# From Pixels to Prognosis: Integrating Wound Image Data in Predictive Model Development

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# Conflict of Interest/Disclaimer Statement

No conflicts of interest to declare.

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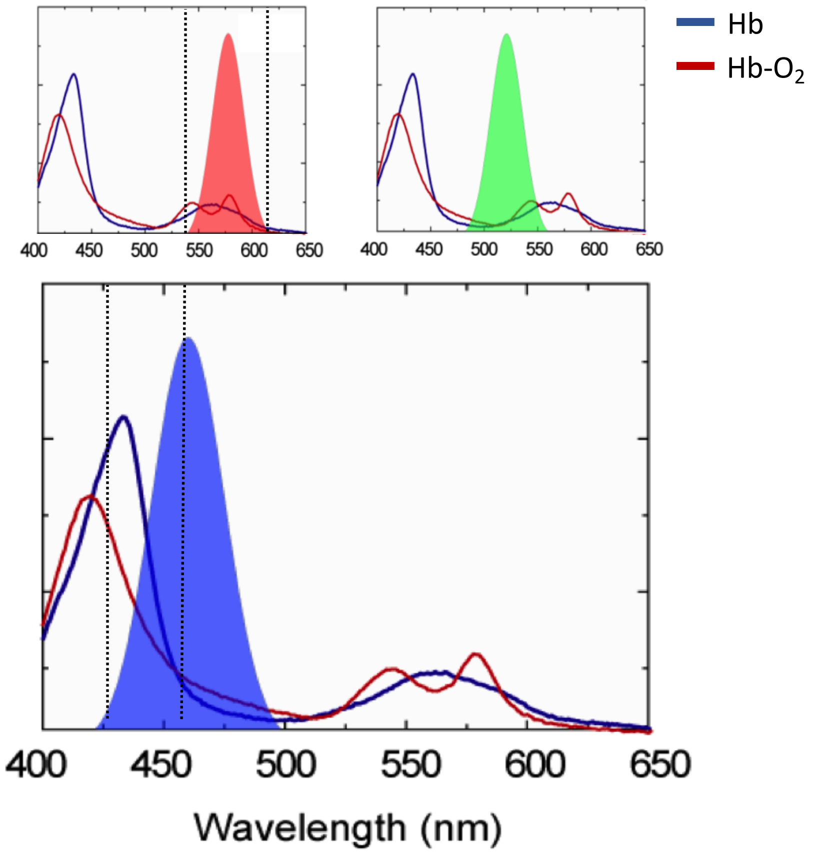
# Using Image Data to Define Wound End States

PLOS | ONE

Radowsky JS, Neely R, Forsberg JA, Lisboa FA, Dente CJ, Elster EA, et al. (2018) Preclosure spectroscopic differences between healed and dehisced traumatic wounds. PLoS ONE 13(9): e0204453 https://doi.org/10.1371/journal

- **Normalized RGB values significantly differed** between healed and dehisced wounds
- **Simple threshold models** (e.g., R-B/($R^2$+$B^2$)) **had poor predictive accuracy** (<65%)
- Hierarchical cluster analysis using 17 variables achieved:
  - **76.6% accuracy, 76.9% sensitivity, 76.5% specificity**

**Hemoglobin Light Absorbance***




*Crane et al. J Am Coll Surg. 2008;206(6):1159–1166

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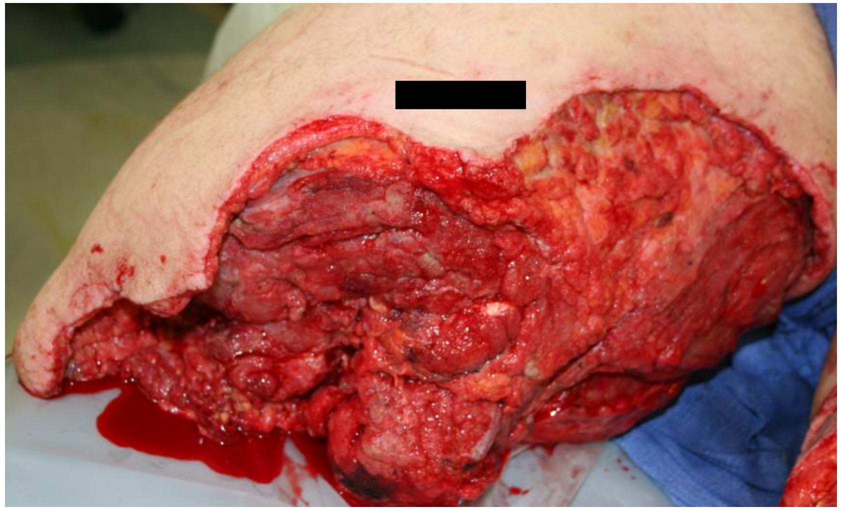
# Materials and Methods

