Development of a Predictive Model for Critical Colonization in Combat-Related Extremity Wounds Using Images

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Conflict of Interest/Disclaimer Statement

No conflicts of interest to declare.

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Critical Colonization in Extremity Trauma

Critical Colonization (CC): Bacterial growth ≥10^5 CFU per gram of wound tissue or microliter of effluent

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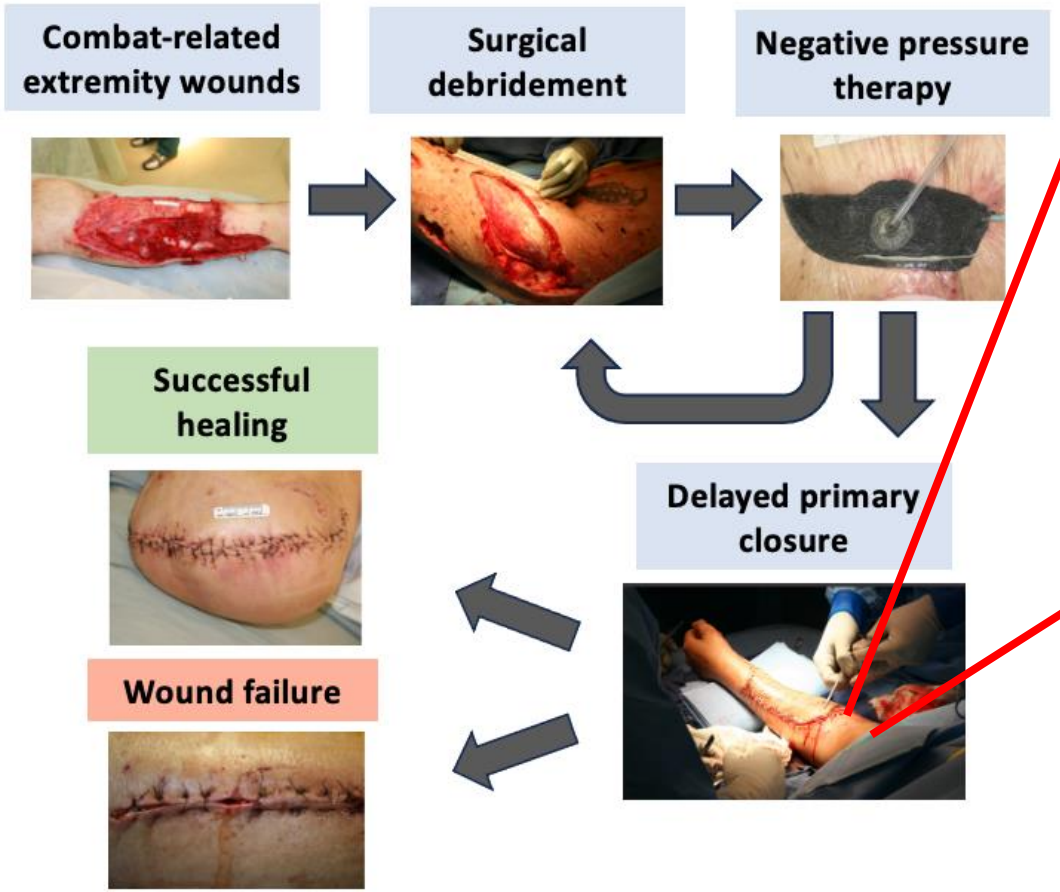

