterior	Mandibular posterior	Maxillary anterior	Maxillary posterior
Group 1	0	5	8	2
Group 2	2	9	3	1



Graph 2. Frequency distribution of sites by their region among two groups

Table 3. Intra-group comparison of mean difference of buccolingual width (mm) between two time intervals of two groups by the Paired t Test

Group	Time Intervals	Mean difference $\pm$ S.E.M.	p-value
Group 1	TO-T1	-2.43667 $\pm$ 0.15045	< 0.001**
Group 2	TO-T1	-3.67533 $\pm$ 0.11592	< 0.001**

NS Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 9 shows the distribution of mean of crestal bone levels on the mesial side (mm) in two groups at different time intervals. It shows that the difference mean of crestal bone level on mesial side (mm) -0.0667 ± 0.1881 between the two groups after one week T1 is $p = 0.726$. The difference mean of crestal bone level on the mesial side (mm) -0.227 ± 0.170 between two groups after 3 months T2 is $p = 0.194$ (Graph 5)

Table 10 shows the distribution of the mean of crestal bone level on the distal side (mm) in two groups at different time intervals. The difference mean $\pm$ SD of crestal bone level on the distal side (mm) 0.2000 ± 0.1604 between the two groups after one week T1 is $p = 0.233$. The difference mean of crestal bone level on the distal side (mm) 0.3133 ± 0.1107 between the two groups after 3 months T2 is $p < 0.05$ (Graph 6)

Graphical representations (Graph 3, Graph 4, Graph 5, and Graph 6) complemented these findings, illustrating trends in buccolingual width, ISQ values, and crestal bone levels across different time intervals and between groups. Overall, the study provided comprehensive insights into the effectiveness

of different implant techniques, demographic influences, and longitudinal changes in key clinical parameters, underscoring the importance of tailored approaches in dental implantology and the need for further research to validate these findings in larger cohorts and longer follow-up periods.

Graph 3, which pertains to Table 4, shows time interval distribution T0 and T1 along the X-axis and mean values of buccolingual width (mm) readings along the Y-axis among the two groups

Graph 4, which pertains to Table 6, shows the time interval distribution T0 and T1 along the X-axis and the mean values of ISQ readings along the Y-axis among two groups Graph 5, which pertains to Table 9, shows the time interval distribution T0 and T1 along the X-axis and the mean values of crestal bone levels on the mesial side (mm) readings along the Y-axis among two groups

Graph 6, which pertains to Table 10, shows the time interval distribution T0, T1 and T2 along the X-axis and the mean values of crestal bone levels on the distal side (mm) readings along the Y-axis among two groups

Table 4. Inter-group comparison of the mean of buccolingual width (mm) between the two groups at different time intervals by the Independent t Test

Time Intervals	Group	N	Mean	Std. Dev.	Mean difference $\pm$ S.E.M.	p-value
T0 (Buccolingual width before procedure)	Group 1	15	3.9913	0.64167	0.03267 ± 0.20971	0.877^{NS}
	Group 2	15	3.9587	0.49795		
T1 (Buccolingual width after 6 months of procedure)	Group 1	15	6.4280	0.32591	-1.20600 ± 0.12683	$< 0.001^{**}$
	Group 2	15	7.6340	0.36750		

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 5. Intra-group comparison of mean difference of ISQ values between two time intervals of the two groups by the Paired t Test

Group	Time Intervals	Mean difference $\pm$ S.E.M.	p-value
Group 1	TO-T1	-2.846 ± 0.465	$< 0.001^{**}$
Group 2	TO-T1	-8.067 ± 0.636	$< 0.001^{**}$

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 6. Inter-group comparison of the mean of ISQ values between two groups at different time intervals by the Independent t Test

Time Intervals	Group	N	Mean	Std. Dev.	p-value
T0 (At the time of implant placement)	Group 1	15	63.53	1.642	0.066 ^{NS}
	Group 2	15	64.53	1.187	
T1 (After 3 months of implant placement)	Group 1	15	66.38	1.387	< 0.001**
	Group 2	15	72.60	2.849	