- **Hypothesis:** Wound image RGB data and clinical variables obtained on the day of delayed wound closure may be used to develop machine learning models to predict wound closure outcomes

- **Patient enrollment/selection:** 73 adult patients with 116 combat-related extremity wounds sustained during OIF/OEF and treated/enrolled at Walter Reed National Military Medical Center

- **Study design:** RGB and red–blue (R–B) features extracted from 104 wound images from the day of delayed wound closure (DWC).
  - Images were first segmented into 100 left-to-right percentile-based column profiles

- **Statistical methods:** Boruta-selected imaging and clinical predictors were incorporated into XGBoost models, and performance was evaluated using 100 iterations of repeated random subsampling using AUC, sensitivity, and specificity



Example of an enrolled patient with a right transfemoral amputation

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# Capturing Color Signal Intensity

RGB profile data

Signal intensity table


| Distance_(pixels) | Intensity | Y1 | Y2 |
|---|---|---|---|
| 0 | 155.7531 | 34.6929 | 33.6867 |
| 1 | 155.0525 | 32.9444 | 32.3673 |
| 2 | 154.5448 | 32.1944 | 30.7454 |
| 3 | 155.5185 | 32.0077 | 30.7593 |
| 4 | 156.5046 | 32.9228 | 30.6497 |
| 5 | 158.3056 | 33.5262 | 31.5077 |
| 6 | 158.4336 | 33.7083 | 30.8272 |
| 7 | 158.0108 | 32.2546 | 29.7562 |
| 8 | 158.2346 | 32.5031 | 29.5139 |
| 9 | 159.2006 | 32.6975 | 30.2330 |
| 10 | 160.1636 | 33.9090 | 31.1759 |
| 11 | 161.2948 | 34.3781 | 32.2685 |
| 12 | 160.7747 | 33.9012 | 31.4738 |
| 13 | 160.4614 | 32.7762 | 30.9707 |
| 14 | 161.0988 | 33.6698 | 31.4151 |
| 15 | 161.6605 | 33.6019 | 32.0694 |
| 16 | 161.2917 | 33.8781 | 31.7454 |
| 17 | 161.6852 | 33.7423 | 32.3333 |
| 18 | 162.1775 | 34.7994 | 32.8951 |
| 19 | 162.4182 | 34.6497 | 33.3426 |
| 20 | 162.1265 | 35.3164 | 33.6157 |
| 21 | 162.9537 | 36.2978 | 35.1590 |
| 22 | 164.2670 | 39.1404 | 37.4444 |
| 23 | 165.7685 | 41.1929 | 39.7855 |
| 24 | 166.2855 | 42.9290 | 41.0633 |
| 25 | 166.1435 | 42.6420 | 41.1312 |
| 26 | 165.1497 | 42.4306 | 40.3657 |
| 27 | 165.6003 | 42.2978 | 40.6975 |
| 28 | 164.8102 | 41.7299 | 39.5725 |
| 29 | 165.1836 | 41.0525 | 39.4167 |
| 30 | 165.4028 | 41.2315 | 39.3179 |
| 31 | 165.6744 | 40.3611 | 39.0725 |
| 32 | 164.5926 | 39.0910 | 37.4769 |
| 33 | 164.5741 | 38.0648 | 37.0586 |
| 34 | 165.2485 | 39.1343 | 37.5571 |
| 35 | 166.1620 | 39.4552 | 38.3380 |
| 36 | 166.7222 | 40.2870 | 38.4738 |
| 37 | 167.6543 | 40.5617 | 39.1559 |
| 38 | 168.5818 | 42.1204 | 39.8241 |
| 39 | 168.8102 | 41.6744 | 39.6389 |
| 40 | 168.6235 | 42.0633 | 38.9769 |
| 41 | 169.9938 | 42.9275 | 39.8549 |
| 42 | 171.1929 | 44.6389 | 40.6435 |
| 43 | 172.1836 | 45.1852 | 41.2006 |
| 44 | 171.7423 | 45.5926 | 40.6960 |
| 45 | 171.8981 | 45.5278 | 40.8966 |
| 46 | 172.2022 | 46.8256 | 41.4645 |
| 47 | 172.7469 | 47.2253 | 42.1790 |

