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ICG-Guided Perfusion Assessment in Mastectomy Flaps during Modified Radical Mastectomy- A Pilot Cohort Study

Nidhi Paswan
Maulana Azad Medical College
Lovenish Bains
lovenishbains@gmail.com

Maulana Azad Medical College
Soukat Ali Khan
Maulana Azad Medical College
Anubhav Vindal
Maulana Azad Medical College

Research Article

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ICG-Guided Perfusion Assessment in Mastectomy Flaps during Modified Radical Mastectomy- A Pilot Cohort Study

Authors: Nidhi Paswan[1], Lovenish Bains[1], Soukat Ali Khan[1], Anubhav Vindal[1]

Affiliations: Department of General Surgery [1], Maulana Azad Medical College, New Delhi, India

First Author: Nidhi Paswan, Resident, Department of Surgery, Maulana Azad Medical College, New Delhi, India

Corresponding Author: Lovenish Bains, Professor, Department of Surgery, Maulana Azad Medical College, New Delhi, India

Authors:

1. Nidhi Paswan, Resident, Department of Surgery, Maulana Azad Medical College,New Delhi, India

   nidhi2208paswan@gmail.com ORCID ID: 0009000425480925
2. Lovenish Bains, Professor, Department of Surgery, Maulana Azad Medical College,New Delhi, India

   lovenishbains@gmail.com ORCID ID: 0000000286270452
3. Soukat Ali Khan, Resident, Department of Surgery, Maulana Azad Medical College, New Delhi, India

   soukatkhan5822@gmail.com ORCID ID: 0009000164974483
4. Anubhav Vindal, Director Professor, Department of Surgery, Maulana Azad Medical College, New Delhi, India

   avindal@gmail.com ORCID ID: 0000-0002-6986-7572

ABSTRACT

Background: Mastectomy skin flap necrosis (MSFN) is a significant complication of Modified Radical Mastectomy, affecting up to 41% of patients and compromising quality of life. This pilot study investigates ICG fluorescence angiography as a real-time, quantitative intraoperative tool for predicting mastectomy skin flap viability.

Methods: A prospective pilot cohort study included 40 patients undergoing Modified Radical Mastectomy over one year. The primary objective was to correlate intraoperative ICG fluorescence imaging with postoperative flap viability assessed by SKIN SCORE; the secondary objective was to evaluate perfusion patterns using ICG fluorescence intensity. ICG angiography analysed 12 regions of interest (ROIs: S1–S6 superior flap, I1–I6 inferior flap) via ImageJ software, with minimum intensities correlated to postoperative necrosis grading.

Results: Of 40 patients, flap necrosis was graded as: B2 epidermal necrosis 12/40 (30%), B3 marginal necrosis 6/40 (15%), C2 partial thickness necrosis 2/40 (5%), and D2–D4 extensive necrosis requiring intervention 4/40 (10%). ICG intensity was significantly lower in the necrosis group (38.79±15.03 units) versus the non-necrosis group (69.37±6.93 units; $p<0.001$). At a 55.0-unit critical threshold, ICG imaging demonstrated 92.9% sensitivity, 100.0% specificity, 100.0% positive predictive value, and 85.7% negative predictive value. Risk stratification confirmed 100% necrosis in low-intensity regions (<55 units), 20% in moderate zones (55–65 units), and 0% in high-intensity areas (>65 units).

Conclusion: Intraoperative ICG fluorescence angiography provides accurate, real-time, objective assessment of mastectomy skin flap viability, shifting evaluation from subjective clinical judgement to precision-based decision-making that enables intraoperative correction. Larger validation studies are needed to establish definitive guidelines and quality-of-life outcomes.

Keywords: Flap necrosis, Mastectomy, Perfusion assessment, Indocyanine Green, Fluorescence angiography.

BACKGROUND

Breast cancer is one of the most significant health challenges facing women globally and a leading cause of cancer-related mortality. In 2022, it affected ~2.3 million women and caused ~670,000 deaths[1-3]. In high-income countries like the United States, ~1 in 8 women (13.1%) will develop it during their lifetime, with ~1 in 43 (2.3%) dying from it, highlighting benefits and limits of early detection and therapy. Globally, incidence varies according to the Human Development Index (HDI); it accounts for ~30% of newly diagnosed malignancies in women and is a leading cause of death among middle-aged women, making it a central focus of women's cancer control strategies worldwide[4].

In India, breast cancer is now the leading cancer in women, with rising incidence and regional variation. The national age-standardized rate is ~25.8 per 100,000, reaching ~34.8 per 100,000 females in urban areas like Delhi. It causes >220,000 new cases yearly, with a mortality rate of ~12.7 per 100,000 highlighting significant gaps in early detection, timely surgery, systemic therapy, and survivorship care[5-6].

Modified Radical Mastectomy (MRM) remains a cornerstone in the surgical management of breast cancer, particularly where breast-conserving surgery is not feasible or appropriate[7]. Despite its standardized nature, MRM is associated with important complications that can affect recovery, quality of life, and reconstructive options. Among these, skin flap necrosis is one of the most serious, with reported incidence ranging from about 5% to over 60% depending on patient factors, technique, and definition[8]. Necrosis may be partial-thickness, limited to superficial skin layers, or

full-thickness, exposing underlying tissues and often requiring surgical debridement, revision, or delayed reconstruction[9]. Numerous strategies have been explored to reduce flap necrosis risk, including preoperative computed tomography angiography to map key perforators, different methods of flap elevation (scalpel, electrocautery, ultrasonic devices), and adjunctive postoperative interventions such as topical nitroglycerin, negative pressure wound therapy, supplemental oxygen, and antiplatelet agents like aspirin[10-15]. Nevertheless, in routine practice, most decisions about flap design and viability are still made visually under white light and depend heavily on the surgeon's subjective judgment of color, capillary refill, temperature, and bleeding characteristics.

The versatility of indocyanine green has led to its adoption across numerous medical specialties, with applications ranging from traditional diagnostic testing to cutting-edge fluorescence-guided surgery. Indocyanine green (ICG) usage in breast surgery has emerged as a valuable tool for the real-time assessment of tissue perfusion through fluorescence imaging[16]. Traditionally, mastectomy skin flap viability has been evaluated using subjective clinical parameters such as color, capillary refill, temperature, and dermal bleeding; however, these methods are highly operator-dependent and demonstrate limited sensitivity, ranging from 10–30%. ICG fluorescence angiography is increasingly utilized for intraoperative assessment of breast flaps, offering a more objective and reproducible evaluation of perfusion, with reported sensitivity of up to 90% and specificity approaching 100% in predicting flap necrosis, although it is associated with higher cost[17]. Only a handful of studies in the literature have focused on the quantitative analysis of ICG fluorescence in breast flaps. Despite these advantages, there remains a need for standardized and quantitative methods to further enhance accuracy and reduce variability. This study therefore focuses on the quantitative assessment of necrosis grading using ICG fluorescence in conjunction with image analysis software (ImageJ), aiming to move beyond subjective interpretation toward more precise and reproducible prediction of flap outcomes.

METHODS

This study was a Pilot Prospective cohort study conducted in the department of Surgery at Maulana Azad Medical College and associated Lok Nayak Hospital, New Delhi. All patients with Breast carcinoma presenting to the surgery department and were planned for Modified Radical Mastectomy were screened and included in the study over a period of 1 year.

A total of 40 patients, 18 years and above females were included in this study, underwent Modified Radical Mastectomy. Patients who were sensitive to contrast agents, had impaired renal function, prior skin irradiation and vascular lesion on skin flap were excluded. All the eligible patients were informed about the procedure (Modified Radical Mastectomy), the expected post-operative course and the possible post- operative complications. Intraoperatively superior and inferior breast flaps were raised using Electrocautery(monopolar) by an experienced surgeon. Intravenous Indocyanine Green (ICG) dye, 7.5mg IV bolus (Aurogreen™ reconstituted in 5ml H_2O) was administered 15 mins before closing the breast flap and Intraoperative ICG NIR fluorescence imaging was performed using Olympus Infrared camera (Visera ELITE II NIR). Superior and Inferior breast flaps pictures were taken by placing camera perpendicular to the flaps at a distance of 15 cm. The breast flaps were closed using Nylon 3-0 sutures (Ethicon), interrupted by simple and vertical mattress sutures whenever required. The collected photos were analysed only at the end of the study once all the data collection had been completed. Indocyanine Green (ICG) fluorescence intensity was measured across 12 regions of interest (ROIs: S1–S6 for the superior flap, I1–I6 for the inferior flap) using ImageJ software (freely available) (Fig.1). The lowest-intensity ROI per patient was identified, and its association with postoperative flap necrosis was noted upto 30 days. The flaps were observed post operatively for any skin changes, discolouration, and flap necrosis was categorised according to SKIN SCORE (Table 1 & Fig.2). Incidence of necrosis in breast flap was noted till postoperative 30

days.

