Section: General Surgery

Original Research Article

SPLIT-THICKNESS GRAFT INTEGRATION POST TUMESCENT VS NON-TUMESCENT HARVESTING TECHNIQUES: A RANDOMIZED CONTROL TRIAL

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ABSTRACT

Background: Split-thickness skin grafting (STSG) is commonly used for coverage of raw areas from trauma, burns, chronic ulcers, and post-excisional defects. Successful graft integration depends on recipient bed vascularity, donor-site handling, graft thickness, and harvesting technique. Tumescent harvesting reduces intraoperative bleeding and may improve graft quality. Hyaluronidase enhances tissue permeability, potentially optimizing tumescent harvesting, but its independent effect on graft take is unclear. **Aim:** To compare STSG integration following non-tumescent harvesting, tumescent harvesting without hyaluronidase, and tumescent harvesting with hyaluronidase. **Materials and Methods:** In this prospective, three-arm randomized trial at a tertiary teaching hospital over 18 months, 84 patients (18–65 years) requiring STSG were randomized into Group A (non-tumescent), Group B (tumescent without hyaluronidase), and Group C (tumescent with hyaluronidase). Grafts were harvested using a standardized Humby's knife. Graft take (%) was assessed on postoperative days 5, 10, and 21. Donor-site healing and complications were recorded. Statistical analysis included repeated-measures GLM, one-way ANOVA, and Chi-square tests ($p < 0.05$). Trial registration: CTRI/2025/05/087112. **Results:** Baseline demographics and wound characteristics were comparable. Graft taken improved over time in all groups ($p < 0.001$). Group C consistently had the highest mean graft take, followed by Group B, then Group A (between-group difference $p = 0.02$). Healing trajectories were similar across groups. Recipient-site complications were fewer in tumescent groups, particularly with hyaluronidase, without added adverse events. **Conclusion:** Tumescent harvesting enhances STSG integration compared to non-tumescent techniques. Adjunctive hyaluronidase provides additional, significant improvement without increasing complications, supporting its use to optimize graft outcomes.

INTRODUCTION

Split-thickness skin grafting (STSG) is a widely used reconstructive procedure for covering raw areas resulting from trauma, burns, infections, chronic ulcers, and post-excisional defects. Successful graft integration depends on recipient bed vascularity, graft thickness, donor-site handling, surgical technique, and patient factors such as comorbidities.
Traditionally, STSG harvesting is performed without infiltration (non-tumescent technique), which may cause increased bleeding, uneven donor surfaces, and prolonged operative time. The tumescent technique, involving subdermal infiltration of a dilute solution with a local anesthetic and vasoconstrictor, reduces intraoperative bleeding, stabilizes the donor site, and facilitates smoother graft harvest, improving early graft adherence and integration.
Hyaluronidase, an enzyme that depolymerizes hyaluronic acid, increases tissue permeability and promotes uniform diffusion of injected solutions. Its adjunctive use in tumescent solutions may enhance graft harvest quality, graft take, and donor-site healing. However, most studies compare tumescent and non-tumescent techniques without isolating the effect of hyaluronidase, making it unclear whether benefits are due to tumescence alone or the enzymatic action.

This prospective, three-arm randomized controlled trial was designed to compare STSG integration following non-tumescent harvesting, tumescent harvesting without hyaluronidase, and tumescent harvesting with hyaluronidase. By standardizing graft thickness, donor site, surgical technique, and postoperative care, the study aims to objectively evaluate the independent effect of hyaluronidase on graft take and donor-site healing, providing clinically relevant evidence to guide optimal STSG harvesting practices.

MATERIALS AND METHODS

This prospective, three-arm randomized controlled trial was conducted in the Department of General Surgery, Aarupadai Veedu Medical College and Hospital, Puducherry, over 18 months, following Institutional Ethics Committee approval and registration with the Clinical Trials Registry of India (CTRI/2025/05/087112). The study adhered to CONSORT guidelines and the Declaration of Helsinki.