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 7. Intra-group comparison of mean difference of crestal bone level on the mesial side (mm) between two time intervals of two groups by the Paired t Test

Group	Time Intervals	Mean difference $\pm$ S.E.M.	p-value
Group 1	T0-T1	-0.3333 $\pm$ 0.1351	0.027*
	T1-T2	-0.7333 $\pm$ 0.1453	< 0.001**
	T0-T2	-1.067 $\pm$ 0.137	< 0.001**
Group 2	T0-T1	-0.4000 $\pm$ 0.1309	0.009*
	T1-T2	-0.8933 $\pm$ 0.1127	< 0.001**
	T0-T2	-1.293 $\pm$ 0.101	< 0.001**

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 8. Intra-group comparison of mean difference of crestal bone level on the distal side (mm) between two-time intervals of two groups by the Paired t Test

Group	Time Intervals	Mean difference $\pm$ S.E.M.	p-value
Group 1	T0-T1	-0.5000 $\pm$ 0.1380	0.003*
	T1-T2	-0.5933 $\pm$ 0.0902	< 0.001**
	T0-T2	-1.0933 $\pm$ 0.0848	< 0.001**
Group 2	T0-T1	-0.3000 $\pm$ 0.0816	0.003*
	T1-T2	-0.4800 $\pm$ 0.0782	< 0.001**
	T0-T2	-0.7800 $\pm$ 0.0712	< 0.001**

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 9. Inter-group comparison of the mean of crestal bone level on the mesial side (mm) between two groups at different time intervals by the Independent t Test

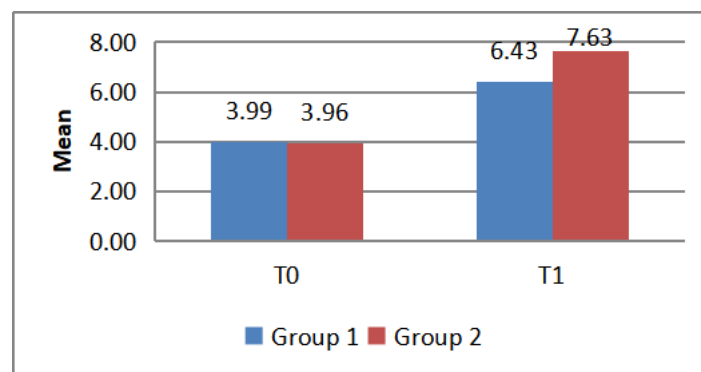
Time Intervals	Group	N	Mean	Std. Dev.	Mean difference $\pm$ S.E.M.	p-value
T0 (Immediate post-op)	Group 1	15	0.00	0.000	0.000	Not calculated
	Group 2	15	0.00	0.000		
T1 (after one week)	Group 1	15	0.333	0.5233	-0.0667 ± 0.1881	0.726 ^{NS}
	Group 2	15	0.400	0.5071		
T2 (after 3 months)	Group 1	15	1.07	0.530	-0.227 ± 0.170	0.194 ^{NS}
	Group 2	15	1.29	0.392		

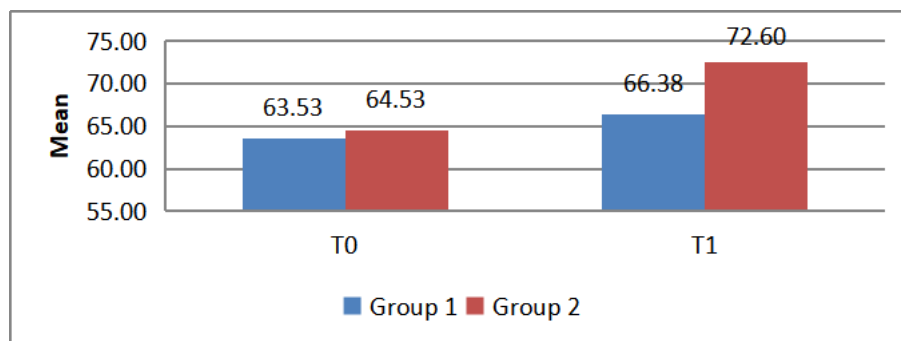
^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

