UniCas Research Initiatives in Medicine and Healthcare

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Abstract

The Artificial Intelligence and Data Analysis Laboratory (AIDA Lab) at the University of Cassino and Southern Lazio (UniCas) has over two decades of experience in advancing artificial intelligence research. The group specialises in Machine Learning, Pattern Recognition, and Deep Learning, with a strong focus on real-world applications, particularly in healthcare. A major research direction involves the design and development of Computer-Aided Diagnosis systems to support prevention, diagnosis, and monitoring of various medical conditions, including Neurodegenerative Diseases, breast cancer, cervical cancer, and motor-related disorders. The AIDA Lab focuses on handwriting analysis to assess cognitive decline and learning disorders, combining static image evaluation with dynamic signal processing. In neurodegenerative research, 3D MRI is used for early Alzheimer's detection. For breast and cervical cancer, image-based methods identify subtle lesions like microcalcifications and cellular changes, supported by the lab's GravityNet architecture for small lesion detection. Gait and movement analysis for Parkinson's disease is also explored, using deep learning models such as cascaded boosting and CNNs to ensure accurate assessments in real-world settings.

Keywords

Neurodegenerative Diseases, Handwriting, 3D Image Analysis, Breast Cancer, Cervical Cancer, Movement Analysis

1. Neurodegenerative Diseases

Neurodegenerative diseases (NDS) are progressive disorders characterised by the gradual disruption of the structure or function of brain cells, neurons. Among the most common are Alzheimer's disease (AD), Parkinson's disease (PD), and Lewy Body Disease (LBD). These conditions have been increasing in recent years due to population growth and ageing, representing a public health burden worldwide. AD is the most common form of dementia, marked by memory loss, cognitive decline, and behavioural changes. PD [1] is primarily known for its motor symptoms such as tremors, rigidity, and bradykinesia, though it can also involve non-motor symptoms, including cognitive impairment. LBD [2] lies at the intersection of these two conditions, characterised by the presence of Lewy bodies, abnormal protein aggregates in the brain, and symptoms that overlap with AD and PD. Though these disorders share some symptoms, they have different causes. Understanding and distinguishing these disorders remains a clinical challenge, moreover, they lack a resolutive cure. An early and accurate diagnosis is essential for patient care, treatment, and therapeutic intervention.

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1.1. Handwriting Analysis for Neurological Disorder Detection

Handwriting is a complex activity that relies on cognitive, motor, and planning abilities. It engages memory, language proficiency, executive skills, and attentional control, making it particularly sensitive to neurological and developmental changes. Thus, handwriting analysis has emerged as a valuable and non-invasive tool for the early detection and monitoring of brain disorders, including neurodegenerative conditions such as AD. Alterations in handwriting, such as changes in linguistic complexity, word choice, dynamics, motor execution, and spatial organisation, can reflect subtle impairments in cognition, memory, and fine motor control. These changes offer early and objective indicators of cognitive decline or learning difficulties, supporting timely diagnosis and intervention. Recognising this potential, the AIDA Lab initiated a structured handwriting acquisition campaign in 2018, based on an experimental protocol comprising 25 writing tasks designed to evaluate cognitive and motor functions [3]. The study involved 174 participants, including 89 with AD and 85 healthy controls, who completed the tasks using a graphic tablet. This device allowed participants to write with a standard-looking pen on A4 paper while simultaneously recording dynamic information. The resulting data were processed to create multiple datasets, including offline scanned images [4], synthetic binary and RGB images [5], as well as collections of features, comprising personal, lognormal [6], and stroke or task dynamic and static features. Our research has advanced along two complementary analytical paths: image-based analysis and dynamic feature analysis. In the context of image-based AD detection, we developed several Artificial Intelligence (AI) approaches using the offline image dataset. Initial investigations [7] examined the effectiveness of various classifier combination strategies to enhance diagnostic accuracy by exploiting handwriting data collected from multiple tasks. The results demonstrated that fusion techniques, particularly the Ranking Diversity approach, significantly outperformed single classifiers, highlighting the benefit of combining information from diverse writing activities. Further exploration [8] involved the application of different deep learning architectures to classify handwriting images. We proposed a three-stage framework involving: task-level classification, automatic selection of the most informative tasks, and fusion of predictions to produce a subject-level decision. This framework led to improved diagnostic performance, highlighting the relevance of integrating multiple tasks and advanced models. Regarding dynamic handwriting analysis, we developed several AI methods to support AD diagnosis using feature datasets. In one study [9], we presented a two-stage multimodal approach using static and dynamic handwriting features, fused with personal ones. For each handwriting task, a machine learning (ML) classifier was trained, producing 25 predictions per subject. In the second stage, a Bayesian Network (BN) modelled the statistical dependencies between these task-level predictions and the AD label. Using the BN's Markov Blanket, a subset of informative tasks was selected, and their predictions were combined. This multimodal combination outperformed single-task classifiers and standard ensemble methods, representing the first study to use a BN for combining classifier outputs in handwriting-based AD detection. Building upon this foundation, we addressed a key limitation in subsequent research [10]. Traditional feature aggregation methods often obscure subtle diagnostic indicators, so we shifted our analytical approach to individual handwriting strokes as fundamental movement units. This stroke-level analysis extracted dynamic and static features from both on-paper and in-air movements, preserving critical kinematic details that aggregate methods typically lose. The ML framework comprised multiple classification strategies alongside robust feature selection techniques to identify the most discriminative stroke-level characteristics. To optimise performance, we developed novel ensemble methods that captured variations at the stroke level while utilising the unique advantages of various classifiers. We applied SHAP to explain model decisions, identifying specific tasks and stroke patterns that consistently provided stronger indicators of AD.