Patients aged 18–65 years requiring split-thickness skin grafting (STSG) for clean wounds were included after informed consent. Exclusion criteria were immunocompromised status, active infection at donor or recipient sites, serum albumin <3 g/dL, hemoglobin <10 g/dL, allergy to lidocaine, adrenaline, or hyaluronidase, and recent smoking.

Based on previous literature, a minimum clinically significant difference of 3% in graft take and 80% power, 28 patients per group were required, totaling 84 patients. Participants were randomized into three groups using computer-generated block randomization with allocation concealment via sealed opaque envelopes. Outcome assessment was single-blinded.

Group A (Non-tumescent): Minimal local infiltration for analgesia only.

Group B (Tumescent without hyaluronidase): Infiltration with lidocaine, adrenaline, and saline/Ringer's lactate.

Group C (Tumescent with hyaluronidase): Same as Group B, with hyaluronidase 1500 IU/L.

A 10–15 minute waiting period was observed after infiltration in Groups B and C. Grafts were harvested using a Humby's knife at uniform thickness (0.012 -- 0.015 inches). Donor-site selection, graft fixation, dressing, and postoperative care were standardized across all groups.

Outcomes and Follow-Up: Primary: Percentage graft take on postoperative days 5, 10, and 21. Secondary: Donor-site healing, time to epithelialization, complications (infection, hematoma, seroma, graft loss), re-grafting requirement, and feasibility/cost-effectiveness of hyaluronidase. Assessments were performed clinically and supplemented with blinded photographic documentation. Patients were followed on POD 5, 10, and 21.

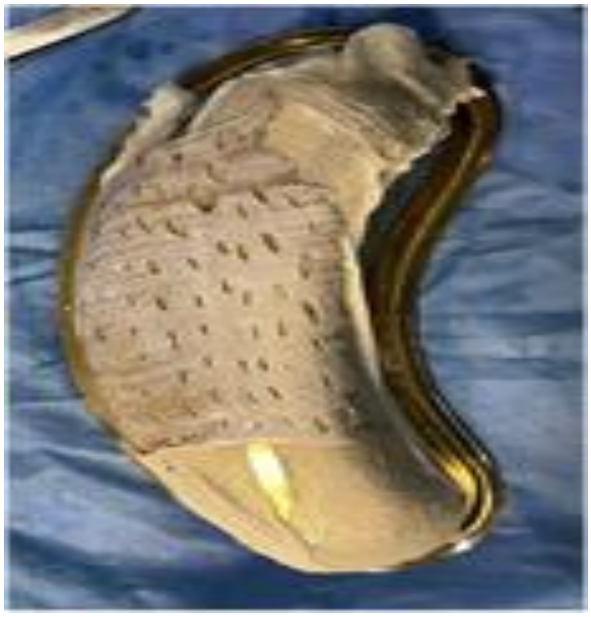

Figure 1: Meshing of graft

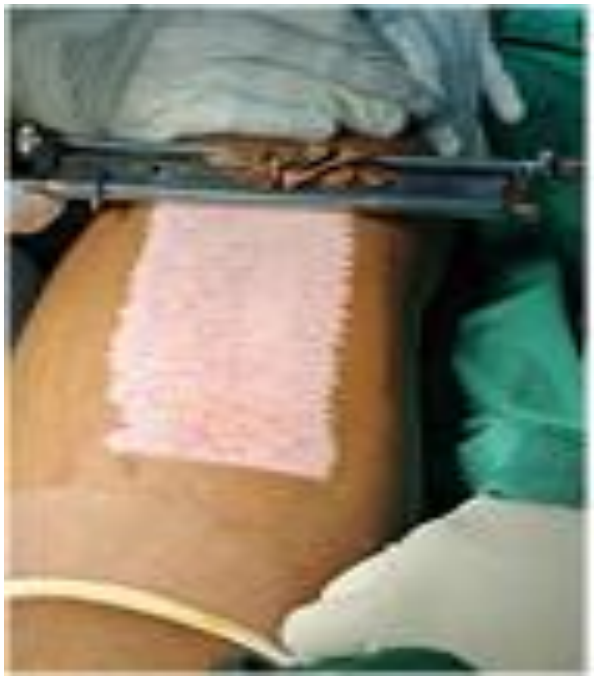

Figure 2: Grafting from donor site

Figure 3A,B,C. Wound pictures of Group A- Non-Tumescent; B- Tumescent; C- Tumescent with hyaluronidase