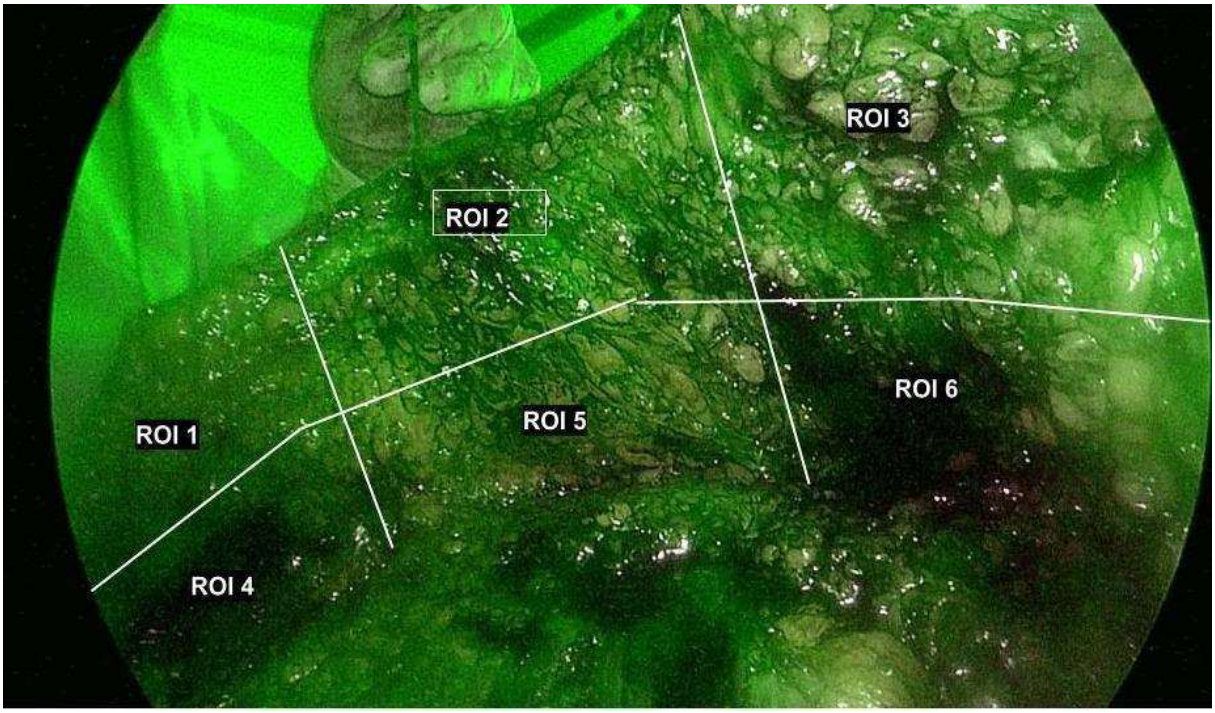


Figure 1: Dividing the inferior flap into 6 quadrants (Region of interest-ROI) for quantitative assessment of tissue perfusion in each quadrant using ImageJ software.

	Depth of tissue ischemic injury		**Surface area involved**
score	Definition	score	Definition
A	No evidence of skin ischemia or necrosis	1	None
B	Color change of skin suggesting impaired perfusion or ischemia (may be cyanosis or erythema)	2	Change involving 1%-10% of breast skin or 1%-10% of NAC
C	Partial thickness skin necrosis resulting in at least epidermal sloughing	3	Change involving 11%-30% of breast skin or 11%-30% of NAC or total nipple involvement
D	Full thickness skin necrosis	4	Change involving >30% of breast skin or >30% of NAC

Table 1: SKIN SCORE by Mayo's clinic[18]

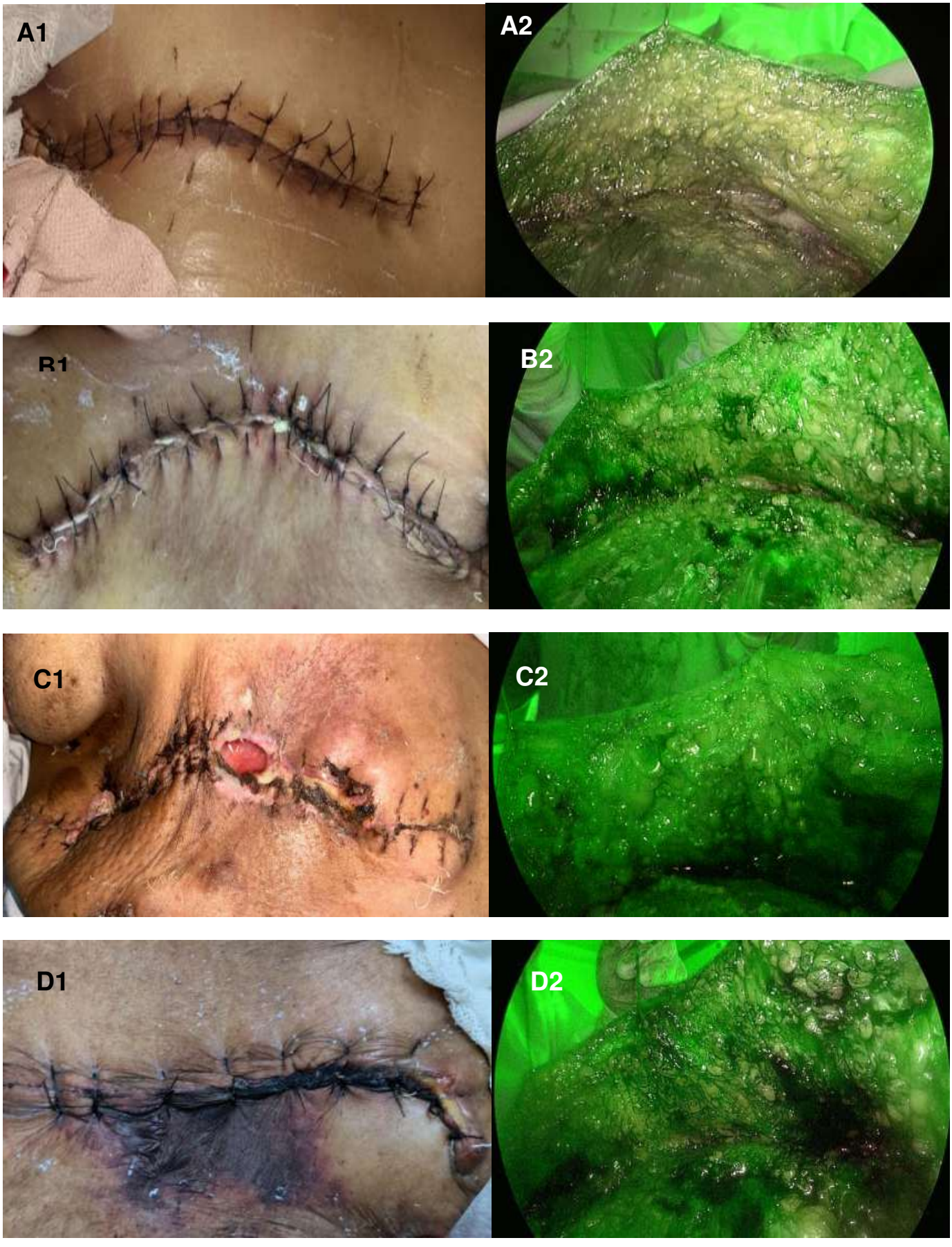

A1
A2
B1
B2
C1
C2
D1
D2

Figure 2: A) Marginal necrosis (B2,B3) B) Partial thickness necrosis(C2,C3), C) Full thickness necrosis (D2,D3), D) Extensive necrosis (D4)

RESULTS

In this study a total of 44 patients were screened, 1 patient developed allergic reactions, 3 patients did not give consent for intraoperative pictures. The age of patients ranged between 18 to 65 years, among which 9 patients had T2 stage, 15 patients with T3 and 16 patients of T4 stage. 25 patients received Neoadjuvant chemotherapy.

