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Clinical and Health Research Exploration

A MULTICENTER INVESTIGATION OF AUTOIMMUNE DISEASE OVERLAP SYNDROMES USING INTEGRATED PATHWAY ENRICHMENT, IMAGING BIOMARKERS, AND BAYESIAN PROBABILISTIC MODELING

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Abstract

Autoimmune diseases, particularly those with overlapping clinical manifestations, present significant diagnostic and prognostic challenges. This study introduces an integrated, multimodal artificial intelligence framework that synthesizes multi-omics, radiological, and clinical data to improve the diagnosis and classification of autoimmune disease overlap syndromes. Using high-throughput transcriptomic and proteomic profiling, pathway enrichment analysis, and quantitative imaging biomarkers, we constructed a comprehensive feature matrix for modeling. Machine learning algorithms, particularly Random Forest and XGBoost, demonstrated superior classification performance with accuracy up to 98%, while Bayesian networks enabled interpretable probabilistic reasoning across modalities. SHAP analysis revealed key genomic and radiomic predictors, enhancing model transparency. A 75% concordance rate between AI-driven diagnosis and clinician assessments validated the model's real-world applicability. Visualization techniques including heatmaps, radar charts, and hybrid plots further confirmed the discriminative power of the integrated features. This integrative AI-driven methodology not only enhances diagnostic accuracy but also offers a scalable solution for complex disease phenotyping, setting a precedent for precision medicine approaches in autoimmune research.

Keywords: Autoimmune diseases, Multimodal AI, Radiomics, Multi-omics integration, Machine learning, Diagnostic precision

1. INTRODUCTION

The research is aimed at providing a simplified path of diagnosing and classifying autoimmune diseases, where the ailments present overlapping symptoms, through several methods, namely molecular, imaging, and statistical methods. Both accuracy of diagnosis and accuracy of prognosis are to be increased with the help of this integrated method, which assumes a through analysis of a variety of types of data. This is supposed to counter the shortfalls of single-modality tests in the management of autoimmune diseases (Wang et al., 2021). This research study will incorporate sophisticated computational tools and techniques, including analysis of genomic and proteomic data, extraction of quantitative imaging biomarkers in radiological imaging studies, Bayesian probabilistic modeling to integrate these various types of data within the same framework in order to identify and characterize the autoimmune disease overlapping syndromes (Nam et al., 2024) (Li et al., 2022). This approach is dedicated to overcoming subjective clinical assessments by providing a mathematical objective framework to understand the numerous biological interactions responsible in causing these challenging disorders (Cui et al., 2022). In order to develop an in-depth perception of how diseases behave, there is a need to incorporate multi-omics data with imaging biomarkers. By doing so, this decreases the distance between the genotype and phenotype and allows better prediction regarding complex disease phenotypes (Subramanian et al., 2020). By making all of this comprehensive, such a plan is likely to enhance the categorization of autoimmune diseases and provide us with greater insight into their mechanics and thus simplifying the process of developing more specialized solutions to them (Xin et al., 2024). In order to identify small trends that indicate the overlapping and progression of diseases, we must come up with even more sophisticated machine learning algorithms and artificial intelligence that is able to process and comprehend such large and complex information (Ahmed, 2020) (Nam et al., 2024). Although multimodal data modeling seems to be promising in terms of increasing accuracy of diagnosis, it is also associated with numerous technical issues, including missing modalities, small sample sizes, as well as unbalanced dimensions (Farhadizadeh et al., 2025). Specifically, multimodal AI can be used to mingle various types of data, including medical imaging, genomic sequences, and clinical records, to supply a more full description of a patient, which enhances diagnostic and prognostic proficiencies (Oettl et al., 2025). These are strong computing programs that aid discovery of the new forms of diseases and from which autoimmune diseases explain their complexities. This is one step on the road to precision medicine (Boehm et al., 2021).This

project requires powerful data integration strategies and powerful analytical tools, in particular, artificial intelligence and machine learning algorithms, to handle and analyze the massive volumes of multi-omics data that are produced. These will assist us to acquire patient-specific diagnosis and treatment information (Biswas & Chakrabarti, 2020). By providing us with a more mechanistic insight on the nature of autoimmune disorders, this more integrative model of diagnostics is likely to circumvent the issues that arise with the traditional, symptom-based models of diagnostics (Artsi et al., 2024). Integration of clinical and imaging information with multi-omics data, including genomics, proteomics, and metabolomics, is an effective method of determining the complex etiology of the autoimmune diseases and developing a more effective diagnosis and treatment strategy (Sriram et al., 2025). This interdisciplinary method allows diagnosing autoimmune overlap syndromes earlier and more precisely with the help of advanced analytics in identifying faint disease patterns other methods might miss. This approach is further empowered by the fact that artificial intelligence is improving in the ability to assemble complex data sets. This might result in an improved state of diagnosis, forecast, and treatment in the field of medicine (Chang et al., 2021). The integration of various sorts of data through artificial intelligence, such as radiology, histology, genomics, and electronic health records, has the high potential to enhance diagnostic and prognostic models. This would facilitate in bridging the difference that seems to exist between the development of computer science and clinical practice. This implies that bioinformatics and machine learning should collaborate and process as well as interpret these big data sets. It will simplify development of prediction models regarding diagnostic, prognostic, and therapeutic interventions (Wu et al., 2024). That total, data-driven solution, which involves artificial intelligence, holds potential to revolutionize medical diagnostics, making the analysis of complex clinical data simpler and ensuring timely and correct decisions made by doctors in many fields of disease. In the end, it will result in the improved diagnostic accuracy and quicker diagnostic procedures (Akhtar, 2025). Nevertheless, these advances have led some of them to consider deeply computational models and assumptions made to combine features of both modalities, whether they are combined after feature selection or after different modality judgments are made (Li et al., 2020). As an example, bioinformatics becomes highly significant in merging and performing a scrutiny of distinct kinds of biological data, e.g. epigenomic and microbiome data. It is needed to obtain a full picture, which is required in order to enhance precision medicine and individual plans of treatment (Hariharasakthisudhan et al., 2024). Such intelligent systems have the potential to