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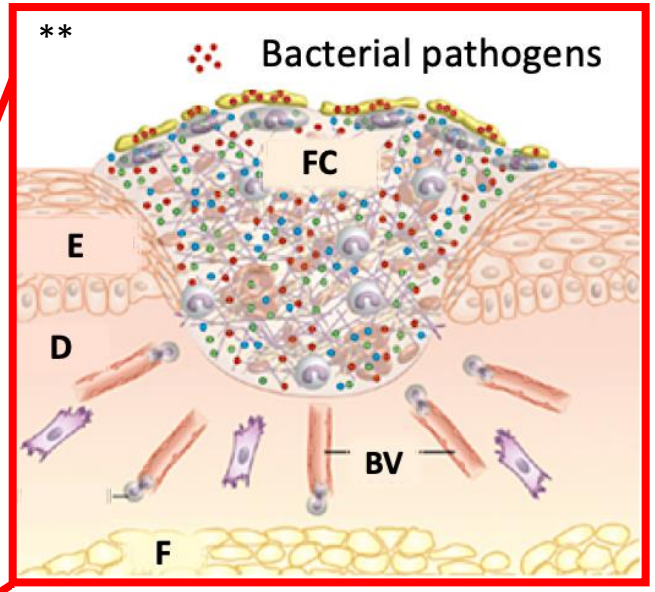
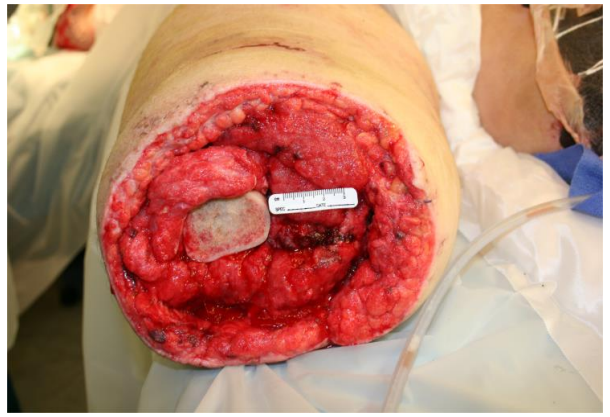


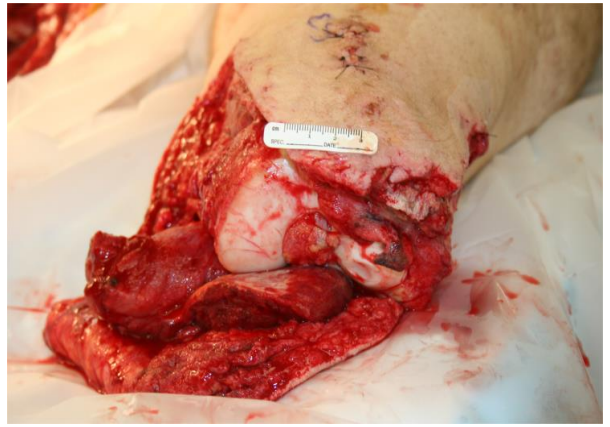
- Granulation tissue
- Neutrophil

E - epidermis D - dermis
F - fat FC - fibrin clot

Closure attempted → eventually healed



Closure attempted → failed



*Modified from Chapter 7, Wound Healing, Leong M and Philips LG in *Sabiston Textbook of Surgery: The Biological Basis of Modern Surgical Practice* 19e, 2012

Modified from *Journal of Investigative Dermatology* (2007) **127, 1018–1029. doi:10.1038/sj.jid.5700715

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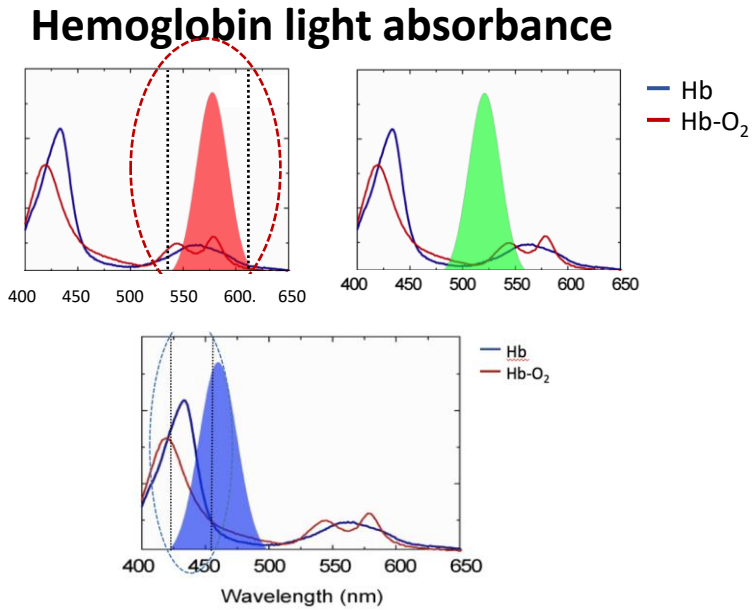
Using Images to Define Wound End States

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 red, green, blue (RGB) intensity 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 (HCA) using 17 variables achieved:
  - **76.6% accuracy, 76.9% sensitivity, 76.5% specificity**