ROI: Central area of wound image was used to generate percentile-based column profiles

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# Exploring RGB Profiles in Extremity Wound Images

- Wound images were analyzed in ImageJ, and red, green, and blue (RGB) pixel intensities were extracted
- RGB intensity profiles were generated from defined wound regions of interest to characterize signs of wound healing

Are these wounds ready for closure?

Successfully closed

Failed

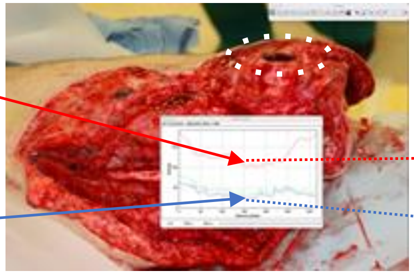
Successfully closed

Failed

Pixel intensity

Red channel

Blue channel

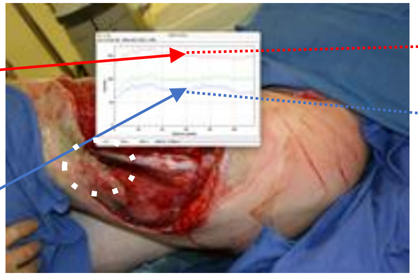


R

B

Red channel

Blue channel

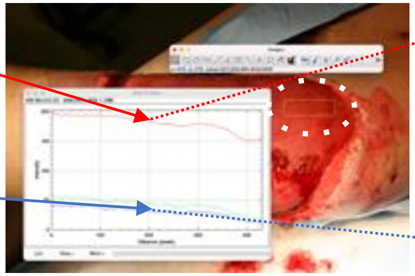


R

B

Red channel

Blue channel



R

B

Based on preliminary/ongoing analyses, these RB profiles are seen in:

Non-viable tissue
Slough
Necrosis

Inflammation
Infection
Purulence

Granulation tissue

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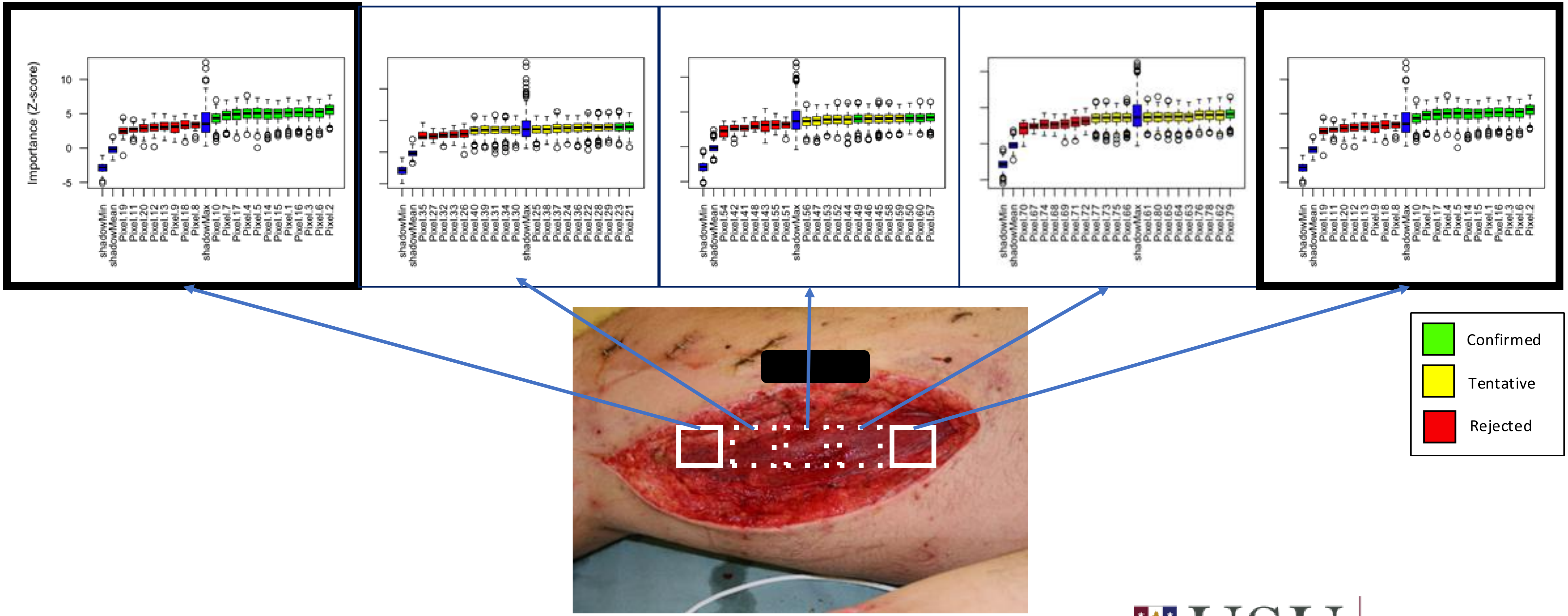
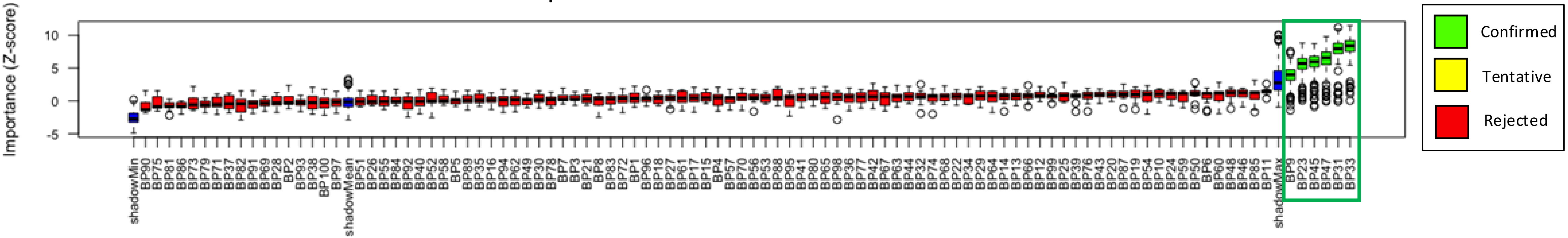
# Regional RGB Analysis Improves Modeling

- Red–Blue (R–B) percentile-based column profile analysis identified wound border regions as stronger predictors of successful delayed wound closure than central wound-bed regions

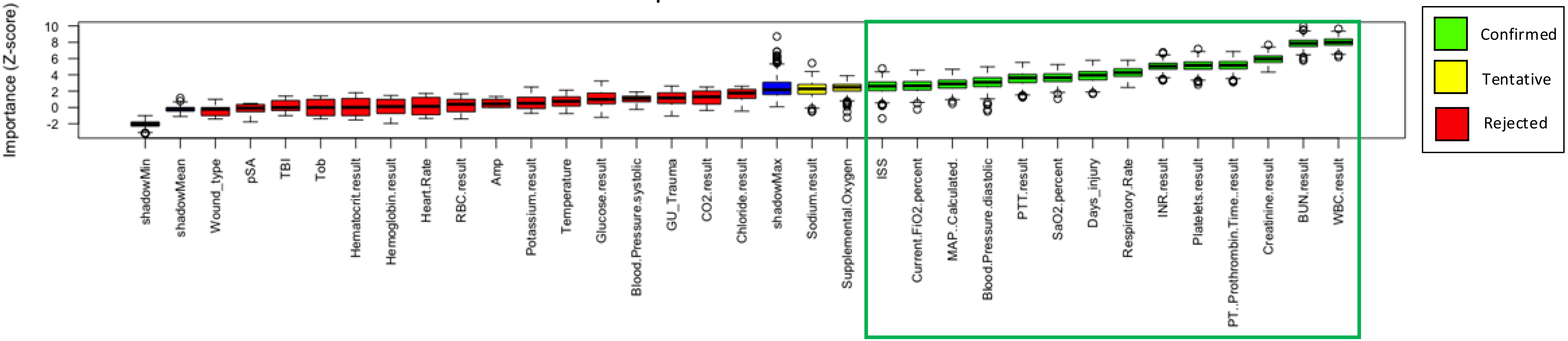


# Identifying the Strongest Predictors of Wound Closure

- The blue channel had the best RGB predictors of successful DWC




- White blood cell count was the best clinical predictor of successful DWC



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# Clinical and RGB Data Emerged as Top Predictors