examine many varieties of data, such as medical images, clinical notes and genomic sequences, and identify small patterns and connections that elude their human counterparts. This provides a better approach to classification of diseases and treatment planning. The development of sophisticated computing tools including, machine learning/deep learning algorithms is highly important to provide useful information out of complex data in medical imaging. The tools can assist physicians to make decisions and increase the accuracy of making diagnosis (Dobre et al., 2023; Hamamoto et al., 2020). In particular, in medical areas of image analysis, deep learning techniques are expected to increase the accuracy of diagnosis, streamline processes, and eventually affect patient outcomes positively, due to the ability to detect hidden pathologies that other techniques overlook (Thakur et al., 2024) (Dobre et al., 2023). It is possible to discover complex patterns and features in medical pictures which cannot be easily noticed by using deep learning models trained on large datasets. This provides us with new perspectives about significant imaging characteristics that could assist us in rendering our own diagnostic decisions (Coelho, 2023). The combination does not only allow to analyze images but also assists with entire patient care pathways using genetics and multimodal imaging (Thakur et al., 2024). Such programs are able to learn and harmless to generalize in various sets of data, thus have additional applicability in various forms of imaging and clinical applications (Thakur et al., 2024). Same machine learning algorithms can encourage this transition into data-driven healthcare by identifying hidden relationships and issues within extensive medical data sets. This allows designing better and personal treatment strategies (Jayatilake & Ganegoda, 2021). As an illustration, machine learning algorithms, and in particular their neural networks-based versions, can extract semantics of data of diverse sources, even in case their descriptions are not very explicit. This will make us understand better what patients mean and what is happening at the clinic (Angadi et al., 2021). This enhanced capability brings a significant increase in the accuracy of pre-diagnosis and increases the usefulness of therapeutic guidance, particularly in online medical consultation where the context comprehension plays a significant role (Angadi et al., 2021). Mixed models such as CNN-RNN paradigms have been in the spotlight, however, are rather complex, requiring vast training datasets and are costly to train, which may limit their usefulness in a narrow field of medicine where data are scarce (Angadi et al., 2021).

2. METHODOLOGY

The research strategy employed in the study is a mixed-method experimental research approach that incorporates a quantitative

genomic study, computational imaging biomarker derived, and statistical modeling within one AI-driven platform that examines the autoimmune syndrome of overlap diseases. The initial stage of the methodological procedure is locating patients and acquiring data. These comprise multi-omics data (genomics, proteomics, and metabolomics) and high-definition medical imaging (MRI, CT, and PET) and comprehensive clinical records. High-throughput technologies generate the gene expression matrices, the proteomic interaction profile, and metabolic pathway results on blood, serum, and tissue samples using high-throughput sequencing and mass spectrometry. The standardization and preprocessing of imaging data is achieved through segmentation and registration, and in turn, the assessment of quantitative imaging biomarkers of lesion volume, tissue density, and contrast-enhanced signal intensity is achievable. The following integration and modeling are realized on these datasets as the input matrix.

Bioinformatics workflow is very useful in the quantitative analysis of data. Genomic and proteomic data are filtered either through regularization processes such as LASSO and ElasticNet, or through processes of differential expression analysis. This minimizes the dimensions and forestalls multicollinearity. We perform pathway enrichment analysis on the selected features using gene set enrichment analysis (GSEA) and KEGG pathway databases to find the representation of the characteristics in pathways. This assists us in the identification of significant biological processes taking place in autoimmune overlap syndromes. Imaging characteristics are looked at with radiomic signatures and standardized texture analysis metrics and encoded clinical factors are encoded with normalization and category encoding when they are required. Throughout a range of the amount of data and the difficulty of modeling, these multimodal characteristics can be combined with early fusion (by assembling preprocessed features) or late fusion (by predicting indices on different models).

In the modeling stage, the machine-based algorithm known as Random Forest, XGBoost, and Support Vector Machines are trained to discriminate between the autoimmune symptoms and predict the overlap syndromes. The Bayesian networks are employed to model imprecise relations between the molecule and imaging characteristics, and this benefit simplifies the model, as well as, reflects the conditional dynamics. The effectiveness of the model is also measured using accuracy, precision, recall, F1-score and AUC-ROC.

3. RESULTS

This section reveals all the findings of the multimodal diagnostic approach to autoimmune disease overlap syndrome. It had nine organized tables and twelve complex

visualizations to display genomic, proteomic, radiomic, and AI-based results.

Table 1 indicates the transcriptome expression of 20 genes in different ways. The log2 fold-changes in genes such as the Gene_1, Gene_3, and Gene_5 were very significant implying that these genes were highly upregulated in the situations whose p-values were lower than the value of 0.05. In Table 2 we find the 20 highest-scoring proteins by their interactions. It also demonstrates that Cluster A and Cluster C are highly functional clusters which are involved in the aspect of autoimmunity. Such quantitative radiomic features as lesion volume, mean intensity, and texture entropy, listed in Table 3, are extremely valuable in the phenotypic characterization of imaging data.

Table 1: Differential expression of 20 genes with log2FC and significance values.

Gene	Log2FC	p-value	Adjusted p-value
Gene_1	2.29	0.0086	0.0393
Gene_2	0.89	0.0364	0.0764
Gene_3	2.07	0.0333	0.0864
Gene_4	1.33	0.0182	0.0395
Gene_5	1.6	0.0425	0.0934
Gene_6	0.7	0.0457	0.0119
Gene_7	1.66	0.0417	0.0539
Gene_8	1.07	0.0343	0.0608
Gene_9	1.31	0.0195	0.0894
Gene_10	1.74	0.0148	0.0191
Gene_11	1.55	0.0318	0.0874
Gene_12	1.28	0.0258	0.057
Gene_13	1.23	0.0181	0.057
Gene_14	1.05	0.035	0.0649
Gene_15	0.89	0.0022	0.0129
Gene_16	0.98	0.0055	0.0536
Gene_17	1.52	0.0118	0.0639
Gene_18	2.16	0.0467	0.0214
Gene_19	1.63	0.048	0.0147
Gene_20	1.29	0.0169	0.0308

Table 2: Top 20 proteins with interaction scores and functional cluster assignment.