**Non-invasive Monitoring of Tissue Oxygenation During Laparoscopic Donor Nephrectomy.* N. J. Crane, P. A. Pinto, D. Hale, F. A. Gage, D. Tadaki, A. D. Kirk, et al. BMC Surg 2008 Vol. 8 Pages 8

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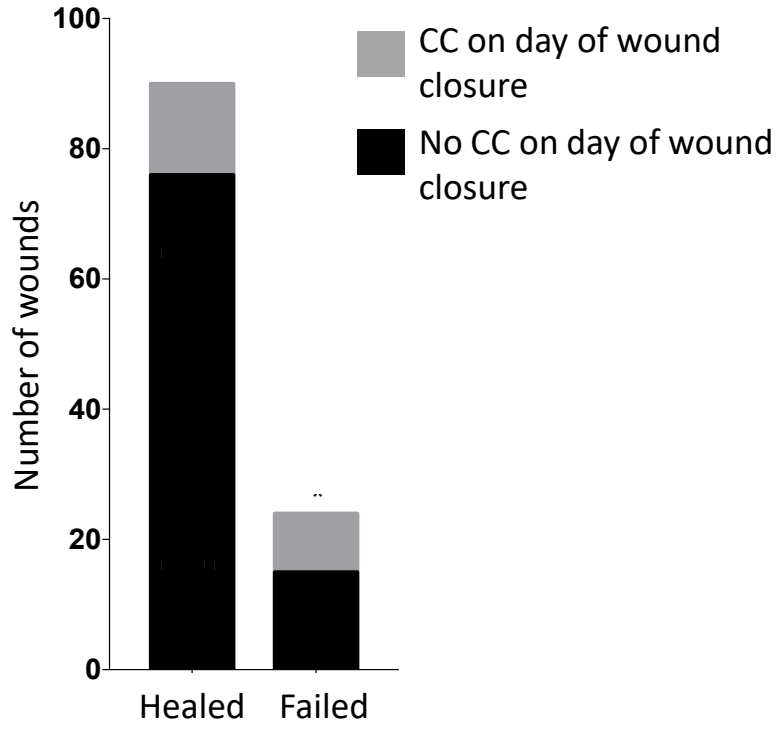
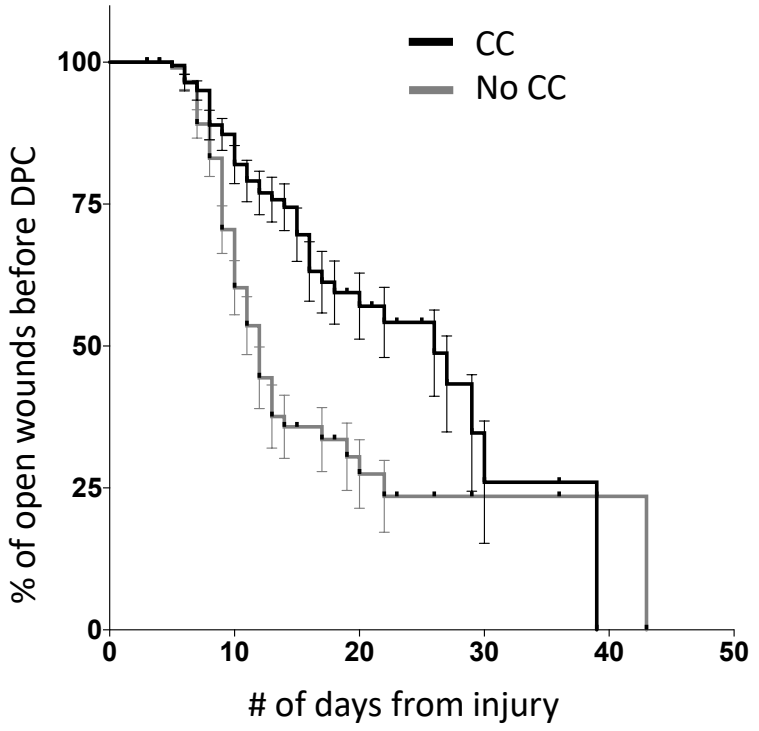
Critical Colonization Associated with Wound Failure

A total of 47 of 116 wounds developed critical colonization (CC) during treatment

Despite antibiotic treatment, 23 wounds were still closed with CC and had increased odds of failure that required reoperation, compared to wounds closed without CC (9 of 23), odds ratio = 2.87 (95% confidence interval = 1.1–7.8)