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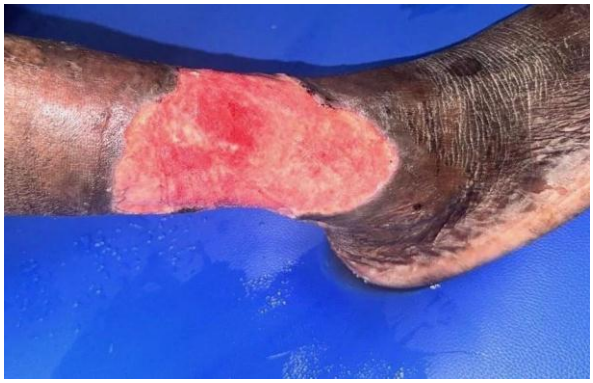

Figure 3A: Non-Tumescent

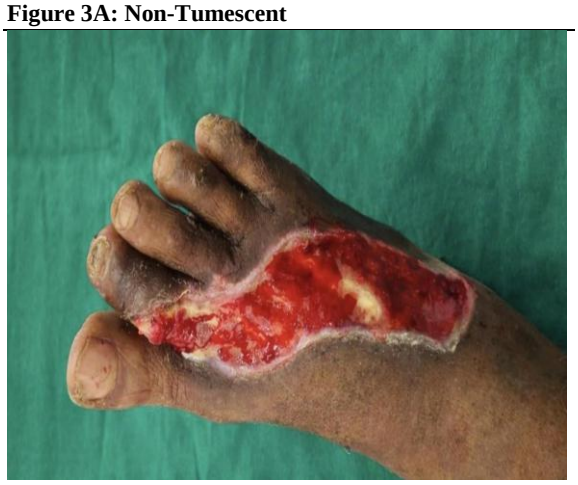

Figure 3B: Tumescent

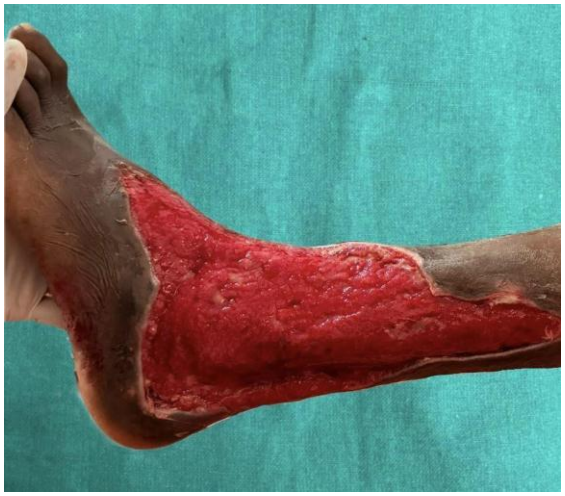

Figure 3C: Tumescent with hyaluronidase

Figure 4A,B,C. Recipient site Post operative day 1 pictures of
Group A- Non-Tumescent; B- Tumescent; C- Tumescent with hyaluronidase