Among 40 patients the incidence of flap necrosis was noted and categorised according to SKIN SCORE- Necrosis Cases: B2: epidermal necrosis 12/40 (30%), B3: marginal necrosis- 6/40 (17%), C2: partial thickness necrosis-2/40 (3%), D2-D4: extensive necrosis requiring intervention-4/40(10%). 16 patients (40%) had no necrosis.(Fig. 3)

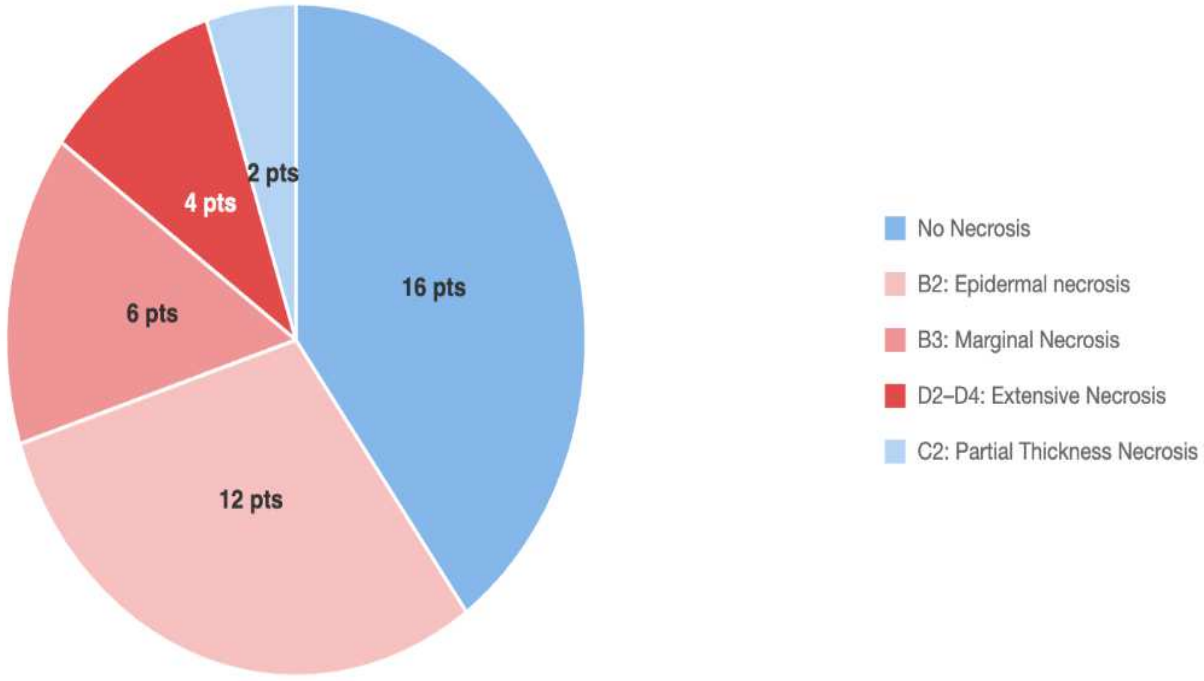


Figure 3: Pie chart showing proportion of necrosis vs no necrosis cases

Patients with necrosis are marked as Group A and patients who did not develop necrosis are marked as Group B for analysis of the study and simplicity of the results.

The age of patients enrolled in the study ranged between 31 to 70 years . The mean age of patients with flap necrosis (group A) was 52.64 ± 11.86 years (95% CI) and patients with no necrosis (group B) was 50.17 ± 6.91 years (95% CI). The statistical analysis reveals that patients with flap necrosis were on average 2.48 years older than those without necrosis. However, an independent t- test showed this difference was not statistically significant ($t = 0.474$, $p = 0.641$). On analysing this data using The Pearson Correlation Coefficient: $r = 0.252$, represents weak positive correlation and Chi-square Test: $\chi^2 = 0.377$, $p = 0.539$ means there is no statistically significant association between comorbidities and necrosis incidence.

SKIN SCORE	Number of patients/Percentage of necrosis	Post-operative day of development	Surgical Intervention
B2	12/30%	Day 2 (n=3) Day-3 (n=8) Day-4 (n=1)	No
B3	6/17%	Day 3 (n=2) Day-4 (n=3) Day-5 (n=1)	No
C2	2/3%	Day 4 (n=2)	No
D2	3/7%	Day 4 (n=2) Day 5 (n=1)	Yes
D4	1/3 %	Day 5 (n=1)	Yes

Table 2: Types of necrosis and post-operative day of development and management

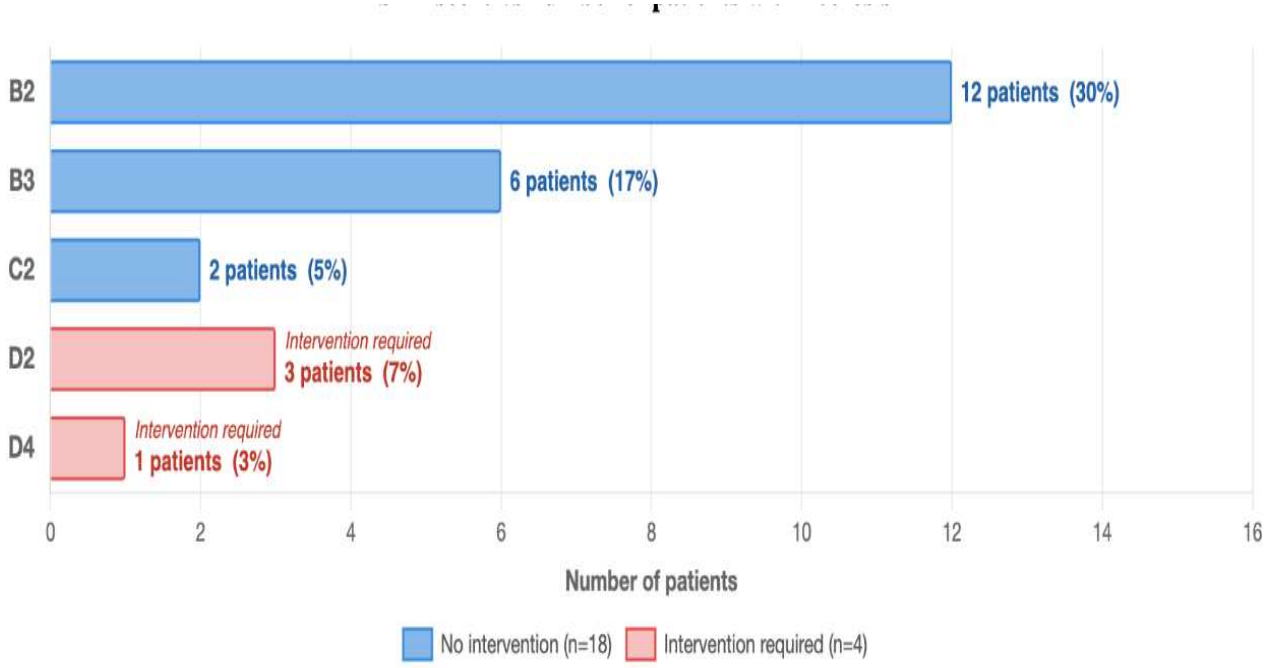


Figure 4: Types of necrosis and postoperative day of development

The study shows most necrosis start as epidermal necrosis (B1–2) and further progress to severe extensive necrosis, some requiring intervention (D2–D4). It was observed that mild–moderate flap necrosis (B2, B3, C2) developed within mean POD = 3.45 ± 1.21 days in 20 patients and Severe flap necrosis (D2,D3,D4) developed within mean POD = 4.67 ± 0.58 days in 4 patients (Table 2 & Fig. 4). The Critical Window Analysis shows early necrosis (≤3 days): 13 patients (55.5%), mid to late necrosis (4–5 days): 11 patients (44.4%). Normality Test (Shapiro–Wilk) was applied and p value was calculated as 0.2326. This means that the

data appears to be normally distributed ($p > 0.05$).The POD distribution range was from 2–5 days. Necrosis which started as epidermolysis and changed to extensive necrosis, POD was selected at the end of reaching complete necrosis (Fig. 5 & 6).