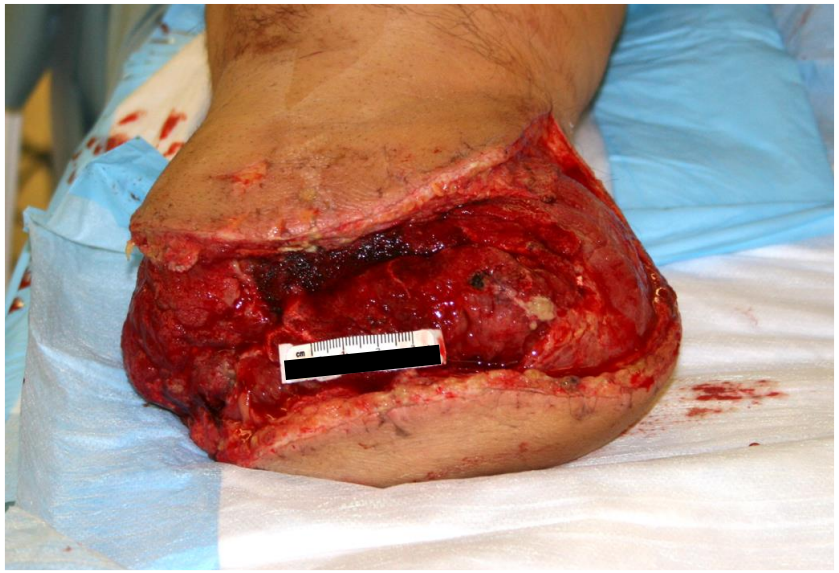
Compared to patients without CC, those with CC experienced prolonged treatment before delayed primary closure (DPC) was attempted ($p<0.01$ CI, log-rank test)



*Unpublished data (Lisboa FA et al.)

Materials and Methods

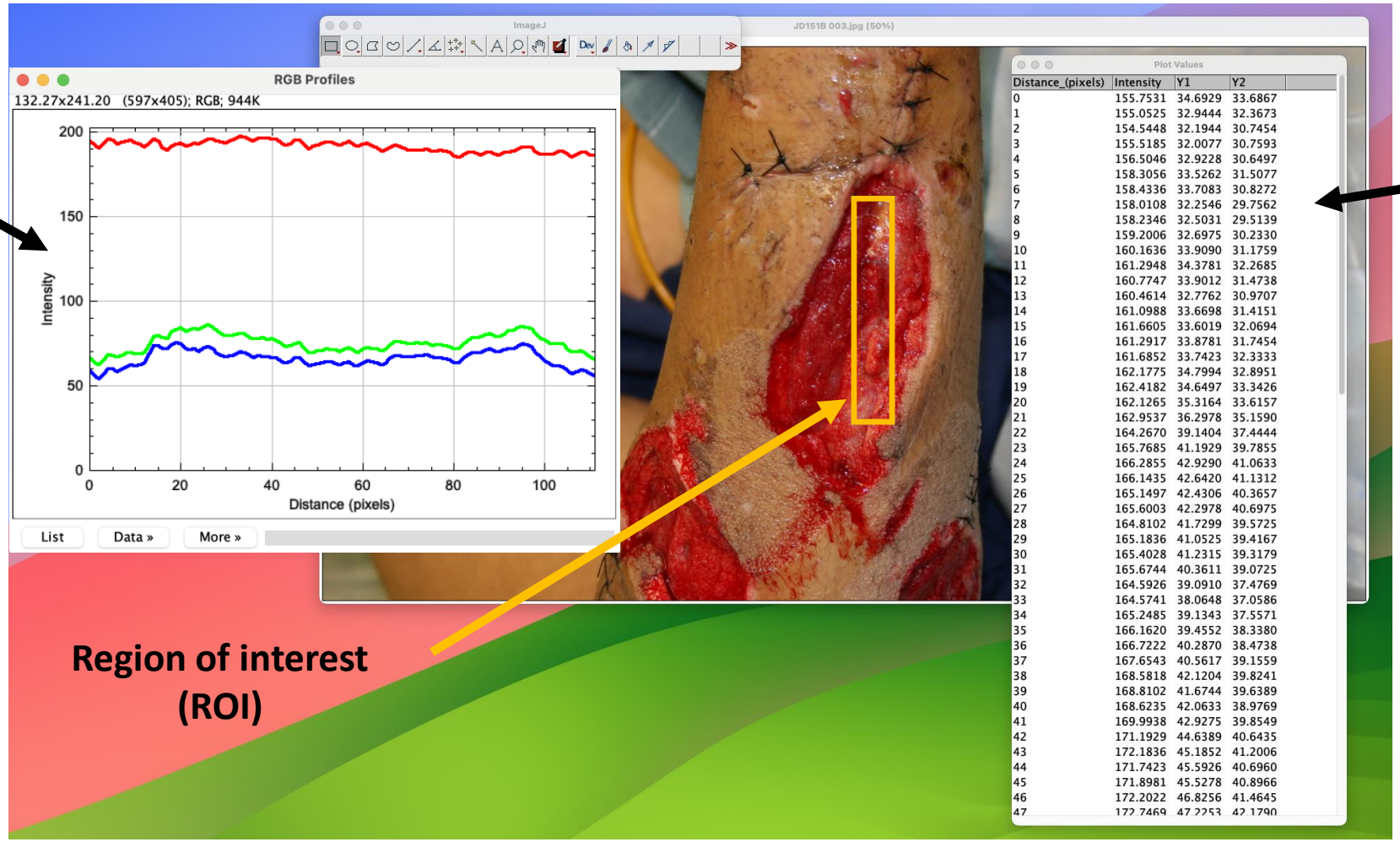
- **Study cohort:** 73 adult patients from the WoundVAC study with 116 combat-related extremity wounds treated at Walter Reed
- **Data and sample collection:** Wound images, effluent, and central wound biopsies collected at each debridement until delayed wound closure (DWC)
- **Image processing:** RGB intensities and red–blue (R–B) differences extracted from 373 wound images using ImageJ. Each image normalized and segmented into 100 left-to-right percentile-based column (PBC) profiles
- **Model development:** Boruta algorithm selected imaging and clinical predictors of CC, which were used in XGBoost binary classification models
- **Model evaluation:** Extreme Gradient Boosting (XGBoost) models were evaluated over 100 random 80/20 stratified train/test splits. A total of 2,000 bias-corrected and accelerated cluster bootstrap resamples were used to estimate 95% confidence intervals (CIs) for area under the ROC curve (AUC), sensitivity, specificity, and Brier score