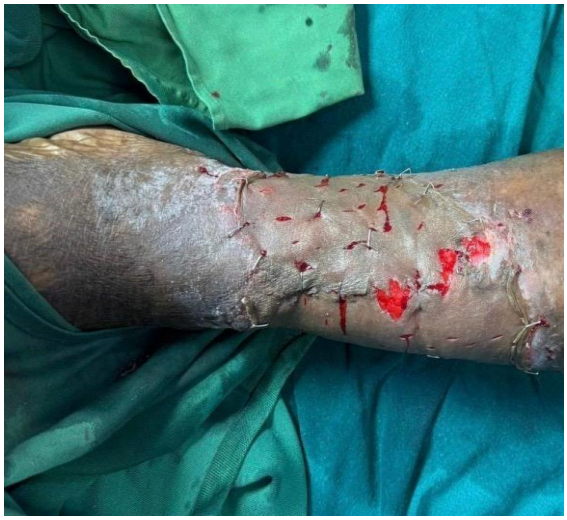

Figure 4A: Non-Tumescent

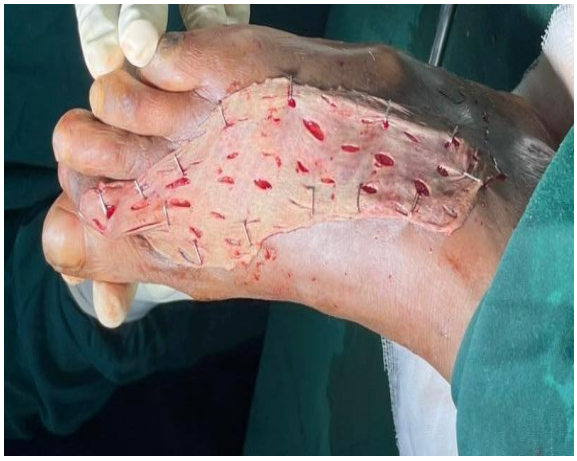

Figure 4B: Tumescent

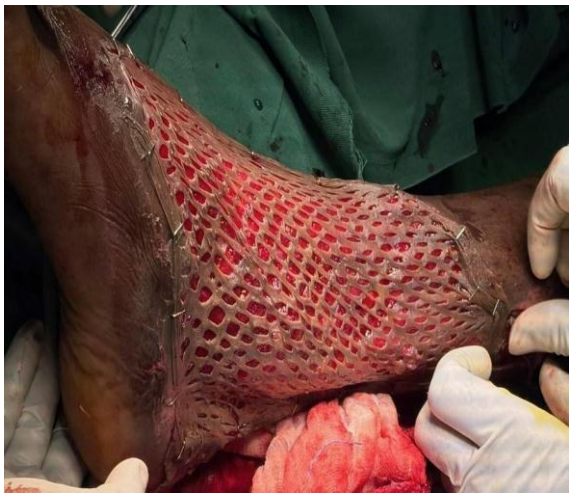

Figure 4C: Tumescent with hyaluronidase

Figure 5A,B,C. Donor site Post operative day 1 pictures of
Group A- Non-Tumescent; B- Tumescent; C- Tumescent with hyaluronidase

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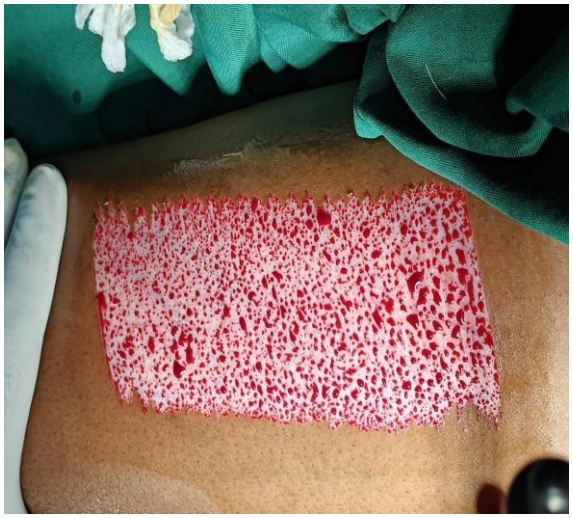