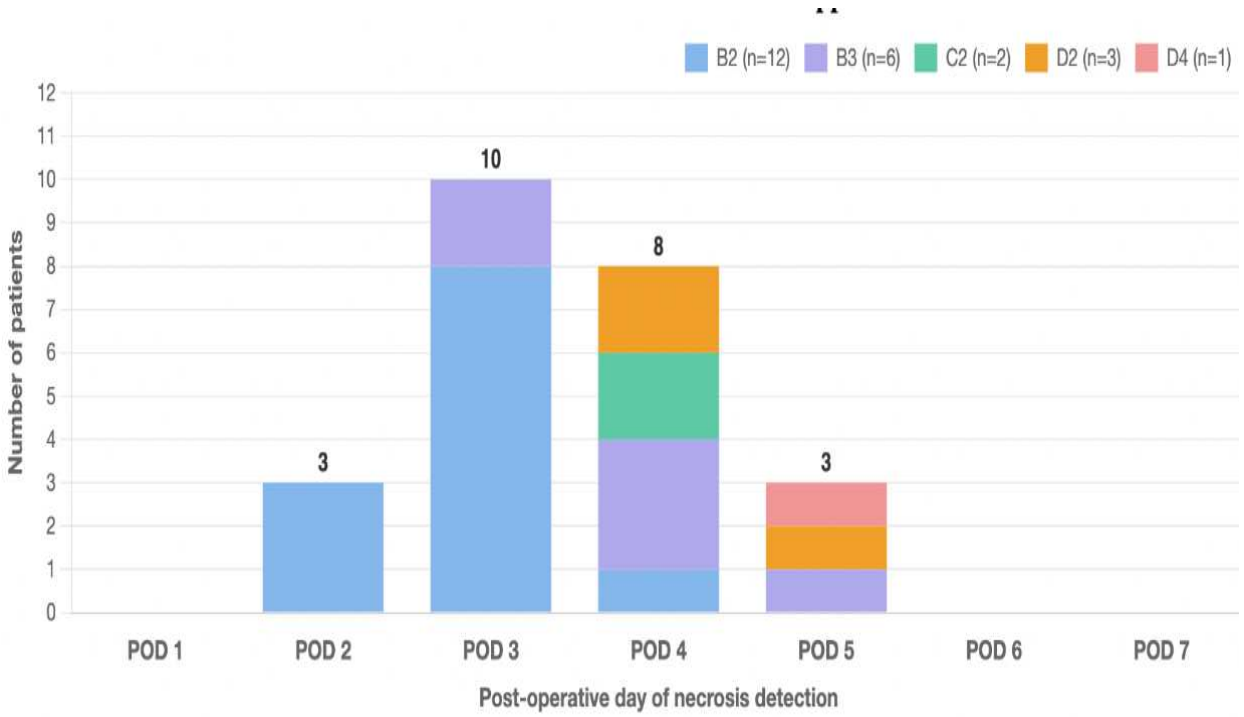


Figure 5: Stacked Bar graph showing POD vs SKIN SCORE (critical surveillance period 2-5 days)

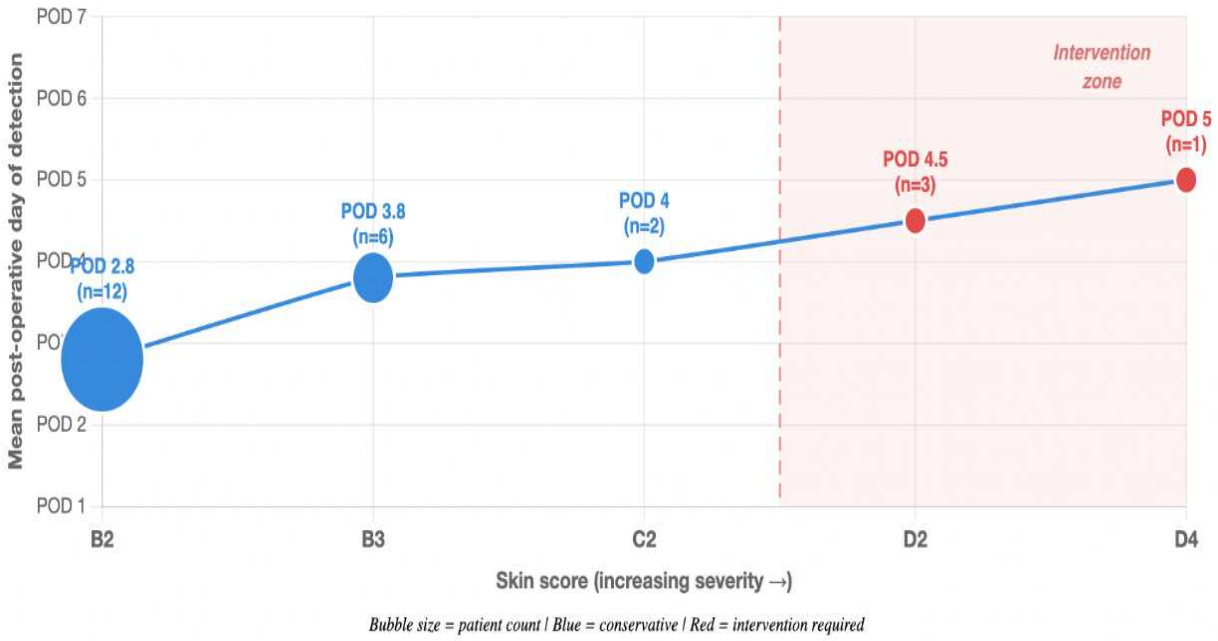


Figure 6: Scatter diagram with trend: The dashed trend line confirms the upward drift: as skin score severity increases, necrosis detection shifts later, and from D2 onward, surgical intervention becomes necessary.

In our study, patients with necrosis (n = 24), showed a mean ICG intensity of 38.79 ± 15.03 units. The intensity values ranged from 14.41 to 57.81 units, with a median of 40.45 units and an interquartile range (IQR) between 26.95 and 51.78 units. In contrast, patients without necrosis (n = 16), who demonstrated a mean ICG intensity of 69.37 ± 6.93 units. Their intensity values ranged from 61.86 to 79.85 units, with a median of 67.50 units and an interquartile range (IQR) between 63.82 and 75.21 units.