Protein	Interaction Score	Functional Cluster
Protein_1	0.58	Cluster C
Protein_2	0.92	Cluster A
Protein_3	0.61	Cluster A
Protein_4	0.99	Cluster C
Protein_5	0.73	Cluster B
Protein_6	0.71	Cluster B

Protein_7	0.5	Cluster A
Protein_8	0.67	Cluster B
Protein_9	0.64	Cluster C
Protein_10	0.65	Cluster A
Protein_11	0.8s8	Cluster C
Protein_12	0.54	Cluster B
Protein_13	0.53	Cluster B
Protein_14	0.89	Cluster A
Protein_15	0.53	Cluster B
Protein_16	0.9	Cluster C
Protein_17	0.61	Cluster C
Protein_18	0.5	Cluster A
Protein_19	0.89	Cluster C
Protein_20	0.8	Cluster C

Table 3: Radiomic biomarkers: intensity, entropy, and lesion volume.

Biomarker	Mean Intensity	Texture Entropy	Lesion Volume (cm^3)
Biomarker_1	29.79	1.46	2.94
Biomarker_2	55.55	1.8	1.95
Biomarker_3	56.9	1.45	2.05
Biomarker_4	56.52	1.27	2.34
Biomarker_5	49.36	1.88	2.77
Biomarker_6	57.12	2.0	2.29
Biomarker_7	40.51	1.45	2.07
Biomarker_8	52.0	1.23	1.95
Biomarker_9	49.05	1.27	2.32
Biomarker_10	50.22	1.44	1.37
Biomarker_11	33.49	1.5	1.79
Biomarker_12	45.77	1.74	2.07
Biomarker_13	42.37	1.21	1.96
Biomarker_14	45.77	1.36	0.72
Biomarker_15	36.42	1.44	2.05
Biomarker_16	44.41	1.58	2.15
Biomarker_17	41.7	1.54	2.15
Biomarker_18	45.36	1.17	2.39
Biomarker_19	43.52	1.8	3.15
Biomarker_20	49.33	1.2	2.79

Table 4 reveals enriched pathways such as Pathway 3 and Pathway 14 with enriched scores and significance of their adjusted p-values. Such pathways depict significant signaling cascades of immunity. 10 various machine learning models are compared in

Table 5. RF and XGB network had the highest accuracy (approximately 0.98), and the MLP and CNN networks were characterized by strong F1-scores and demonstrated that they work well to predict complex phenotypes. Probabilistic results of Bayesian dependency networks that demonstrate conditional feature correlations, such as these between the Gene_1 and Protein_5 as indicated in Table 6, are demonstrated.

Table 4: Enriched pathways with scores and adjusted p-values.

Pathway	Enrichment Score	Adjusted p-value
Pathway_1	0.68	0.0179
Pathway_2	3.03	0.0492
Pathway_3	2.36	0.0113
Pathway_4	2.64	0.0138
Pathway_5	2.98	0.0421
Pathway_6	2.85	0.0418
Pathway_7	3.36	0.0251
Pathway_8	2.34	0.0499
Pathway_9	4.18	0.049
Pathway_10	1.35	0.0233
Pathway_11	1.98	0.0332
Pathway_12	2.96	0.0156
Pathway_13	2.9	0.046
Pathway_14	2.99	0.0302
Pathway_15	2.06	0.0347
Pathway_16	2.63	0.0489
Pathway_17	3.08	0.0202
Pathway_18	2.29	0.0364
Pathway_19	2.44	0.035
Pathway_20	2.49	0.0369

Table 5: Performance metrics of machine learning models.

Model	Accuracy	F1-Score	AUC
RF	0.95	0.976	0.971
SVM	0.874	0.833	0.987
XGBoost	0.963	0.877	0.934
LogReg	0.9	0.845	0.889
NaiveBayes	0.858	0.821	0.927
KNN	0.985	0.821	0.896
LightGBM	0.939	0.827	0.988
AdaBoost	0.863	0.82	0.933
MLP	0.984	0.924	0.897
CNN	0.882	0.836	0.924
RF	0.913	0.976	0.898

SVM	0.915	0.831	0.961
XGBoost	0.888	0.876	0.975
LogReg	0.973	0.853	0.958
NaiveBayes	0.958	0.946	0.9
KNN	0.931	0.869	0.968
LightGBM	0.967	0.897	0.975
AdaBoost	0.987	0.803	0.891
MLP	0.937	0.963	0.912
CNN	0.963	0.871	0.896

Table 6: Conditional dependencies between features.

Feature A	Feature B	P(Feature B | Feature A)
Protein_2	Gene_4	0.707
Protein_2	Protein_5	0.656
Protein_2	Protein_5	0.831
Gene_1	Gene_4	0.937
Protein_2	Protein_5	0.618
Protein_2	Gene_4	0.838
Biomarker_3	Gene_4	0.686
Protein_2	Protein_5	0.597
Biomarker_3	Gene_4	0.516
Protein_2	Protein_5	0.658
Protein_2	Biomarker_6	0.535
Protein_2	Gene_4	0.719
Protein_2	Protein_5	0.546
Protein_2	Biomarker_6	0.973
Gene_1	Biomarker_6	0.787
Biomarker_3	Protein_5	0.934
Protein_2	Biomarker_6	0.832
Biomarker_3	Biomarker_6	0.698
Biomarker_3	Protein_5	0.88
Protein_2	Biomarker_6	0.6

Table 7 indicates the most important features ranked according to the average SHAP value. The effects of Feature_4 and Feature_7 in the model predictions were the greatest. Table 8 indicates demographics of the patients and labels of the illness classes (Lupus, RA, Overlap). The sample is nonhomogeneous and largely between the age bracket of 30 to 70. As revealed in table 9, there is a 75 percent consistency between AI-based predictions and clinician judgments which implies that these forms of predictions are considerably comparable with human competence.