Figure 5A: Non-Tumescent

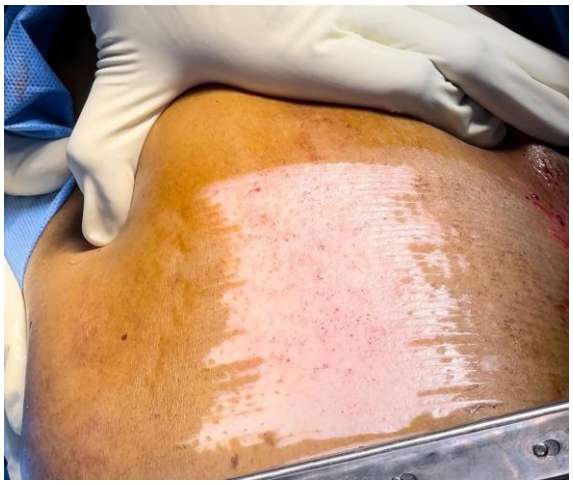

Figure 5B: Tumescent

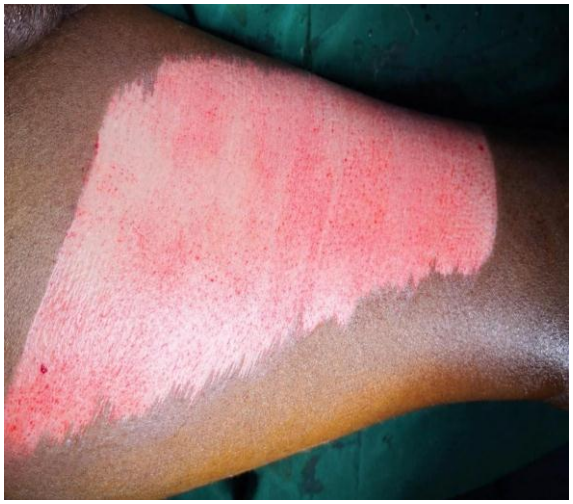

Figure 5C: Tumescent with hyaluronidase

Figure 6 A,B,C. Recipient site Post operative day 5 pictures of
Group A- Non-Tumescent; B- Tumescent; C- Tumescent with hyaluronidase