Table 10. Inter-group comparison of the mean of crestal bone level on the distal side (mm) between two groups at different time intervals by the Independent t Test

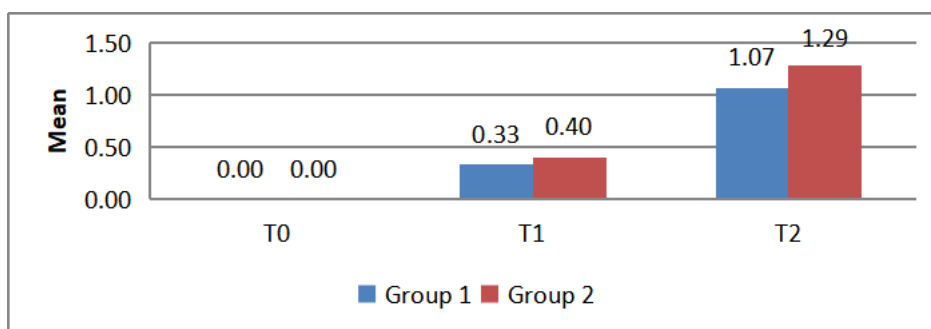
Time Intervals	Group	N	Mean	Std. Dev.	Mean difference $\pm$ S.E.M.	p-value
T0 (Immediate post-op)	Group 1	15	0.00	0.000	0.000	Not calculated
	Group 2	15	0.00	0.000		
T1 (after one week)	Group 1	15	0.500	0.5345	0.2000 ± 0.1604	0.223 ^{NS}
	Group 2	15	0.300	0.3162		
T2 (after 3 months)	Group 1	15	1.093	0.3283	0.3133 ± 0.1107	0.009 ^{**}
	Group 2	15	0.780	0.2757		

^{NS} Not significant $p > 0.05$, * Significant $p < 0.05$, ** Highly significant $p < 0.001$

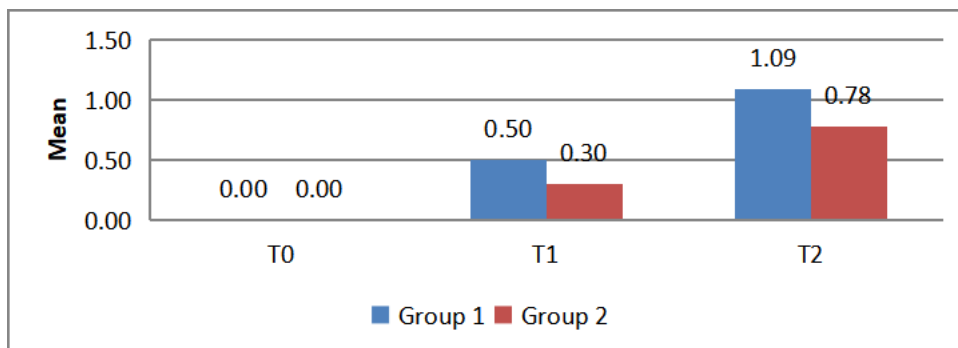
**Graph 3.** Comparison of mean of buccolingual width (mm) between the two groups at different time intervals



Graph 4. Comparison of mean of ISQ values between the two groups at different time intervals



Graph 5. Comparison of mean of crestal bone level on the mesial side (mm) between two groups at different time intervals



Graph 6. Comparison of mean difference of crestal bone level on the distal side (mm) between two groups at different time intervals

Discussion

In recent decades, dental implants have revolutionized treatment for patients with missing teeth by offering reliable long-term outcomes through osseointegration. However, a significant challenge remains in cases where the alveolar ridge lacks sufficient width for successful implant placement. Adequate bone width of 1 to 1.5 mm on both the labial and lingual/palatal aspects of the implant site is crucial for predictable results⁷. To address this,

various surgical techniques have been proposed, including alveolar ridge split osteotomy and osseodensification, as alternatives to traditional bone grafting methods.