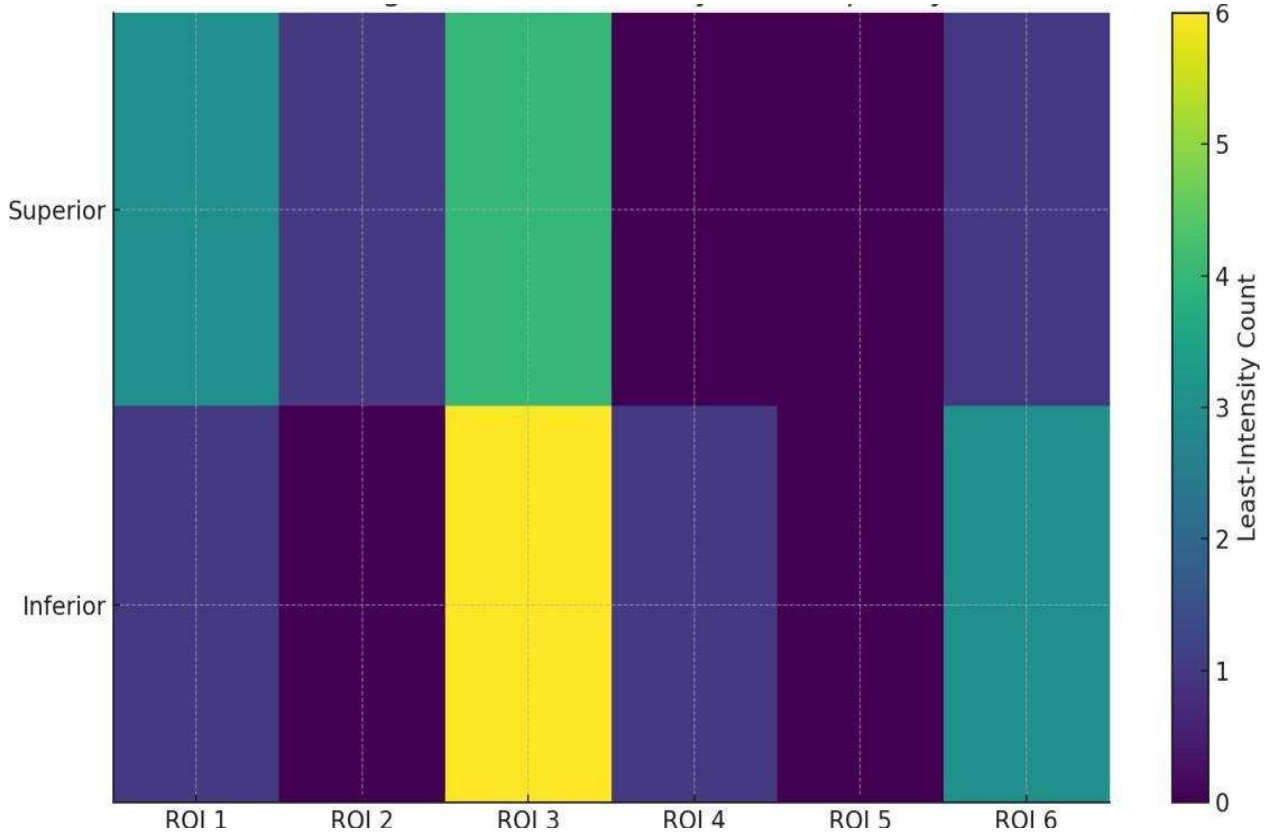


Figure 7: Ski diagrams showing the most frequent locations of least-intensity ROIs, suggesting anatomical predilection zones in an individual patient.

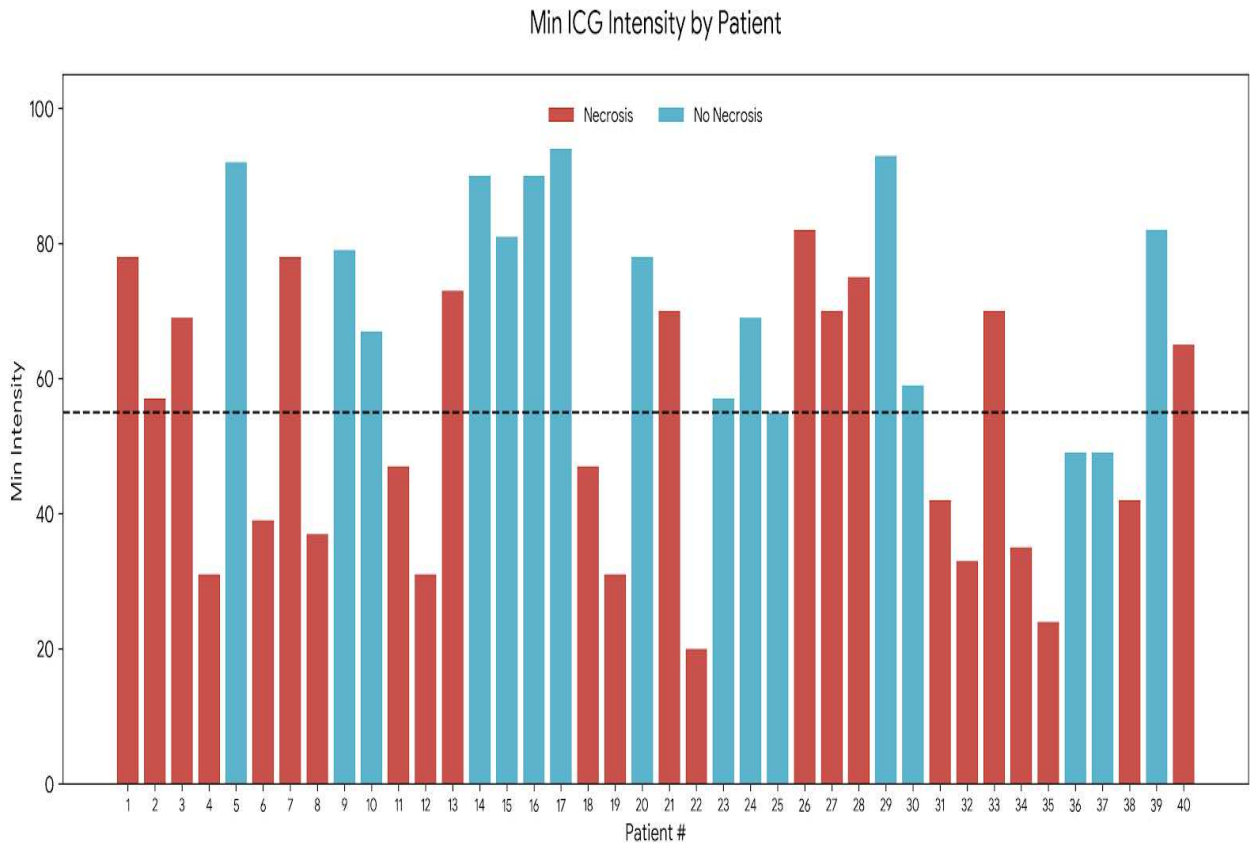


Figure 8: Minimum intensity by necrosis status (n=40), Critical threshold measured at 55.0 units

This histogram graph shows the minimum ICG intensity found across all ROIs for each patient. Red bars indicate patients who developed flap necrosis, while blue bars represent patients without necrosis. The horizontal dashed line at 55.0 represents the calculated **critical value threshold using.** The *critical intensity* threshold that best separates patients who developed necrosis from those who did not was calculated. The optimal cut-off (critical intensity value) was derived using Youden's J index(J-0.119) - (55.0 units)- any ROI with intensity below this value is highly predictive of postoperative necrosis. The Accuracy of the study was 75.0% (30/40 total cases correctly classified) and Positive Predictive Value was 92% (22/24 patients predicted to have necrosis).Based on ICG intensity levels, patients were categorized into three groups: low intensity (<55 units), moderate intensity (55–65 units), and good intensity (>65 units). The low ICG intensity group demonstrated a sensitivity of 92.9%, specificity of 100.0%, and an overall accuracy of 95.0%. The positive

predictive value (PPV) was 100.0%, while the negative predictive value (NPV) was 85.7%. In the moderate ICG intensity group, the sensitivity was 7.1%, specificity 33.3%, and accuracy 20.0%. The PPV was 100.0%, and the NPV was 77.8%. For the good ICG intensity group, the sensitivity was 33.3%, specificity 100.0%, and accuracy 80.0%. This group also showed a PPV of 100.0%.



Figure 9: Sensitivity and specificity between the 3 groups.