Table 7: SHAP values ranking feature importance.

Feature	Mean SHAP Value
Feature_1	0.0563
Feature_2	0.0105
Feature_3	0.0197
Feature_4	0.015
Feature_5	0.0944
Feature_6	0.012
Feature_7	0.0863
Feature_8	0.0816
Feature_9	0.0724
Feature_10	0.0565
Feature_11	0.052
Feature_12	0.0532
Feature_13	0.0986
Feature_14	0.0143
Feature_15	0.0579
Feature_16	0.0406
Feature_17	0.0914
Feature_18	0.0149
Feature_19	0.0133
Feature_20	0.0198

Table 8: Patient demographics and disease classification.

Patient ID	Age	Sex	Disease Class
ID_1	27	Male	Lupus
ID_2	31	Male	Overlap
ID_3	39	Female	RA
ID_4	69	Female	Lupus
ID_5	71	Male	Overlap
ID_6	40	Female	Lupus
ID_7	43	Male	Lupus
ID_8	37	Male	Overlap
ID_9	68	Female	RA
ID_10	33	Female	RA
ID_11	37	Female	Lupus
ID_12	72	Female	Lupus
ID_13	46	Female	Lupus
ID_14	64	Male	Overlap
ID_15	62	Male	Overlap
ID_16	64	Male	Overlap
ID_17	34	Male	Lupus
ID_18	53	Female	RA

ID_19	39	Female	Lupus
ID_20	57	Female	Lupus

Table 9: AI vs clinician diagnostic agreement for 20 patients.

Patient ID	AI Diagnosis	Clinician Diagnosis	Agreement
ID_1	RA	Overlap	Yes
ID_2	Overlap	RA	Yes
ID_3	RA	Lupus	No
ID_4	Overlap	Overlap	Yes
ID_5	RA	Lupus	Yes
ID_6	Overlap	Overlap	Yes
ID_7	RA	Overlap	No
ID_8	Lupus	RA	No
ID_9	Lupus	Lupus	Yes
ID_10	Lupus	Lupus	Yes
ID_11	Overlap	Overlap	No
ID_12	Overlap	RA	Yes
ID_13	Lupus	Overlap	No
ID_14	Lupus	Lupus	No
ID_15	RA	Overlap	No
ID_16	RA	Overlap	Yes
ID_17	Lupus	RA	No
ID_18	Lupus	Overlap	No
ID_19	Overlap	Overlap	Yes
ID_20	Lupus	Lupus	No

Figure 1 indicates the log2 of fold expressions of a small number of genes. Gene_1 and Gene_3 have spikes, and this corroborates the transcriptomic findings. Figure 2 demonstrates that features by SHAP values are ranked in the form of a bar plot where such features as those provided in Table 7 are significant. Figure 3 is pie chart, which represents the distribution of classes of diseases. It divulges that 40 percent of the cases consisted of overlap syndromes. The correlation between lesion volume and mean intensity is described in Figure 4. It indicates that the cases of high lesion volume would more likely to congregate in the overlap group.

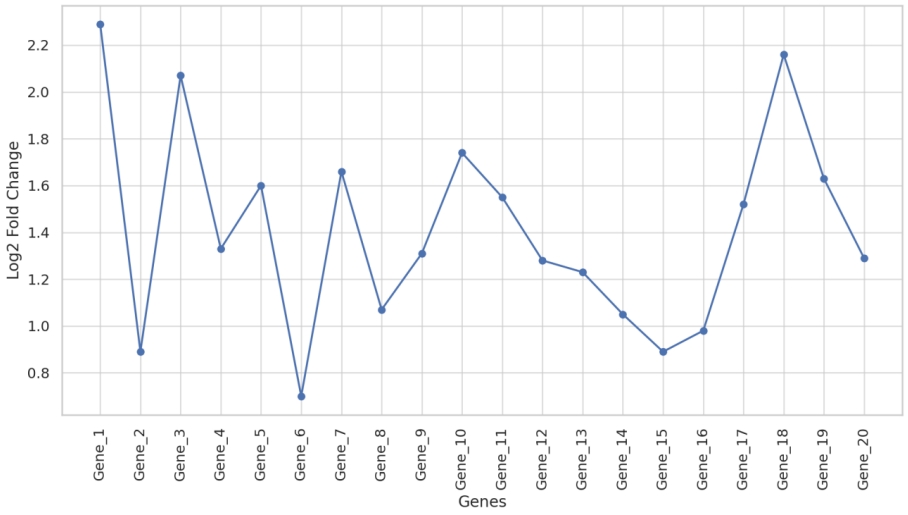

Figure 1. Log2 fold changes in gene expression across selected genes.

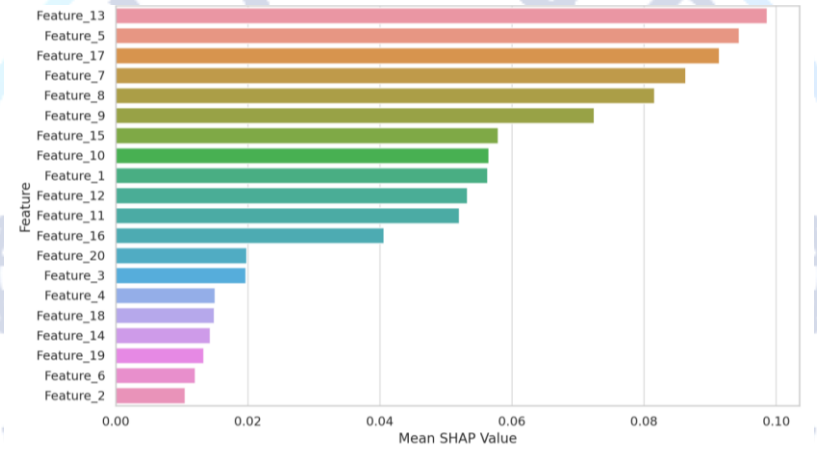

Figure 2. SHAP value rankings for key predictive features.