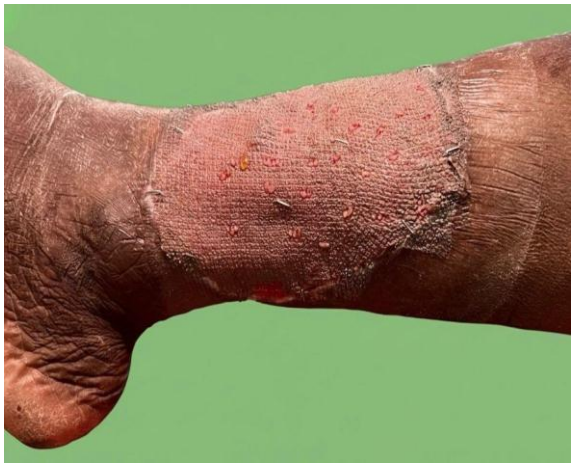

Figure 6A: Non-Tumescent

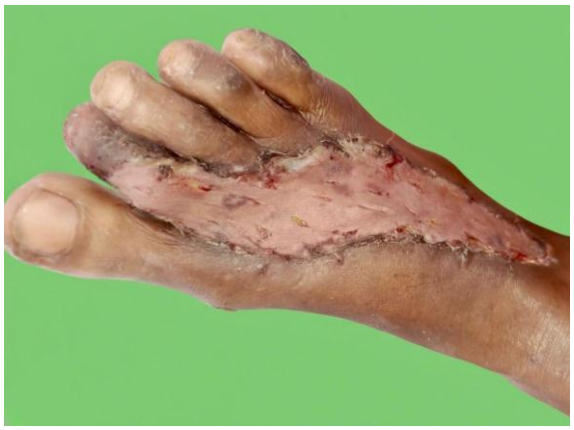

Figure 6C: Tumescent

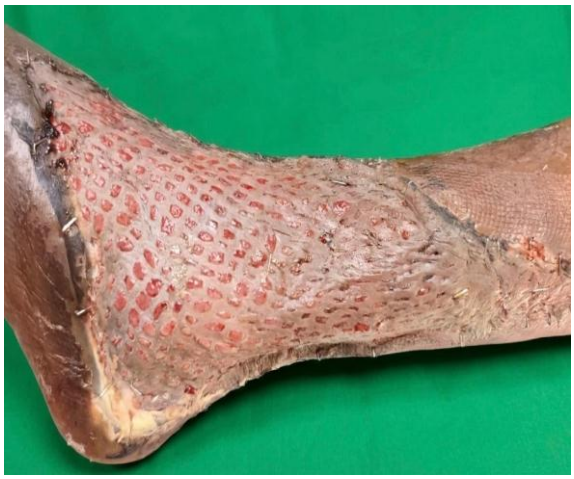

Figure 6C: Tumescent with hyaluronidase

Data were analyzed using SPSS v28. Continuous variables were expressed as mean ± SD and compared using ANOVA or Kruskal–Wallis test; categorical variables were analyzed using Chi-square or Fisher's exact test. Post-hoc comparisons evaluated the effects of tumescence, hyaluronidase, and their combination. A p-value <0.05 was considered statistically significant.

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RESULTS

Age Distribution

Table 1 and Figure 6 depict the baseline age distribution of participants across the three study groups, categorized into four age groups: 18–30, 31–45, 46–60, and >60 years. Despite these descriptive differences, statistical analysis using the Pearson Chi-square test revealed no significant association between age group and study group allocation (χ^2 = 7.346, p = 0.290). This indicates that the age distribution was comparable across all three groups, thereby confirming baseline demographic homogeneity prior to intervention.

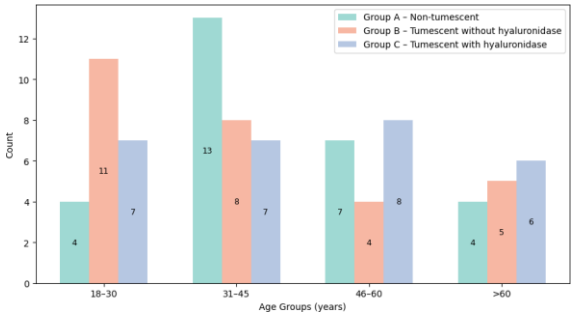

Figure 7. Baseline Age Distribution Across Study Group

Sex and Occupational Distribution

As shown in Table 2 and Figure 2A, statistical analysis using the Pearson Chi-square test demonstrated no statistically significant association between sex and study group allocation (χ^2 = 1.149, p = 0.563). Table 2 and Figure 2B illustrates the occupational profile. Although minor numerical variations were observed, differences were not statistically significant (χ^2 = 6.691, p = 0.754). Overall, sex and occupational distributions were comparable across groups.

Table 1: Baseline Age Distribution of Study Participants (n = 84)

Age group (yrs)	Group A (n=28) n(%)	Group B (n=28) n(%)	Group C (n=28) n(%)	χ^2	p-v alu e†
18–30	4 (14.3)	11 (39.3)	7 (25.0)	7.34	0.29
31–45	13 (46.4)	8 (28.6)	7 (25.0)	-	
46–60	7 (25.0)	4 (14.3)	8 (28.6)	-	
>60	4 (14.3)	5 (17.9)	6 (21.4)	-	

†Pearson Chi-square test; p < 0.05 considered statistically significant.

Table 2: Baseline Sex and Occupational Distribution (n = 84)

Varia ble	Categ ory	Group A n(%)	Group B n(%)	Group C n(%)	p-val ue†
	Male	15 (53.6)	11 (39.3)	13 (46.4)	
Sex	Femal e	13 (46.4)	17 (60.7)	15 (53.6)	0.56
	Unskil led	4 (14.3)	7 (25.0)	7 (25.0)	
	Skilled	7 (25.0)	6 (21.4)	2 (7.1)	
	Prof/S emi	5 (17.9)	6 (21.4)	4 (14.3)	
	Home maker	7 (25.0)	7 (25.0)	9 (32.1)	
Job	Retire d	3 (10.7)	1 (3.6)	3 (10.7)	0.75
	Studen t	2 (7.1)	1 (3.6)	3 (10.7)	

Figure 2A–2B. Baseline Sex and Occupational Distribution

Wound and Graft Characteristics

Table 7 and Figures 7A–7D show the descriptive distribution of wound and graft characteristics. The mean area to be grafted was 143.49 ± 58.10 cm². The mean tumescent volume used was 191.07 ± 144.04 cm³. Graft thickness exhibited minimal variability (0.40 ± 0.06 mm), indicating standardized harvesting.