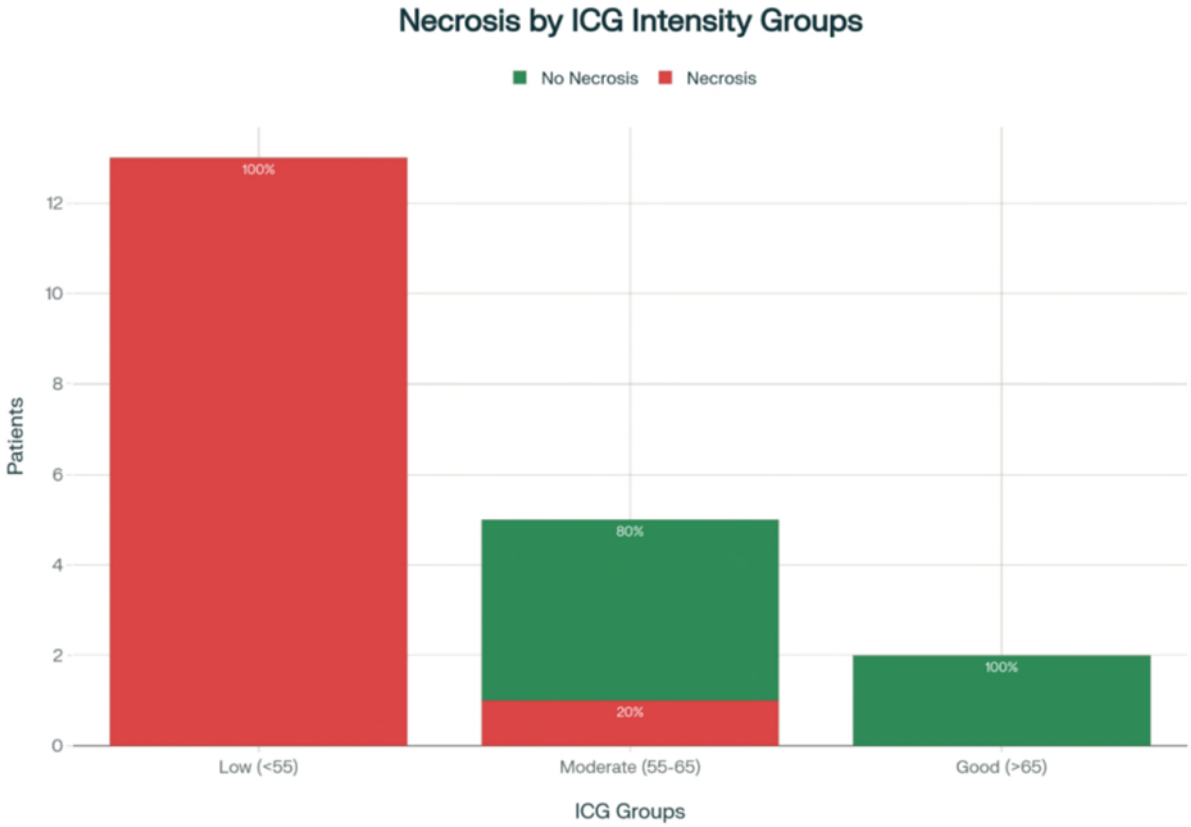


Figure 10: Necrosis prediction below threshold between 3 groups

In the low ICG Intensity Group (<55 units), 22 patients were identified to have lower than threshold ICG intensity. Amongst them 100% of the patients developed necrosis of different grades. In moderate ICG Intensity Group (55-65 units), 10 patients had intensity between 55-65 units, amongst which 2 developed necrosis (20%) and the rest 8 had no necrosis (80%). Lastly in the good ICG Intensity Group (>65 units): 8 patients had high intensity values and both of them had no necrosis in the postoperative period (100%).

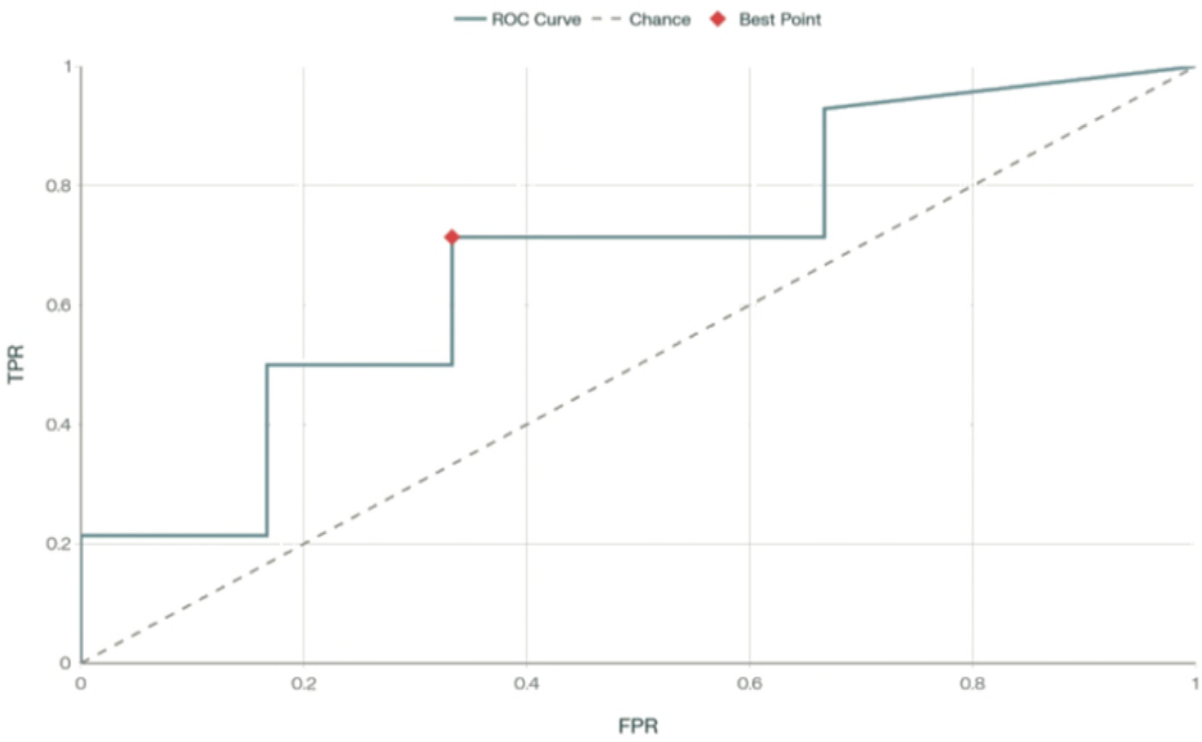


Figure 11: ROC curve showing good discriminatory ability (AUC- 0.857), convex curve

The Diagnostic Performance Area Under Curve (AUC): 0.857, (95% Confidence Interval: 0.389 - 0.921 (estimated). On analysing this data, the ROC curve interprets good discriminatory ability. Clinical Significance of the ROC is that the use of ICG fluorescence is better than random chance (AUC > 0.5). The shape of the ROC is a convex curve above the diagonal reference line which represents the Optimal Point: Sensitivity 92.9%, Specificity 100%.

DISCUSSION

Breast cancer is one of the most significant oncological challenges facing women worldwide, constituting a global health impact. The International Agency for Research on Cancer (IARC) estimates that in 2022, breast cancer affected 2.3 million women globally and resulted in 670,000 deaths[1-3]. Modified Radical Mastectomy (MRM) continues to be a key surgical approach in the management of breast cancer. However, among its potential complications, mastectomy skin-flap necrosis (MSFN) is particularly concerning, with reported incidence rates reaching as high as 41%.[4]. There is a wide range of flap necrosis which reflects differences in definition criteria, patient populations, surgical techniques, and follow-up protocols. The Mayo Clinic's development of the validated Skin Ischemia and Necrosis (SKIN) scoring system represents a significant advancement in standardizing MSFN assessment[18]. It helps surgeons predict the risk of mastectomy skin-flap necrosis (MSFN) in the early postoperative period, helps in early identification of compromised skin, allowing timely interventions. This system employs a dual-component scoring methodology: depth assessment using a 4- point letter score (A through D, representing no necrosis through full-thickness necrosis) and area assessment using a 4-point numerical score (1 through 4, representing 0% through >30% surface area involvement). This standardization facilitates more accurate comparisons between studies and enables better characterization of necrosis severity.

Indocyanine green (ICG) angiography has substantially advanced the intraoperative assessment and prevention of flap necrosis across various reconstructive techniques, as documented by multiple large studies and meta-analyses. Wang et al. (PMID: 37165852) conducted a meta-analysis of 22 studies on DIEP flaps, finding ICG significantly reduced fat necrosis rates (10.89% vs 21.53%, p=0.004, 53% risk reduction, RR 0.47) and reoperation rates (10.42% vs 32.82%, p=0.03, 59% reduction, RR 0.41) by enabling precise perfusion assessment and tissue excision[19]. Similarly, Thomas et al. (PMC12028749) studied 53 ALT flaps using combined