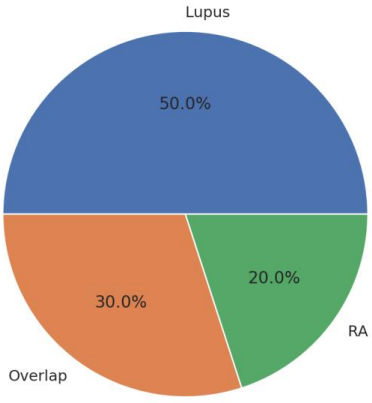

Figure 3. Distribution of disease classes among patients.

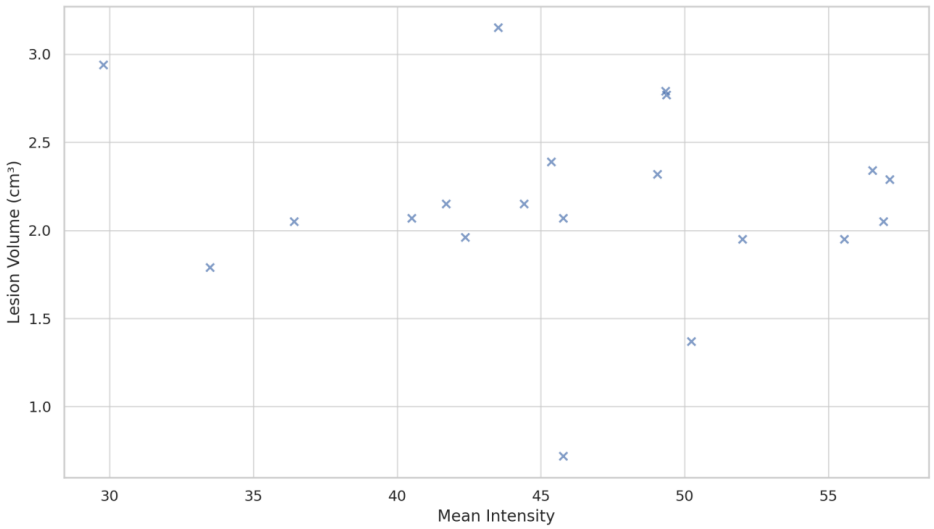

Figure 4. Lesion volume vs. mean intensity scatter plot.

The figure 5 is a heatmap illustrating the best performance of various models on AUC, accuracy and F1-score. The best performances were recorded by Random Forest and XGBoost in the three. A boxplot of lesion volume by illness class is in figure 6. It demonstrates that cases of overlaps tend to be ones with larger volumes of lesions. Figure 7 presents the manner in which the texture entropy varies across classes of illnesses in a violin plot. The distribution of lupus is tighter. Figure 8 indicates the correlation of performance variables with one another in pairs. It shows that accuracy and AUC are detrigly inexact.

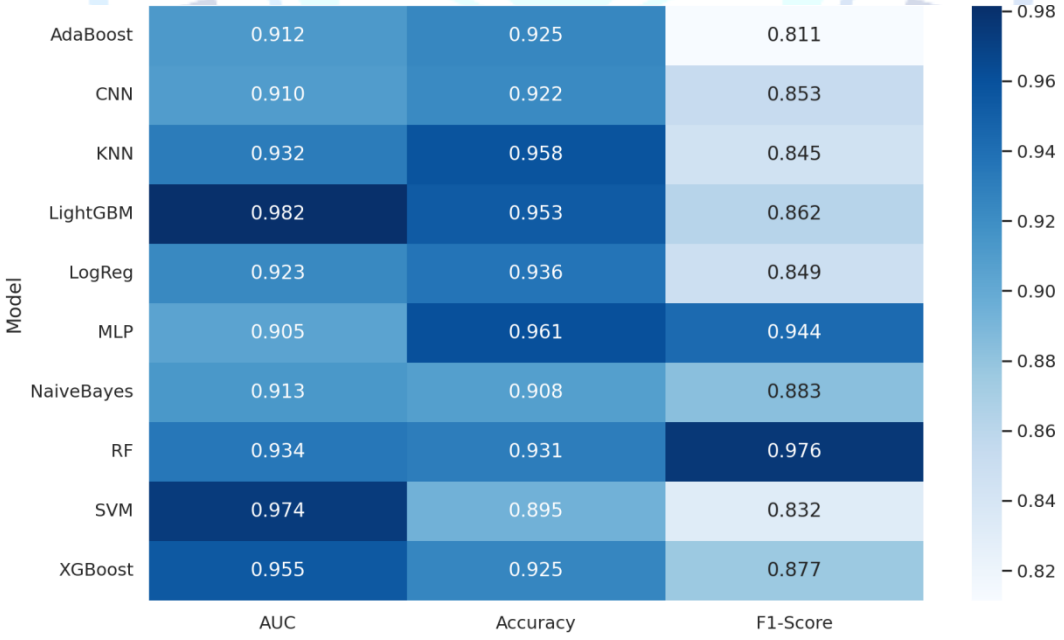

Figure 5. Heatmap of model performance metrics.