An extremity wound closed with CC that went on to fail, requiring reoperation

Capturing Color Signal Intensity

RGB profile data



Signal intensity table

Region of interest (ROI)

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

Generating Percentile-Based Column (PBC) Profiles

Image Processing

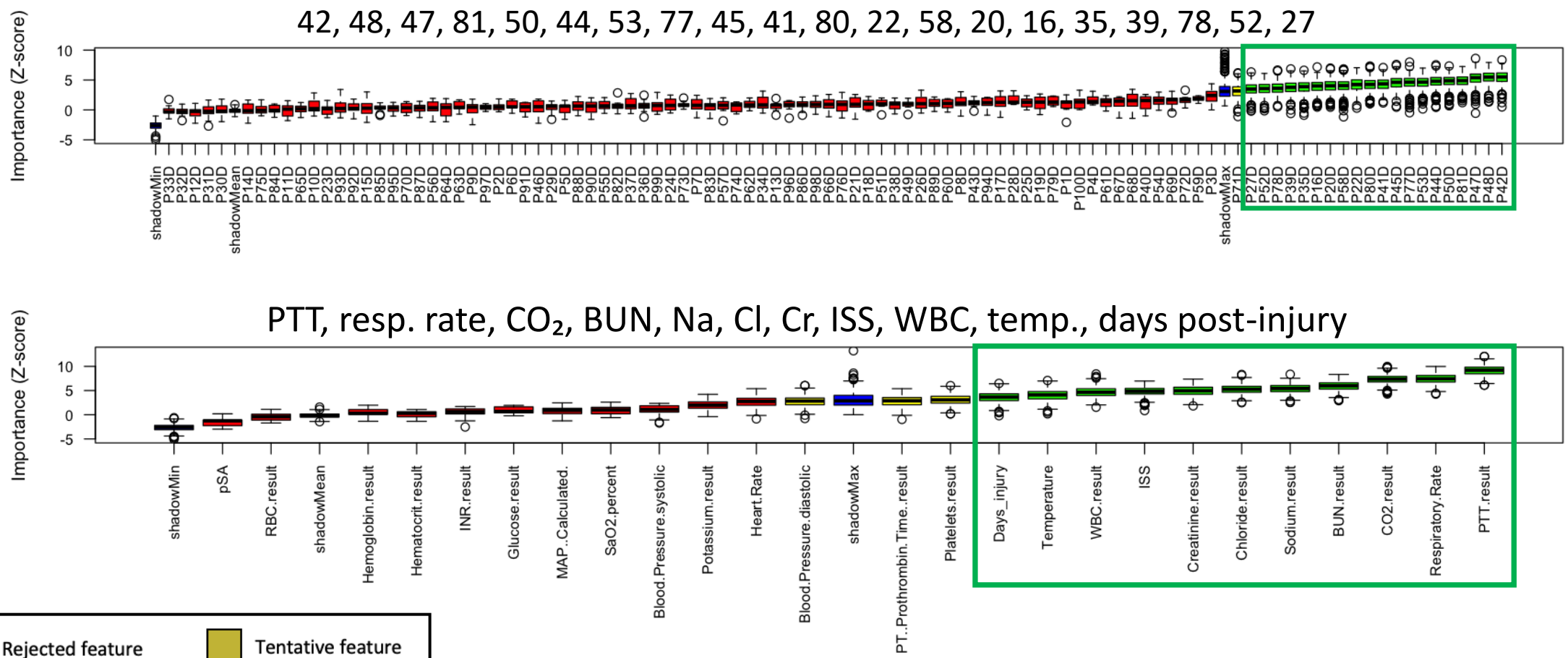
- RGB profiles were normalized to the minimum intensity value within each profile to reduce baseline signal variation across images
- Profiles were resampled into 100 left-to-right percentile-based columns (PBCs) spanning the wound from one margin to the other, standardizing wounds of different sizes