| Rank | Variable Name | Description / Notes |
|---|---|---|
| 1 | **BP33** | Blue channel profile percentile region 33 |
| 2 | **WBC.result** | White blood cell count result |
| 3 | **BP31** | Blue channel profile percentile region 31 |
| 4 | **BUN.result** | Blood urea nitrogen result |
| 5 | **BP47** | Blue channel profile percentile region 47 |
| 6 | **BP45** | Blue channel profile percentile region 45 |
| 7 | **Creatinine.result** | Serum creatinine result |
| 8 | **BP23** | Blue channel profile percentile region 23 |
| 9 | **PT..Prothrombin.Time..result** | Prothrombin time result |
| 10 | **Platelet.result** | Platelet count result |
| 11 | **INR.result** | International normalized ratio |
| 12 | **Respiratory. Rate** | Breaths per minute |
| 13 | BP9 | Blue channel profile percentile region 9 |
| 14 | **Days_injury** | Days since injury |
| 15 | **SaO2.percent** | Oxygen saturation (%) |
| 16 | PTT.result | Partial thromboplastin time |
| 17 | Blood.Pressure.diastolic | Diastolic blood pressure |
| 18 | MAP..calculated. | Mean arterial pressure (calculated) |
| 19 | Current.FiO2.percent | Fraction of inspired oxygen (%) |
| 20 | ISS | Injury severity score |

- Twenty candidate predictors were selected and ranked using the Boruta feature selection algorithm
- Models were developed using combinations of top-ranked RGB and clinical predictors
- Based on preliminary model performance, 4 RGB-derived predictors and 9 clinical predictors were selected for final model development and validation (shown in red boxes)

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# Predictor Directionality for Successful Closure

| Predictor | Association with successful DWC | Approximate favorable range | Interpretation |
|---|---|---|---|
| BP47 | Higher | > 15 (blue-channel intensity, AU*) | Favorable wound-bed characteristics |
| BP31 | Higher | > 8 (blue-channel intensity, AU*) | Favorable wound-bed characteristics |
| BP33 | Lower | < 15 (blue-channel intensity, AU*) | Favorable wound-bed characteristics |
| BP45 | Lower | < 12–14 (blue-channel intensity, AU*) | Favorable wound-bed characteristics |
| WBC | Lower | < 15–18 $\times 10^3$ cells/µL | Lower inflammation |
| Platelet Count | Lower (within normal range) | 150–450 $\times 10^3$ platelets/µL | Lower inflammation |
| INR | Lower | < 1.15–1.20 | Normal coagulation |
| Prothrombin Time (PT) | Lower | < 17 seconds | Normal coagulation |
| Respiratory Rate | Lower | < 16–17 breaths/min | Lower physiologic stress |
| BUN | Lower | < 15–20 mg/dL | Better physiologic condition |
| Creatinine | Normal physiologic range | ~0.7–1.5 mg/dL | Preserved physiologic reserve |
| Days from Injury | Intermediate timing | ~8–11 days | Optimal closure timing |
| $SaO_2$ | Higher (within physiologic range) | 97–99% oxygen saturation | Adequate oxygenation |