preoperative color-coded duplex sonography (CCDS) and intraoperative ICG, achieving 100% flap survival (zero losses), avoiding unnecessary perforator dissection in 16 cases, and cutting operative time by 19% (216±47 vs 268±71 min, p=0.006)[20]. Also, Choudhary et al. (PMID: 37435339) analyzed 877 free flaps retrospectively, showing ICG lowered partial flap loss (0.45% vs 5.00%, p<0.001, 91% reduction), re-exploration rates (3.65% vs 10.00%, p<0.001, 64% reduction), and was cost-effective, though complete flap loss was similar (1.36% vs 2.10%, p=0.44); they also validated warm saline soaks for perfusion[21].Several individual studies illustrate the mechanisms and clinical impact of ICG angiography in breast flaps, requiring high definition camera which was highly cost effective. Phillips and Lanier demonstrated a reduction in skin flap necrosis incidence from 41.2% to 23.4% after implementing intraoperative ICG. Their protocol relies on identifying poorly perfused zones in real-time and excising or modifying flap design, thus preventing necrosis post-mastectomy. This study encompassed all necrosis grades (A1–D4 SKIN SCORE), including mild epidermolysis to extensive necrosis. The distribution of necrosis severity in our cohort revealed that epidermolysis(B2) was observed in 12/40 (30%), marginal necrosis(B3) was in 6/40 (15%), partial thickness necrosis (C2) was in 2/40 (5%) and extensive necrosis requiring intervention(D2-D4) was found in 4/40(10%)[22]. Many published reports focus solely on clinically significant necrosis requiring reoperation (grades D2–D4). The lower incidence of necrosis rate as compared to our study (10%) was likely due to a more subjective method of necrosis measurement and intraoperative flap revision. This observation supports the use of the SKIN SCORE system, which provides standardized criteria for each grade and has been validated for inter-observer reliability. This study was an observational study to measure ICG related flap viability, therefore, no intervention was done intraoperatively. Azzena et al. conducted a prospective study of 50 patients undergoing immediate implant-based breast reconstruction post-mastectomy, comparing intraoperative ICG angiography (Group A) to clinical assessment (Group B) for skin flap perfusion. Group A showed 28% overall necrosis

(16% severe requiring revision, 12% minor), while Group B had 36% complications (24% severe, 12% mild). These findings align with our study, where ICG accurately predicted the 17% severe necrosis rate (4/24 cases)[23].

The mean duration of appearance of necrosis in our cohort of 40 patients was 3.71 ± 1.20 days (95% CI: 3.02 - 4.41). Flap necrosis typically manifested around the 3rd postoperative day, with a standard deviation of 1.20 days, indicating moderate variability in timing starting from epidermal necrosis and further progressing to extensive necrosis. The POD distribution of appearance of necrosis ranges from 2-6 days (epidermal necrosis starting at 2nd day and maximum necrosis observed at 6th day). The Critical monitoring period was found to be the first 5 postoperative days which account for 92.9% of cases. Early surveillance should begin immediately postoperatively and special attention be given to patients with low intensity intraoperative.

ICG Angiography Perfusion Assessment and Quantitative Analysis

This study also demonstrated that patients who developed necrosis had significantly lower mean ICG intensities (38.79 ± 15.03 units) compared to those without necrosis (69.37± 6.93 units). The lowest intensity ROI for each patient was strongly linked to the necrosis outcome. Patients with necrosis generally had much lower ROI intensities than those without necrosis [t-test ($t(18) = –4.736$, $p < 0.001$)]. The critical threshold analysis in our study yielded a cut-off value of 55.0 units using Youden's J index, with sensitivity of 92.9% and specificity of 100% in the low ICG group. ImageJ software was used for quantitative assessment of ICG fluorescence intensity across 12 regions of interest (6 superior flap ROIs and 6 inferior flap ROIs). Individual minimum ranged from 14.41 to 142.76 units. Spatially, the most frequent least-intensity ROIs were S1, S3, and I3, suggesting anatomical predilection for distal ischemia in inferolateral and superomedial quadrants. The ROC curve analysis in our study yielded an AUC of 0.857, indicating good discriminatory ability. These align with Komorowska-Timek et al.'s study of 68

mastectomy flaps, which identified the inferolateral quadrant (analogous to I3/S4 regions) as prone to low perfusion due to vascular watershed zones. Furthermore, Baum et al. quantified relative fluorescence (% of maximal) and demonstrated that minimum below 30% relative intensity correlated with 90% of necrosis cases[24].

This analysis supports the hypothesis that the region with the least intraoperative ICG fluorescence intensity is most likely to undergo postoperative necrosis. The identified critical ICG intensity threshold provides a potential clinical guide for intraoperative decision-making, flap design, and postoperative risk stratification.

Clinical Implications

An area under the curve (AUC) of 0.857 reflects good predictive performance of the ICG test,

indicating strong overall diagnostic utility for detecting necrosis and guiding postoperative management. The test characteristics further support this: a “good” ICG result demonstrates 100% specificity, meaning it is highly reliable for ruling out necrosis and serves as an reliable negative predictor, whereas a “low” ICG value shows 92.9% sensitivity and 100% specificity, making it a good positive predictor for identifying patients truly at risk. Clinically, this translates into clear decision thresholds: patients with ICG values below 55 should be considered high risk and managed with immediate intervention or very close monitoring due to the strong association with necrosis and adverse outcomes. In contrast, patients with ICG values above 65 can generally receive standard postoperative care, as their likelihood of necrosis is very low based on the test’s high specificity and negative predictive value. Those with intermediate ICG values between 55 and 65 fall into a gray zone where enhanced monitoring, individualized risk assessment, and possibly adjunctive tests or imaging are warranted to refine decision-making and avoid both overtreatment and missed complications.

Clinical decision-making can be guided by ICG values: patients with an ICG of less than 55 require immediate intervention or very close monitoring due to higher risk, whereas those with an ICG above 65 can generally proceed with standard postoperative care. For patients with ICG values between 55 and 65, an intermediate approach is recommended, involving enhanced monitoring and individualized management based on clinical judgment and patient-specific factors.

Study Strengths

Firstly, the prospective observational design enabled real-time intraoperative ICG perfusion measurements to be directly correlated with postoperative flap outcomes, thereby reducing recall and selection bias while strengthening causal inference. Secondly, the application of a standardized regional ROI-based analysis across predefined flap zones allowed systematic identification of hypoperfused areas at greatest risk of necrosis. Thirdly, postoperative outcomes were assessed using the validated SKIN SCORE grading system, which is an objective, standardized scale for evaluating the spectrum of flap necrosis ranging from superficial epidermolysis to full-thickness tissue loss. Fourthly, the application of a receiver operating characteristic (ROC) curve and a Youden's J statistic derived 55-unit threshold provides an optimized, evidence-based cutoff for intraoperative risk stratification and targeted clinical interventions to enhance overall flap survival.

Study Limitations

Firstly, as a single-center pilot study, the findings may have limited generalizability due to institutional variations in patient populations and practices. Secondly, the relatively small sample size (n = 40) limits statistical power and may affect the robustness and external validity of the proposed perfusion threshold. Thirdly, flap thickness and the impact of neoadjuvant therapy were not specifically evaluated. Although eligible patients were included according to study criteria and procedures were standardized and flaps raised by experienced surgeons, these factors may have influenced perfusion characteristics.

CONCLUSION

This pilot prospective cohort study demonstrates that intraoperative indocyanine green (ICG) fluorescence angiography effectively assesses mastectomy skin flap viability and perfusion. Patients developing necrosis had significantly lower mean ICG intensities (38.79 ± 15.03 units) versus those without (69.37 ± 6.93 units; $t(18) = -4.736$, $p<0.001$). Diagnostic performance showed AUC 0.857, with a 55-unit threshold optimal for identifying high-risk regions—yielding 92.9% sensitivity, 100% specificity, and 95% accuracy for low-intensity areas.

These findings indicate that intraoperative ICG mapping can reliably identify high-risk regions, particularly in medial portions of superior and inferior flaps supporting its use as an adjunct to clinical judgment for surgical planning, intraoperative decision-making, risk stratification, and postoperative monitoring. At the same time, variability in performance across low, moderate, and good intensity groups underlines the need for refinement and external validation of perfusion cut-offs in moderate intensity group showing skewed data. Larger, multicenter trials are needed before the technique can be standardized and widely integrated into routine breast cancer surgery.

Table 3. Baseline Patient Demographics and Clinical Characteristics

Characteristic	Necrosis Group (n=24)	No Necrosis Group (n=16)	p-value
Age (years, mean ± SD)	52.64 ± 11.86	50.17 ± 6.91	0.641
95% CI	45.80 – 59.49	42.91 – 57.42	—
Female, n (%)	24 (100)	16 (100)	—
Comorbidities present, n (%)	6 (42.9)	2 (33.3)	0.539
Diabetes mellitus	4	0	—
Hypertension	3	2	—
Hypothyroidism	0	1	—
NACT received, n (%)	17 (92.9)	8 (83.3)	—

Data are presented as mean ± SD, n (%), or 95% CI as indicated. p-values by independent t-test (continuous) or chi-square test (categorical). CI = confidence interval; NACT = neoadjuvant chemotherapy.