- The resulting PBC-based RGB profiles provided quantitative imaging features for machine-learning model development

Model Development

- Wounds were labeled based on the subsequent development of CC, establishing the training dataset
- RGB-derived features from each PBC, together with relevant clinical variables, were used as candidate predictors
- The Boruta feature selection algorithm identified the most informative imaging and clinical predictors of CC
- Selected features were used to train XGBoost machine learning models for prediction of CC development

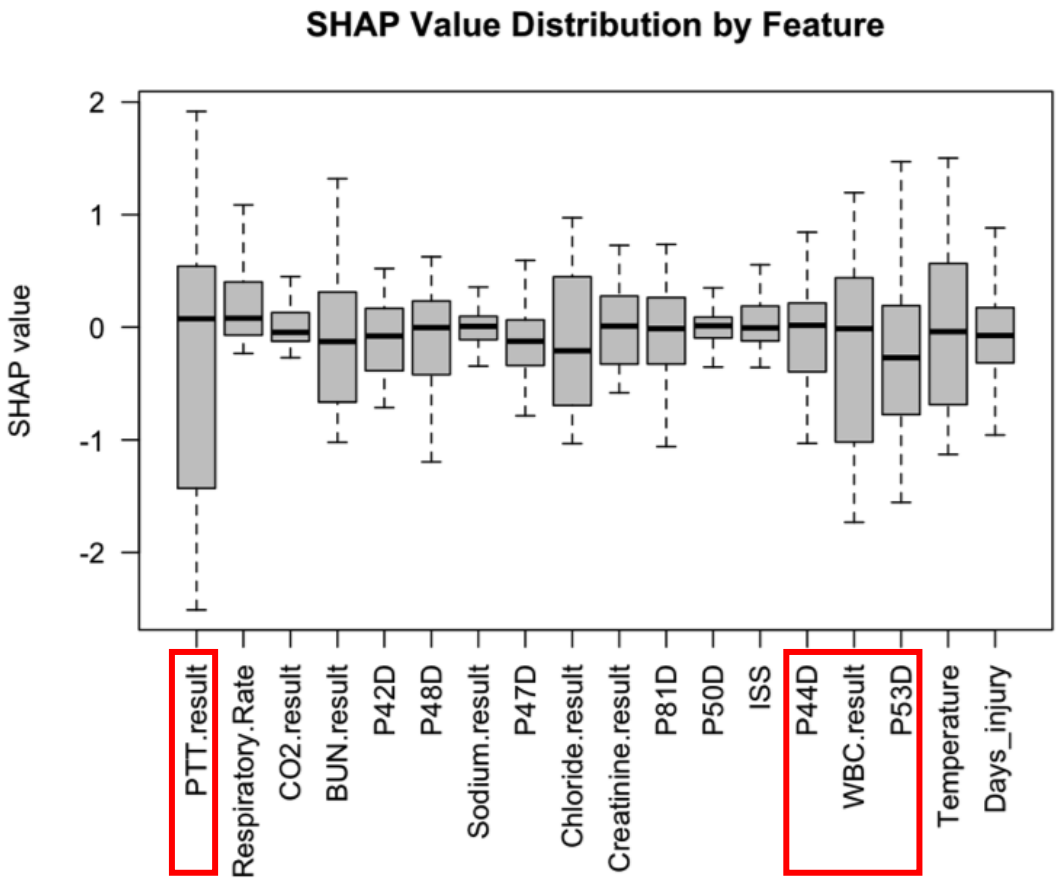
RGB and Clinical Data Variables are Associated with CC