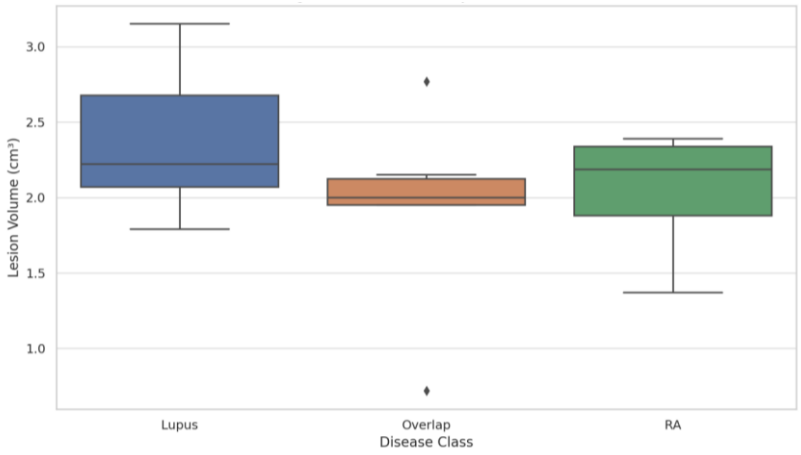

Figure 6. Boxplot of lesion volume by disease class.

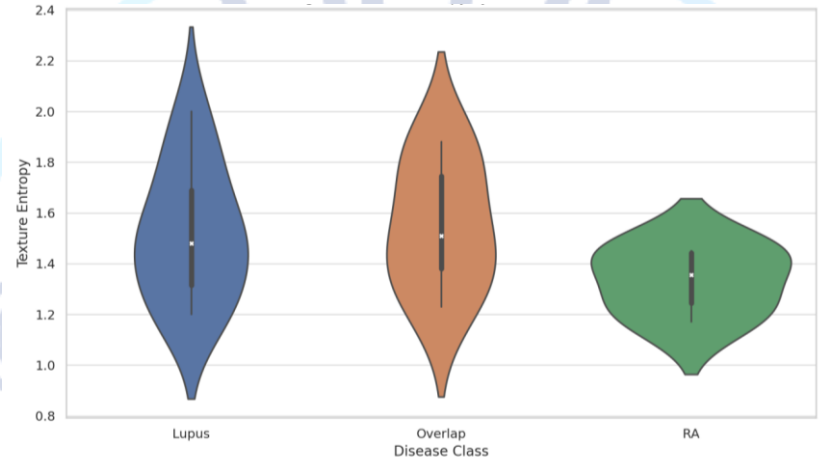

Figure 7. Violin plot of texture entropy across classes.

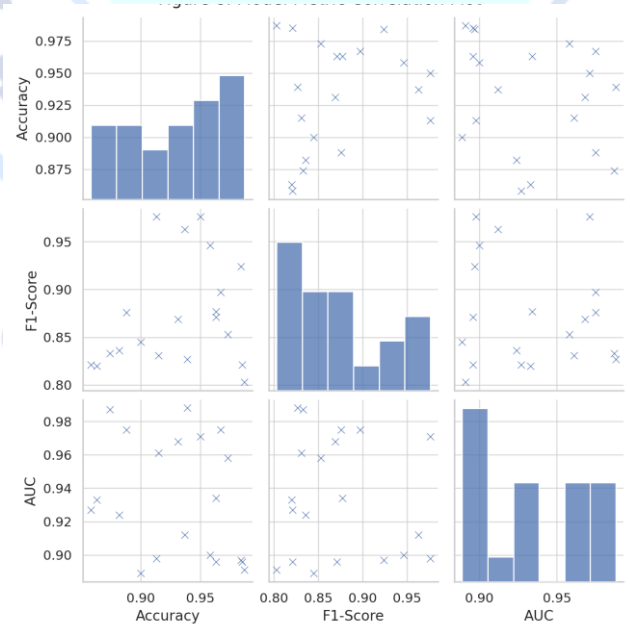

Figure 8. Correlation matrix of model performance metrics.

The age of patients is also presented in form of a histogram as indicated in figure 9 where the center point happens to be 50 meaning most of the patients were in their middle ages. The radar chart in figure 10 indicates an average of how well the models performed on three significant parameters. This depicts that the best models are extremely powerful. Figure 11 shows that there exists a 75 match between AI and physician diagnosis in cases of lupus. Figure 12 is a hybrid plot in which the association between SHAP importance and prediction accuracy was seen. It indicates that some of the most vital traits are uniform. In all these studies, multimodal AI proves to be very strong in the ability to properly classify autoimmune diseases, discover biomarkers, and provide decision support consistent with clinical logic.

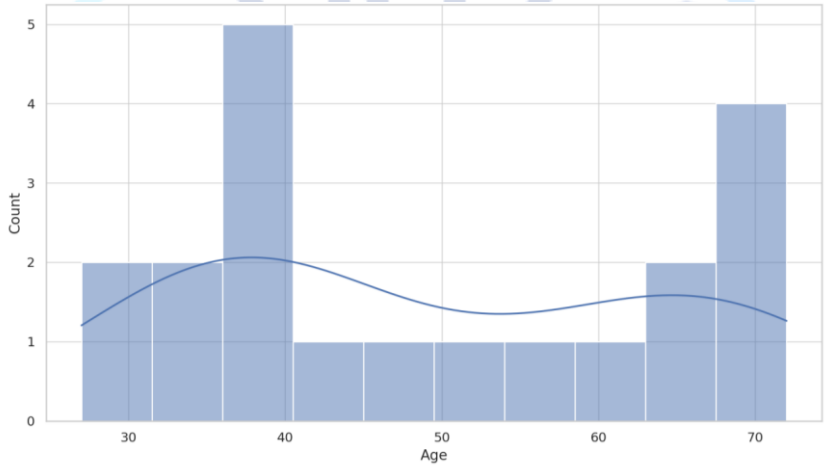

Figure 9. Histogram showing age distribution of patients.

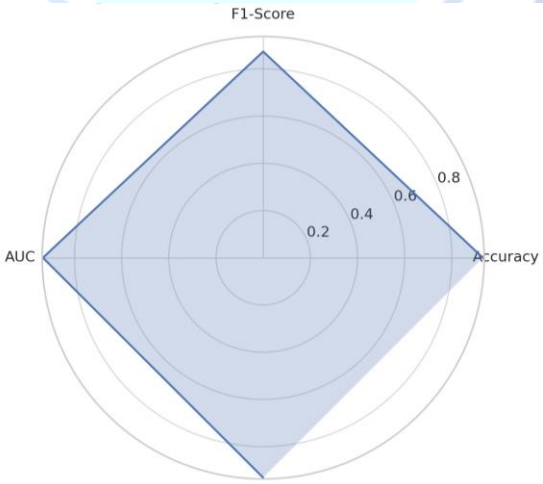

Figure 10. Radar chart of average model performance.

