UNIVERSITY OF CAMBRIDGE

Executive Summary

Feasibility and sensitivity study of radiomic features in photoacoustic imaging of patient-derived xenografts

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1. Introduction

Breast cancer is a serious disease that affects around 2.3 million women every year [1]. We recognise multiple subtypes of breast cancer for better diagnostics, among which this work focuses on the luminal B and basal subtypes [2, 3]. Photoacoustic acoustic imaging is an emerging non-invasive technique that has seen progress in detecting tumours in a clinical setting [4, 5, 6]. However, manual inspection can be expensive and inefficient, so radiomic features [7] have been considered as indicators for the state of the tissue. The primary goal of this work is to replicate and extend the work by Escudero Sanchez et al. [8], evaluating the discriminative power of radiomic features under various conditions and methodologies.

2. Objectives

Our objectives in this study were to:

- Reaffirm the main discoveries of Escudero Sanchez et al. [8], up to confirming which radiomic features have the most predictive potential.
- Investigate the implications of tweaking components of the pipeline, and whether any changes affect the final conclusions.
- Verify whether we can apply standard data science techniques in light of the small dataset size.

3. Methodology

The research methodology in this project involved exploring the data, after which applying two separate studies into the sensitivity of each feature with respect to data collation factors, as well as the power of the features to distinguish between the aforementioned tumour models.

Using the data provided by Escudero Sanchez et al. [8], extracted in the original study, we first applied a form of sensitivity analysis using multi-factor ANOVA. We register a η^2 measure for each feature-factor pair that tracks what fraction of the feature variance can be explained by the given set of factors. Ideally, we want features that are highly sensitive to the underlying model, but not to other factors, such as the grey level quantisation, image reconstruction method, or the wavelength used for PAI. We further explored an unbalanced version of the ANOVA and report the effects of including all samples.

In the larger part of the study, we implore a model discrimination analysis, which aims to determine the predictive capabilities of a set of radiomics. The features were normalised to the effects of the volume of interest (VOI) as described in Escudero Sanchez et al. [9], a step we further explore in our work. The proposed method for measuring the feature importance was through fitting a random forest classifier on a reduced feature set and obtaining the respective SHAP values [10], which are a proxy for determining how well the classifier would do without the underlying feature. The original study used the Kruskal-Wallis statistical test [11] that can discriminate between different distributions, in our case emerging from the cancer subtypes. The respective p-values are used alongside the Benjamini-Hochberg correc-

tion [12], to select the most discriminative features. Finally, to obtain the reduced feature set, one of each pair of correlated features was disregarded if they passed a certain threshold α_{corr} of the RMCorr (Repeated Measures Correlation) [13] metric. We explore the pipeline, making modifications in the initial feature reduction phase by substituting the Kruskal-Wallis test with the Kolmogorov-Smirnov one or with the sequential forward selection method [14]. Finally, we consider the effects of cross-validation and the choice of classifier on the final outcome.

4. Results

The obtained results confirm the findings of the original work [8], and extend the applicability of the framework. First of all, we discerned 4 features that are sensitive to the tumour model - *FO Skewness, FO Kurtosis, FO* 10^{th} *Percentile*, and *NGTDM Coarsensess*, with no significant differences between balanced and unbalanced ANOVA. Furthermore, we reaffirmed that features are more sensitive to the model upon standardising for grey-level binning and the reconstruction algorithm. This would allow for features to potentially be used across different settings, granted that the factors are kept consistent.

We also achieve comparable results in the model discrimination analysis section of the project. Changes in the feature reduction components did not yield any significant deviations in the conclusions, with 2-3 features varying among the top 9 in each ablation study. However, according to our implementation of the VOI normalisation procedure [9], a more standardised approach is required to ensure replicable findings. Furthermore, cross-validation was found to robustify the performance and was applied when investigating other models for importance inference. While the gradient boosting classifier was underdetermined under such a small dataset, the logistic regression produced results that had significant overlap with the original, they were more in line with the sensitivity analysis, likely due to the linear nature of the model. Finally, we arrive at a final list of features that have shown promise in predicting the breast cancer subtype:

- FO Skewness
- FO 10^{th} Percentile
- FO 90^{th} Percentile/RMS
- GLCM Sum of Squares
- NGTDM Strength
- GLCM Cluster Prominence

5. Discussion

This study replicates and extends previous work [8], serving as a viability study for PAI radiomics in clinical use. In order for PAI radiomics to become feasible, their viability must be thoroughly validated across a multitude of settings. The framework we described can be used as a first step towards such an exploration, with the results emphasising the need for using machine learning standard practices to generalise the methodology across all components.

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References

[1] Freddie Bray, Mathieu Laversanne, Hyuna Sung, Jacques Ferlay, Rebecca L Siegel, Isabelle Soerjomataram, and Ahmedin Jemal. Global cancer statistics 2022: Globocan estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA: a cancer journal for clinicians*, 74(3): 229–263, 2024.

[2] Erasmo Orrantia-Borunda, Patricia Anchondo-Nuñez, Lucero Evelia Acuña-Aguilar, Francisco Octavio Gómez-Valles, and Claudia Adriana Ramírez-Valdespino. Subtypes of breast cancer. *Breast Cancer [Internet]*, 2022.

[3] Ozlem Yersal and Sabri Barutca. Biological subtypes of breast cancer: Prognostic and therapeutic implications. *World journal of clinical oncology*, 5(3):412, 2014.

[4] Mohammad Mehrmohammadi, Soon Joon Yoon, Douglas Yeager, and Stanislav Y Emelianov. Photoacoustic imaging for cancer detection and staging. *Current*

Molecular Imaging (Discontinued), 2(1): 89–105, 2013.

[5] Srivalleesha Mallidi, Geoffrey P Luke, and Stanislav Emelianov. Photoacoustic imaging in cancer detection, diagnosis, and treatment guidance. *Trends in biotechnology*, 29(5):213–221, 2011.

[6] Keerthi S Valluru and Juergen K Willmann. Clinical photoacoustic imaging of cancer. *Ultrasonography*, 35(4):267, 2016.

[7] Janita E Van Timmeren, Davide Cester, Stephanie Tanadini-Lang, Hatem Alkadhi, and Bettina Baessler. Radiomics in medical imaging—"how-to" guide and critical reflection. *Insights into imaging*, 11(1):91, 2020.

[8] Lorena Escudero Sanchez, Emma Brown, Leonardo Rundo, Stephan Ursprung, Evis Sala, Sarah E Bohndiek, and Ignacio Xavier Partarrieu. Feasibility and sensitivity study of radiomic features in photoacoustic imaging of patient-derived xenografts. *Scientific Reports*, 12(1):15142, 2022.

[9] Lorena Escudero Sanchez, Leonardo Rundo, Andrew B Gill, Matthew Hoare, Eva Mendes Serrao, and Evis Sala. Robustness of radiomic features in ct images with different slice thickness, comparing liver tumour and muscle. *Scientific reports*, 11(1):8262, 2021.

[10] Scott M Lundberg and Su-In Lee. A unified approach to interpreting model predictions. *Advances in neural information processing systems*, 30, 2017.

[11] Patrick E McKight and Julius Najab. Kruskal-wallis test. *The corsini encyclopedia of psychology*, pages 1–1, 2010.

[12] JA Ferreira and AH Zwinderman. On the benjamini–hochberg method. 2006.

[13] Jonathan Z Bakdash and Laura R Marusich. Repeated measures correlation. *Frontiers in psychology*, 8:252904, 2017.

[14] Michael Alin Efroymson. Multiple regression analysis. *Mathematical methods for digital computers*, pages 191–203, 1960.