The study discussed herein aimed to compare bone expansion techniques using Densab[®] burs versus ridge split with expanders for implant placement in narrow ridges. Thirty implants were placed across 11 patients, with sites randomized into two groups. Group 1 utilized the RST for bone expansion, while

Group 2 employed the ODT. Age was a critical factor influencing technique selection, with younger patients typically better suited for RST due to superior bone quality and healing capabilities, whereas OD was preferred for older patients with compromised bone density⁸.

Results showed promising outcomes for both techniques, with successful implant integration observed in the majority of cases over a six-month follow-up period. Two implants in Group 1 failed, potentially due to low bone density, a known risk factor for implant failure, especially in the maxillary anterior region. The OD group demonstrated significantly greater bone expansion compared to the RST group, attributed to the unique properties of Densah[®] burs, which compact bone laterally without causing fractures, thereby facilitating effective ridge expansion.

In 2019, Tretto et al.⁹ conducted a comprehensive literature review on implant preparation methods and found that OD has produced encouraging and promising biomechanical outcomes.

Chan in 2013 assessed the amount of ridge expansion achieved with screw expanders. His findings indicated that the use of screw spreaders or expanders increased the ridge width by an average of 0.79 mm¹⁰.

The primary stability of implants was evaluated using Resonance Frequency Analysis (RFA) with the Osstell[™] ISQ device, showing a statistically significant increase in stability over the three-month postoperative period for both groups. This method proved effective in monitoring osseointegration progress and implant stability, crucial for long-term success. Radiographic evaluation using intraoral periapical radiographs revealed minimal crestal bone loss, essential for maintaining implant stability and overall success.

As for complications, a systematic review by Lin et al.¹¹ concluded that according to seven studies, ARS can have problems during or after surgery, such as exposure, infection, poor split, dehiscence, fracture, paraesthesia, and soft tissue retraction^{12,13-18}. Furthermore, if OD drills are not used in conjunction with abundant irrigation, they have been discovered to raise the temperature and may cause the nearby osteoblasts to necrotize¹⁹.

Complications were minimal, with only two cases of thin buccal cortical plate fractures observed in the mandibular posterior region in the patients of Group 1. This underscores the importance of careful patient selection and

technique application to minimize adverse events during implant procedures. Overall, the study supports OD as a potentially superior technique for achieving adequate bone expansion and implant stability in narrow ridges compared to traditional ridge splitting methods.

In conclusion, while both RST and ODT offer viable solutions for implant placement in narrow ridges, OD appears to provide greater bone expansion and stability advantages. Further research and larger-scale studies are warranted to confirm these findings and optimize treatment protocols for enhancing dental implant outcomes in patients with ridge deficiencies.

Conclusion

This study compared the Ridge Split Technique (RST) and the Osseodensification Technique (ODT) for dental implant placement in narrow ridges. Both techniques demonstrated practicality and predictability with significant increases in ridge thickness and minimal complications. However, the data strongly favored OD for enhancing implant primary stability and achieving a greater buccolingual width. Osseodensification, utilizing Densah[®] burs, showed superior performance in terms of implant stability over time and mitigated risks associated with buccal cortical plate fractures, which are common with ridge splitting.

Key findings included successful ridge expansion with both techniques, evidenced by increased primary stability as measured by Resonance Frequency Analysis (RFA). The study highlighted crestal bone loss of 1.0 to 2.0 mm at three months post-implantation, underscoring the importance of subcrestal implant placement to maintain stability. Ultimately, the study rejected the Null Hypothesis and supported the Alternate Hypothesis I, affirming OD as a more patient-friendly and effective method for implant placement in narrow ridges.

However, the study acknowledged limitations such as a small sample size and short follow-up duration, necessitating larger prospective cohorts and randomized control trials to further validate the clinical efficacy and long-term success of OD in diverse patient populations. This research underscores the evolving landscape of implant dentistry, emphasizing the need for refined techniques that enhance predictability and patient outcomes.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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