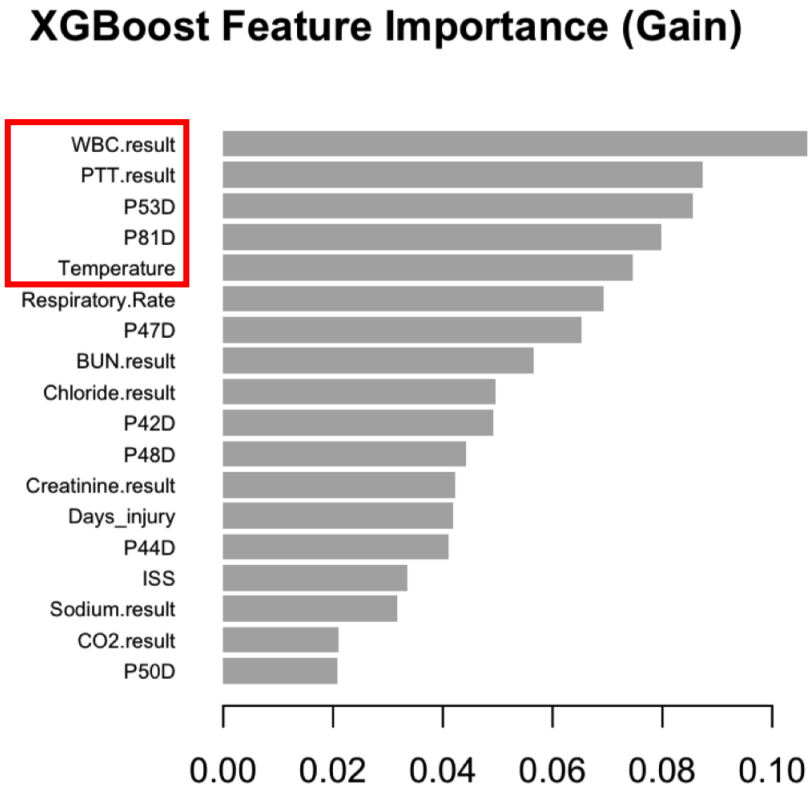
The Boruta algorithm identified 20 R–B difference PBC profiles and 11 clinical variables associated with CC



PBC Profiles + Clinical Values Best Predict CC

- Best-performing XGBoost classification model: 7 R–B PBC profiles (42, 48, 47, 81, 50, 44, 53) and 11 clinical variables: PTT, resp. rate, CO_2, BUN, Na, Cl, Cr, ISS, WBC, temp., days post-injury
- Model performance: AUC 0.76 (95% CI 0.71–0.80), sensitivity 0.71 (95% CI 0.64–0.77), specificity 0.67 (95% CI 0.63–0.72), Brier score 0.19 (95% CI 0.17–0.23)





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Summary and Way Forward

Summary:

- Critical colonization (CC) is associated with prolonged time to delayed wound closure and may increase the risk of wound failure when present at the time of closure
- RGB-derived red–blue (R–B) image features, combined with routinely collected clinical variables, showed moderate ability to predict CC (AUC 0.76)

Way forward:

- Perform external validation in additional cohorts
- Explore local pixel relationships
- Improve image processing techniques to better define wound area
- Evaluate additional machine learning approaches

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