Table 3: Descriptive Statistics of Wound/Graft Characteristics

Variable	Min	Max	Mean ± SD
Area (cm²)	38	250	143.49 ± 58.10
Duration (days)	9	88	48.42 ± 23.98
Tum. Vol (cm³)	0	411	191.07 ± 144.04
Thickness (mm)	0.30	0.50	0.40 ± 0.06

Wound and Graft-Related Parameters

Table 9 presents the comparison across groups. The mean area to be grafted and mean wound duration were comparable (p > 0.05). A highly significant difference was observed in tumescent volume (p < 0.001) due to study design. Mean graft thickness was similar across groups (p = 0.182).

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Table 4: Comparison of Wound and Graft-Related Parameters

Variab le	Grp A Mean±SD	Grp B Mean±SD	Grp C Mean±SD	p-val ue†
Area (cm²)	133.1 ± 60.1	151.8 ± 57.1	145.5 ± 57.5	0.479
Dur (days)	54.9 ± 24.8	43.0 ± 23.5	47.4 ± 22.9	0.173
Vol (cm³)	0.00 ± 0.00	259.9 ± 47.8	313.3 ± 56.8	<0.00 1*
Thick (mm)	0.42 ± 0.06	0.40 ± 0.06	0.39 ± 0.06	0.182

Statistically significant (One-way ANOVA)

Graft Uptake Across Follow-up

Repeated-measures GLM analysis (Table 10) revealed a significant effect of time ($p < 0.001$), indicating progressive improvement. The between-group effect was significant ($p = 0.026$). Group C demonstrated consistently higher mean graft take, followed by Group B and Group A.

Table 5: Repeated Measures GLM Analysis of Graft Take (%)

Time	Group A	Group B	Group C
Day 5	73.8 ± 10.9	76.1 ± 11.0	79.2 ± 11.6
Day 10	78.4 ± 8.7	81.1 ± 9.9	84.8 ± 10.5
Day 21	82.9 ± 8.0	85.1 ± 9.2	87.4 ± 10.8
Between-subjects effect (Group): F=3.84, p=0.02* Within-subjects effect (Time): F=18.92, p<0.001*			

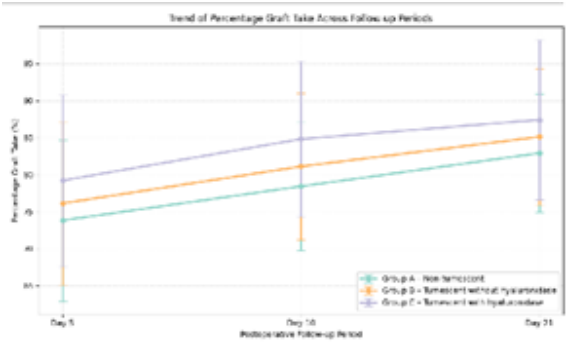

Figure 8: Longitudinal Comparison of Percentage graft uptake at Day 5, Day 10, and Day 21 Across the Three Study Groups

Recipient Site Complications

Table 11 shows complications on Day 5. Complications were most frequent in Group A. Partial graft loss occurred in 25.0% of Group A vs 14.3% in Group C. The proportion of patients without complications was highest in Group C (46.4%).