*AU: Arbitrary Units

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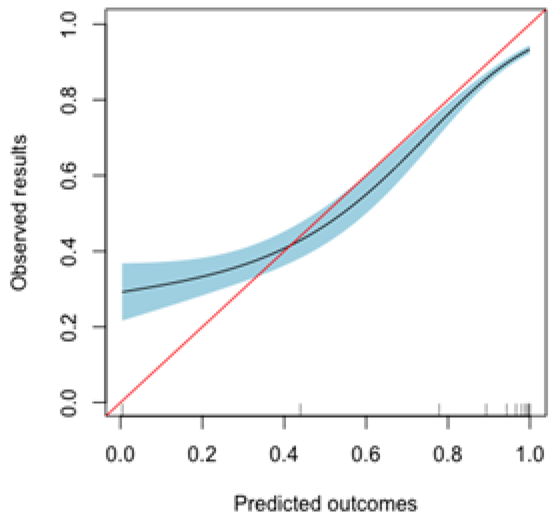
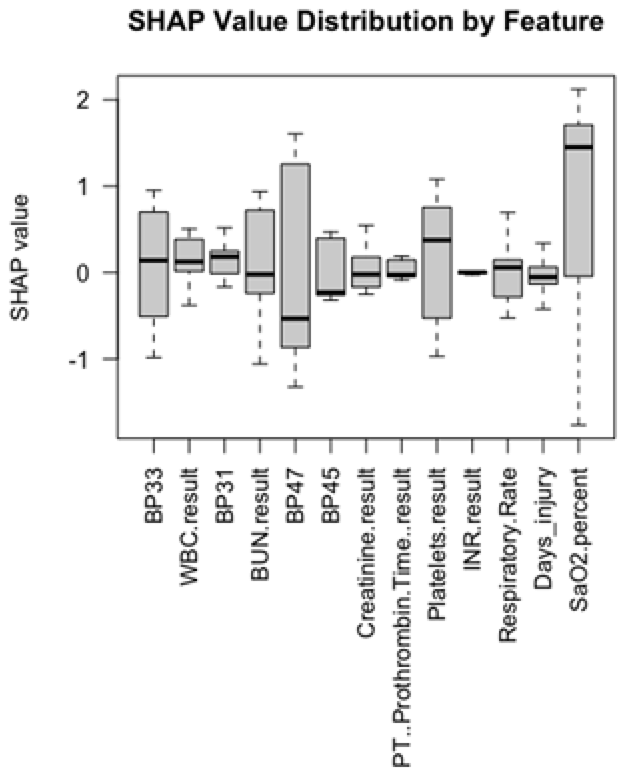
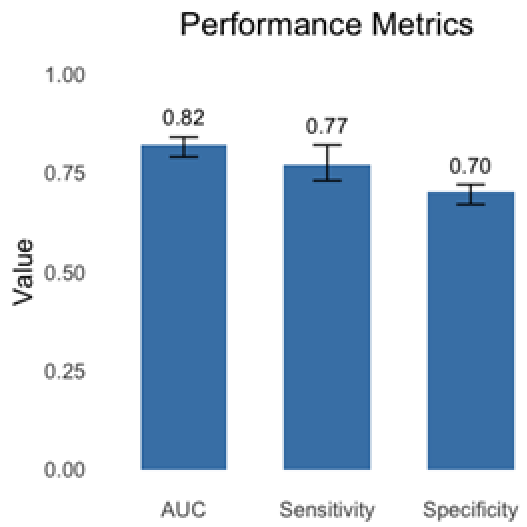
# Combined Modeling Achieved High Accuracy

- Combining wound image features with clinical data yielded strong prediction of delayed wound closure outcomes (AUC = 0.82), demonstrating the feasibility of an integrated imaging-clinical decision-support approach

- **SHAP values** quantify the contribution of each variable to a single prediction. Values indicate how much a variable increases (positive) or decreases (negative) the predicted outcome relative to the model's average output

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# Summary and Way Forward

- **Key Findings**
  - RGB wound profiles may capture visual signatures of tissue healing and readiness for DWC
  - Red–Blue (R–B) wound border profiles were more informative predictors of closure success than central wound regions
  - Successful closure was associated with: favorable wound image characteristics, lower inflammation, normal coagulation, lower physiologic stress, adequate peripheral oxygenation, and closure within an optimal post-injury window
    - Blue-channel profiles (31, 33, 45, and 47) were the strongest image-derived predictors of DWC
    - The key clinical variables for predicting successful wound closure were: WBC, BUN, creatinine, PT, platelet count, INR, respiratory rate, days post-injury, and oxygen saturation
  - The final XGBoost model combined four blue-channel image features and nine clinical variables, and it demonstrated strong internal performance (AUC = 0.82)
  - If these findings generalize, wounds with imaging and physiologic characteristics consistent with adequate oxygenation and favorable wound-bed conditions may be more likely to heal successfully

- **Next Steps**
  - Investigate wound- and tissue-component findings, including visual indicators of healing (such as signs of infection, necrosis, and granulation tissue formation), in coordination with RGB data
  - Evaluate deep learning approaches to characterize local spatial relationships among pixels and tissue features to refine model performance
  - Validate the model and key predictors in independent patient cohorts to assess generalizability and confirm performance across diverse wound types and clinical settings