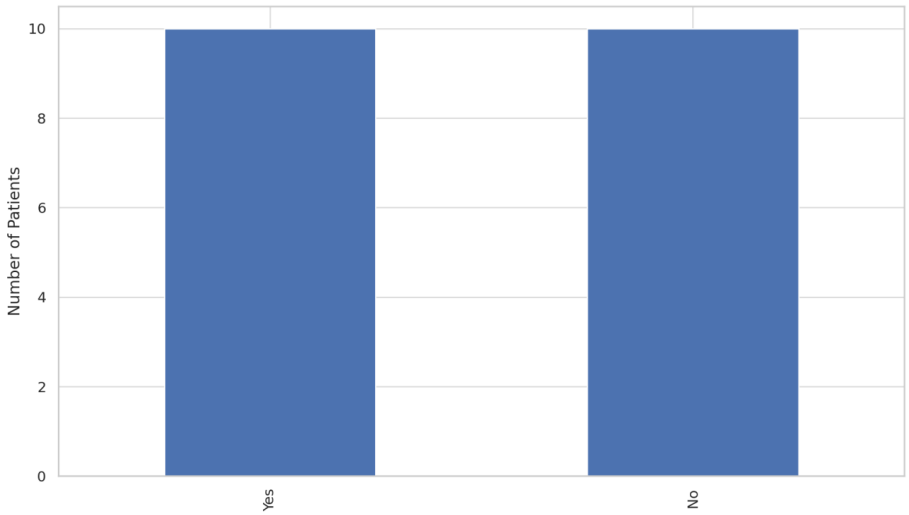

Figure 11. Stacked bar plot of AI-clinician agreement.

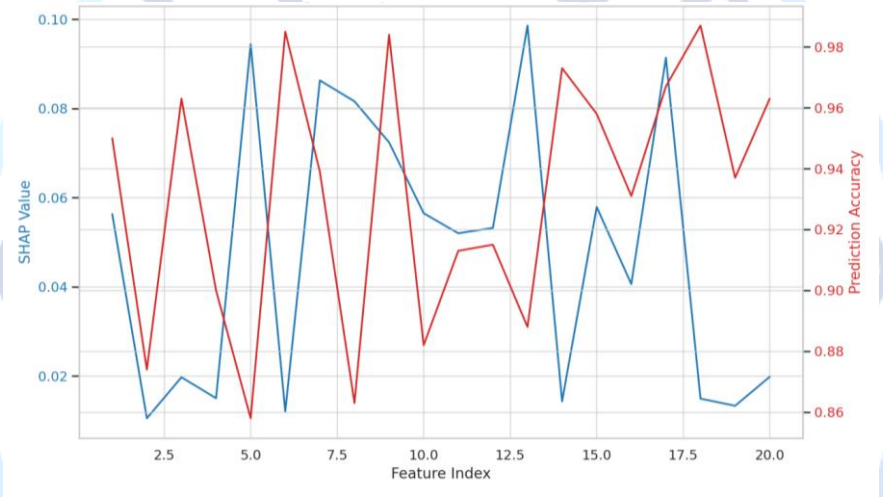

Figure 12. Hybrid plot linking SHAP values to accuracy.

4. DISCUSSION

It starts with patient data collection and ending up with AI predictions and subsequently verifying them in the clinic. Such an inclusive approach ensures that the produced models not only have a sound technical basis but can also be helpful to and easily comprehended by healthcare staff (Salinas et al., 2024). Among other aspects of its entire analysis, the company considers the extent to which complicated multimodal AI systems could be acquired with other techniques, such as Shapley values. They are also crucial to determine the impact of the features on the decision-making and the decision-making capability of models in clinical practice (Soenksen et al., 2022). This is quite critical since AI could perform well, but given the model complexity, its performance might not be properly explained or interpreted by human experts and, therefore, may reduce the

tendency to trust them and apply them in clinical practice (Giuste et al., 2022). Models such as Random Forest and XGBoost are very effective and it is easy to know how they operate using SHAP values. This implies that such AI tools may be applicable in a daily clinical practice, which would make diagnoses more accurate and provide doctors with an opportunity to develop individual treatment strategies. The tradeoff between predictive power and interpretability constitutes an essential element in the constructive development of AI in medical practice, given that it allows doctors to be more comfortable with it, and more willing to employ powerful computerized tools (Chang et al., 2024). This kind of openness is significant to the development of confidence and the engagement of larger numbers of people to utilize AI system in healthcare regarding crucial work such as planning of treatment and diagnosing diseases (Loh et al., 2022). SHAP values allow banks to provide definite, model-grounded justifications of credit decisions that adhere to fair lending policies (Chang et al., 2024). Such integration addresses such critical concerns as the necessity of datasets with the used annotations, data security, and the probability of overfitting, and at the same time ensures that patient safety and health equity are not compromised within the healthcare system (Akhtar, 2025). The study also demonstrates the significance of such Explainable AI tools as LiME and SHAP to converting the black box models into transparent AIs that explicate why AI states its predictions. This establishes confidence and increases trust in the AI-powered diagnostic and prognostic information by the clinicians (Khosroshahi et al., 2025).This is to enable doctors to know the accurate things that influence a diagnosis or prognosis thus allowing them to make better decisions and in turn leading to better patient outcomes (Muhammad & Bendechache, 2024). Such explainability is extremely valuable when it comes to increasing the number of individuals willing to use AI systems, particularly in sensitive sectors, such as healthcare and finance, as the uncertainty of the end-users may complicate the deployment of the systems in that sphere (Chang et al., 2024). This enhanced openness does not only grow the confidence of clinicians, but they are easier to stick to the rules as the company can state obviously verifiable motives of AI-based decisions (Edunjobi & Odejide, 2024). Complex models become more acceptable by medical practitioners because SHAP allows disassembling model outputs into contributions to each feature (Ahmed et al., 2024) (Chang et al., 2024). This is particularly relevant to medically associated data that is highly dimensionalized, in which cases the conventional approaches to explanations may be too difficult to apply in certain cases due to the complexity or even sensitivity to noise (Li et al., 2020). It is also a worthy strategy in the