Table 6: Recipient Site Complications Day 5

Comp.	Grp A n(%)	Grp B n(%)	Grp C n(%)	p-value†
Nil	4 (14.3)	8 (28.6)	13 (46.4)	0.03*
Infectio n	8 (28.6)	6 (21.4)	4 (14.3)	
Hemato ma	6 (21.4)	5 (17.9)	3 (10.7)	
Graft loss	7 (25.0)	5 (17.9)	4 (14.3)	
Seroma	3 (10.7)	4 (14.3)	4 (14.3)	
Total	28 (100)	28 (100)	28 (100)	

Donor Site Outcomes

Excellent donor site healing (>95% epithelialization) at Day 10 was most frequent in Group C (50.0%) compared to Group A (25.0%). Group C also had the highest rate of "Nil" complications (64.3%).

Table 7: Donor Site Epithelialization Day 10

Healing	Group A	Group B	Group C	p-value†
Exc. (>95%)	7 (25.0)	10 (35.7)	14 (50.0)	0.03*
Good (80-95%)	14 (50.0)	13 (46.4)	11 (39.3)	
Fair (60-79%)	7 (25.0)	5 (17.9)	3 (10.7)	

Table 8: Donor Site Complications

Comp.	Group A	Group B	Group C	p-value†
Nil	8 (28.6)	12 (42.9)	18 (64.3)	0.02*
Infection	8 (28.6)	7 (25.0)	4 (14.3)	
Hematom a	7 (25.0)	6 (21.4)	4 (14.3)	
Delay Heal	5 (17.9)	3 (10.7)	2 (7.1)	

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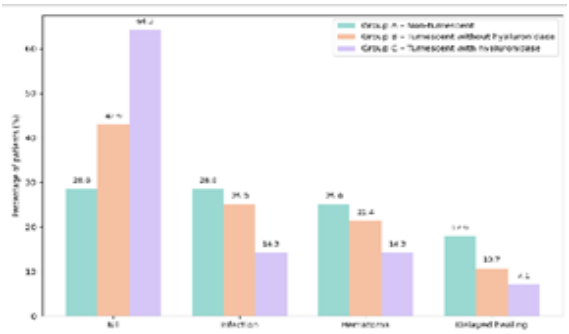

Figure 9: Distribution of Donor Site Complications Across Study Groups

Overall Graft Outcome

Excellent graft outcome was highest in Group C (53.6%), compared to Group B (35.7%) and Group A (25.0%).

Table 14: Overall Graft Outcome

Outcome	Group A	Group B	Group C	p-value†
Poor	6 (21.4)	4 (14.3)	2 (7.1)	0.03*
Good	15 (53.6)	14 (50.0)	11 (39.3)	
Excellent	7 (25.0)	10 (35.7)	15 (53.6)	

CONCLUSION

Split-thickness skin graft (STSG) survival depends on both recipient-bed vascularity and atraumatic graft harvesting with preservation of dermal microcirculation. In this study, comparable baseline demographic, wound, and laboratory parameters across groups ensured valid outcome comparisons.

The non-tumescent technique showed lower graft uptake and higher early complication rates, likely related to increased donor-site bleeding, uneven graft thickness, and greater tissue trauma, which can disrupt plasmatic imbibition and inosculation. Tumescent harvesting alone improved graft integration, consistent with evidence that vasoconstriction, reduced bleeding, and mechanical expansion of tissues create a firm donor surface that facilitates uniform dermatome movement and graft thickness.

The addition of hyaluronidase resulted in the highest graft uptake at all postoperative assessments, demonstrating benefit beyond tumescence alone. Hyaluronidase depolymerizes hyaluronic acid, increasing tissue permeability and promoting uniform diffusion of the tumescent solution. This likely produces more homogeneous vasoconstriction, even tissue expansion, and a consistent harvesting plane while reducing shear trauma, thereby preserving dermal capillary networks essential for early inosculation and revascularization.

Graft uptake improved over time in all groups, reflecting the normal biological progression of graft healing. The lower complication rate in the hyaluronidase group further suggests improved early graft stability. Overall, hyaluronidase-augmented tumescence represents a safe and effective refinement of STSG harvesting that enhances graft integration without increasing complications, and may be considered a valuable adjunct in routine grafting practice.

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