Table 4. Incidence and Classification of Mastectomy Skin Flap Necrosis (SKIN Score)

SKIN Score	Description	n / Total (%)	Mean POD ± SD	Range	Surgical Intervention
A1	No necrosis	16 / 40 (40%)	—	—	No
B2	Epidermolysis	12 / 40 (30%)	3.33 ± 1.37	2 – 5	No
B3	Marginal necrosis	6 / 40 (17%)	4.00 ± 1.00	3 – 5	No
C2	Partial thickness	2 / 40 (3%)	3.00 ± 1.41	2 – 4	No
D2	Full thickness	3 / 40 (7%)	4.00	4	Yes
D4	Full thickness (>30%)	1 / 40 (3%)	5.00	5	Yes

Overall Necrosis	—	24 / 40 (60%)	3.71 ± 1.20	2 – 6	3 / 18 (21.4%)

SKIN Score classification per Mayo Clinic criteria. POD = postoperative day. Mild–moderate: B2, B3, C2; Severe: D2–D4. Surgical intervention = debridement and/or VAC therapy.

Table 5. ICG Fluorescence Intensity Analysis by Necrosis Status

Parameter	Necrosis Group (n=14)	No Necrosis Group (n=6)	p-value
ICG Minimum Intensity (ImageJ units)			
Mean ± SD	38.79 ± 15.03	69.37 ± 6.93	< 0.001*
Median	40.45	67.50	< 0.001†
Range	14.41 – 57.81	61.86 – 79.85	—
IQR	26.95 – 51.78	63.82 – 75.21	—
Effect Size			
Cohen's d	–2.279 (Large)	—	—
t-statistic (df)	t(18) = –4.736	—	< 0.001

**Independent t-test; †Mann-Whitney U test. ICG intensity measured as mean greyscale values (0–255 scale) via ImageJ software on minimum-intensity ROI per patient. IQR = interquartile range.*

Table 6. Diagnostic Performance of ICG Fluorescence Angiography (Threshold: 55 Units)

Diagnostic Parameter	Value	95% CI	p-value

ROC Curve Analysis			
Area Under Curve (AUC)	0.857	0.389 – 0.921	< 0.001
Optimal threshold (Youden's J)	55.0 units	J = 0.119	—
At Threshold < 55 units			
Sensitivity	92.9% (13/14)	—	0.002
Specificity	100.0% (6/6)	—	0.031
Accuracy	95.0% (19/20)	—	—
Positive Predictive Value (PPV)	100.0%	—	—
Negative Predictive Value (NPV)	85.7%	—	—

ROC = receiver operating characteristic; AUC = area under curve; PPV = positive predictive value; NPV = negative predictive value. Optimal threshold determined by Youden's J index. Bold p-values indicate statistical significance (p < 0.05).

Table 7. ICG-Based Risk Stratification and Necrosis Outcomes

ICG Intensity Group	n (%)	Necrosis, n (%)	No Necrosis, n (%)	PPV / NPV	Recommended Action	p-value
Low (< 55 units)	22 (53.3)	22 (100.0)	0 (0.0)	PPV: 100%	Immediate intervention / close monitoring	< 0.001*
Moderate (55 – 65 units)	10 (33.3)	2 (20.0)	8(80.0)	—	Enhanced monitoring, individualized approach	0.024
Good (> 65 units)	8(13.3)	0 (0.0)	8(100.0)	NPV: 100%	Standard postoperative care	0.016

**Fisher's exact test. Risk stratification based on minimum ICG fluorescence intensity per patient (ImageJ units). All patients with ICG < 55 units developed necrosis; no patient with ICG > 65 units developed necrosis.*

Table 8. Postoperative Timeline of Flap Necrosis Development

POD Category	Patients, n	% of Necrosis Cases	Cumulative %	SKIN Score Range
POD 2	3	14.3	14.3	B2, C2
POD 3	10	35.7	50.0	B2, B3
POD 4	8	21.4	71.4	B2, B3, C2, D2
POD 5	3	21.4	92.9	B3, D3, D4
POD 6	0	0	—	—
Overall	**24**	**100.0**	**—**	**Mean: 3.71 ± 1.20 days**

POD = postoperative day. Critical monitoring window: 92.9% of necrosis cases manifested by POD 5. Shapiro-Wilk normality test: p = 0.233 (normally distributed). Necrosis progressing through stages was classified at final extent.

Table 9. Anatomical Distribution of Least-Perfused Regions of Interest (ROIs)

Least-Intensity ROI	Frequency (n)	% of Necrosis Cases	Flap Location
I3	8	35.7	Inferior – Medial
S3	8	28.6	Superior – Medial
I6	4	7.1	Inferior – Lateral
S6	1	7.1	Superior – Lateral
S1	1	7.1	Superior
I4	1	7.1	Inferior – Central
Other	1	7.1	—

ROI = region of interest; S = superior flap; I = inferior flap. Medial regions (S3, I3) accounted for 64.3% of necrosis-associated least-intensity zones, representing anatomical predilection sites for hypoperfusion.

Figure Legends

Figure 1: Dividing the inferior flap into 6 quadrants(Region of interest-ROI) for quantitative assessment of tissue perfusion in each quadrant using ImageJ software.

Figure 2 : a) Marginal necrosis (B2,B3) b) Partial thickness necrosis(C2,C3), c) Full thickness necrosis (D2,D3), d) Extensive necrosis (D4)

Figure 3: Pie chart showing proportion of necrosis vs no necrosis cases.

Figure 4: Types of necrosis and post-operative day of development

Figure 5: Stacked Bar graph showing POD vs SKIN SCORE (critical surveillance period 2-5 days)

Figure 6: Scatter diagram with trend

Figure 7: Ski diagrams showing the most frequent locations of least-intensity ROIs, suggesting anatomical predilection zones in an individual patient.

Figure 8: Minimum intensity by necrosis status (n=40), Critical threshold measured at 55.0 units

Figure 9: Sensitivity and specificity between the 3 groups.

Figure 10 : Necrosis prediction below threshold between 3 groups

Figure 11 : ROC curve showing good discriminatory ability (AUC- 0.857), convex curve

Table Legends

Table 1: SKIN SCORE by Mayo's clinic

Table 2: Types of necrosis and post-operative day of development and management

Table 3. Baseline Patient Demographics and Clinical Characteristics

Table 4. Incidence and Classification of Mastectomy Skin Flap Necrosis (SKIN Score)

Table 5. ICG Fluorescence Intensity Analysis by Necrosis Status

Table 6. Diagnostic Performance of ICG Fluorescence Angiography (Threshold: 55 Units)

Table 7. ICG-Based Risk Stratification and Necrosis Outcomes

Table 8. Postoperative Timeline of Flap Necrosis Development

Table 9. Anatomical Distribution of Least-Perfused Regions of Interest (ROIs)

Abbreviations

ICG: Indocyanine green, NACT: Neoadjuvant chemotherapy, MRM: Modified Radical Mastectomy

Ethics approval and consent to participate

Written consent for the publication of this study was obtained from the patient. The study was approved by the **Institutional Ethics Committee (IEC) of Maulana Azad Medical College and Associated Hospital** (Lok Nayak Hospital), New Delhi, approval reference number is **F.1/IEC/MAMC/MD/MS(108/01/2024/No.154)**.

This study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments; and Indian Council Medical Research guidelines as applicable in the country.

Consent for Participation

Written informed consent was obtained from all participants prior to enrolment.

Consent for publication

Written informed consent for the publication of this study and for the accompanying images was obtained from the patient. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Data Availability statement (DAS)

All data generated or analyzed during this study are included in this article.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LB conceptualized the manuscript and reviewed the literature. NP,LB analyzed data, and made major contributions to the writing of the manuscript, performed the clinical examination, surgical treatment, and clinical follow-up. NP,LB,SAK,AV performed final review and editing of the manuscript. All authors have read and approved the final version of the manuscript.

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Declaration of generative AI and AI-assisted technologies in the manuscript preparation process.

During the preparation of this work the authors used [Perplexity / Chatgpt] in order to summarize the data and results in tabular form. After using this tool/service, the authors reviewed and edited the content as needed and take(s) full responsibility for the content of the published article.

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