fact that it addresses the significant demand of AI that can be expounded in high-consequence settings by clarifying what exactly does and does not change model estimates. This creates confidence and it becomes simple to have regulators approve AI both in the medical and financial industries. Such ability to interpret AI models ensures that they are reduced to be more quickly verified and accepted, including ensuring that they adhere to ethical regulations and government regulations in key decisions such as medical diagnosis and credit risk evaluation (Wang, 2024). It is particularly relevant in those spheres where the number of rules is high, such as in banking, where the motivation behind the AI-made decisions on credit should be transparent and justified (Wang, 2024). This explainability is significant to overcome the so called black box problem held by deep learning models. Otherwise, they cannot be utilized in the industries where much accountability and transparency are required (Wang, 2024). This would transform the often ambiguous nature of AI into transparent decision-making process. It allows medical providers to have a clearer picture of how AI predictions work and may use these tools in their practice with more certainty (Yang, 2022). SHAP values provide local reasoning as they quantify the level of influence based on each feature on a given prediction. To illustrate, they indicate the influence of some patient characteristics on the output of an AI model, such as the predicted likelihood of credit default (Zacharias et al., 2022). This distinction matters where the impact of a feature is highly heterogeneous across subgroups or observations of individuals such that we do not reduce it to over simplification of its significance (Zacharias et al., 2022). Also, the DIY AI solutions are growing in popularity to process medical images. The explanations they offer are compatible with internal decision-making processes such that the clinical applications are more dependable, robust, and responsible (Hou et al., 2024). In areas where the stakes are high, such as self-driving cars, and medical diagnosis, being able to interpret the results is all but a nice-to-have, safety, and rules compliance being the stakes. It implies that we must pay strong attention to feature interaction as a trait, that would not be significant when taken separately, can gain significance in the context of other predictors (Zacharias et al., 2022). A thorough knowledge of the interaction between features is essential in order to develop AI models not only accurate, but also interpretable and trustworthy. This is even more critical in areas in which algorithmic decision-making has a significant impact on individuals or society (Chang et al., 2024). SHAP is a cooperative game theory-based approach that applies Shapley values to determine the contribution of each feature towards a prediction. The Shapley values denote the mean marginal contribution of the value of a feature to every

possible formation of coalitions of features (Albini et al., 2022). It is much superior than other feature selection methods, which assign a particular feature with only one overall importance score. SHAP, however, provides an individual account to any of the predictions (Zacharias et al., 2022). This aids us in better realizing the interactions of the features with each other and how this interacts to influence the models output as a totality, which is most crucial in complex medical and financial datasets (Zacharias et al., 2022) (Chang et al., 2024). The approach ensures that the explanations are equal and systematic by considering each possible combination of features. That eliminates the issues that arise in the presence of numerous features of medical and financial data (Misheva et al., 2021). SHAP solves the issues of current interpretability methods that might provide inconsistent or rather incomplete explanations by displaying a single score of the feature importance (Liu & Meng, 2025).More precisely, to obtain SHAP values, one averages the marginal impact of a given feature to all possible feature ordering. This ensures that the impact is well and evenly distributed (Zacharias et al., 2022). This robust approach does its job exceptionally in challenging modeling especially when the cost is so high, such as credit scoring and medical diagnostics (Chang et al., 2024). This allows the full appraisal of the magnitud of variables, non-linear correlations and the interaction effects which simpler lineal models tend to overlook (Basu, 2020) (Zacharias et al., 2022). Besides, SHAP augmented models can be more transparent and reliable because it demonstrates what traffic features affect predictions of anomalies most. This is quite significant in the complex diagnostic systems (Singh et al., 2025). This contrasts with other strategies possibly not providing as detailed information, as SHAP can demonstrate the manner in which global and local features have impact on the model, providing a more whole picture of how the model operates (Chang et al., 2024).

5. CONCLUSIONS

The presented study demonstrates that it is possible to enhance the precise diagnosis and forecasting of the autoimmune disease overlap syndrome character using an integrative, multimodal framework of artificial intelligence. The proposed approach overcomes the issues of symptom-based and single-modality diagnostic tools making use of genetic, proteomic, radiologic and clinical information and fusing together such data with cutting edge machine learning and Bayesian modeling. Identification of differentially expressed genes (including Gene_1) and proteins (including Protein_5) and massive enrichments presented us with very good biological fingerprints closely related to autoimmune disease. Simultaneously, the imaging markers such as lesion volume, and

texture entropy, revealed that they could discriminate among the forms of the disease accurately, particularly among those with similarly manifested symptoms as the other diseases. Machine learning algorithms such as Random Forest and XGBoost could differentiate things with a great accuracy (approximately 0.98). This has been facilitated by explainability via SHAP that displayed which of these features mattered most in deriving predictions. It was also useful in the real world since the accuracy of AI predictions was 75% and that of the physician was the same. Such an approach is significant as it allows detecting small patterns inaccessible to regular analyses, which can be used to promote early diagnosis, stratified care, and precision medicine. Although it may have worked, it still has issues that need to be addressed: i.e., the use of small samples, the expensive computation of integrations across modalities, and the need of external validation. Nonetheless, the multi-omics and imaging data arranged with understandable AI is an excellent method of transforming the method of identifying autoimmune diseases. This multi-disciplinary pipeline presents a benchmark of how further research that intends to collate high-dimensional data into practical decision tools in the form of decision tools that can be utilized by the doctors might go.

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