1.2. Advances in 3D MRI Analysis, Explainability, and Unsupervised Learning

Magnetic Resonance Imaging (MRI) is a non-invasive technique crucial for diagnosing and monitoring neurodegenerative diseases like Alzheimer's (AD). High-resolution 3D scans reveal structural brain changes, such as atrophy, especially in the hippocampus, that correlate with tau buildup and cognitive decline, making MRI essential for early detection. Diffusion models have recently advanced generative modelling in images, but their potential as unsupervised representation learners in medical imaging remains underexplored. Their structured latent spaces could support robust, semantically meaningful embeddings for downstream tasks like disease classification. Deep learning has already transformed MRI analysis. Earlier approaches relied on hand-crafted features and classical machine learning, while CNNs and Vision Transformers now enable automatic feature extraction. 3D CNNs capture spatial context but need large labelled datasets. As a workaround, many use 2D slicing along anatomical planes (axial, coronal, sagittal), trading spatial coherence for efficiency. Interpretability remains a key barrier to clinical deployment. Clinicians need models to provide transparent, region-specific explanations. Inspired by how radiologists read MRIs slice-by-slice, we developed AXIAL [11], a soft-attention model that processes 2D slices and generates 3D attention maps, enabling voxel-level localisation of AD-related changes. AXIAL consistently highlights clinically relevant regions like the hippocampus and amygdala, outperforming post hoc methods like Grad-CAM in focus and reproducibility. Building on this interpretability foundation, we introduced Latent Diffusion Autoencoders (LDAE)[12], a diffusion-based framework for unsupervised learning in 3D imaging. Operating in a compact latent space, LDAE enables 20× faster inference and high-fidelity reconstruction. Despite no labels, it learns semantically rich embeddings that support tasks like AD classification and age regression. It also enables counterfactual generation: transforming an AD brain scan into a plausible cognitively normal version while preserving subject-specific anatomy, offering insights into disease progression and potential interventions.

2. Medical Image Analysis

2.1. Advances in AI-based Detection and Diagnosis in Breast Imaging

Breast cancer remains the most commonly diagnosed cancer among women and a leading cause of cancer-related mortality. Early detection significantly increases survival rates, and various imaging modalities, like mammography and Digital Breast Tomosynthesis (DBT), are central to screening and diagnostic efforts. However, each modality presents unique challenges. While mammography enables the identification of early markers such as microcalcifications, its 2D nature can hinder lesion visibility due to tissue overlap. DBT addresses this by offering 3D imaging, which enhances lesion conspicuity but increases interpretation complexity and time. Recent developments in artificial intelligence, especially deep learning, have shown great promise in automating and improving various tasks in breast imaging, such as lesion detection, classification, and localisation [13, 14, 15, 16]. Our first contribution focuses on the detection of calcification clusters in mammography, a key early sign of malignancy. We propose the use of Swin Transformers as a powerful backbone for feature extraction, capturing both local and global contextual information via a hierarchical self-attention mechanism [17]. In a comprehensive study using the large-scale OMI-DB dataset, we compared transformer-based backbones with traditional CNNs (including ResNet, EfficientNet, and ConvNeXt) across three detection heads (RetinaNet, RepPoints, and Deformable DETR). The Swin-B model, paired with the RepPoints head, outperformed all convolutional counterparts, achieving a sensitivity of 80.67% at 0.1 false positives per image and demonstrating statistically significant superiority. Notably, the transformer-based model showed strong generalisation to the external InBreast dataset without retraining, highlighting its robustness and potential for real-world deployment. The second line of work addresses the classification of DBT volumes and efficient visual summarisation of 3D breast scans. Given the volumetric nature of DBT, interpretation can be time-consuming and mentally taxing. We introduce a novel neural architecture that jointly classifies DBT scans as benign or malignant and generates a synthetic 2D projection containing diagnostically relevant content. This is accomplished by computing a 3D saliency map that identifies discriminative regions within the DBT volume. A 2D diagnostic image is then produced by sampling a surface through this saliency space, effectively collapsing the 3D structure into an interpretable 2D representation. Remarkably, a standard CNN trained on these synthetic 2D images achieves performance comparable to models trained directly on full 3D volumes. We trained the model on the OMI-DB dataset and evaluated it on the BCS-DBT dataset, demonstrating strong generalization capabilities.

2.2. Computational Cytology for Cervical Cancer Screening

Computational cytology focuses on the automated analysis of microscopic images to support early cancer diagnosis and improve consistency in clinical decision-making. Among the most common applications, cervical cancer screening remains a major public health priority, as the disease is largely preventable through the early detection of precancerous cellular changes. Conventional screening methods, such as Pap smears or liquid-based cytology, rely on the manual examination of slides by trained cytotechnologists and pathologists. However, this process is time-consuming, subjective, and prone to diagnostic variability. The presence of overlapping cells, inconsistent staining patterns, imaging artefacts, and a wide range of nuclear morphologies makes the manual assessment of cytological samples particularly challenging, often leading to false negatives or false positives. Computational cytology applies AI-driven techniques to extract and analyze morphological features automatically. In particular, the detection and segmentation of cell nuclei represent critical steps for the identification of atypical cells and for the development of accurate diagnostic pipelines. The AI-driven deep-learning tools standardize cytological evaluation, reduces diagnostic errors, and alleviates the workload of clinical professionals. These technologies not only enhance diagnostic reproducibility but also offer scalable solutions to support population-wide screening programs, especially in resource-constrained settings. In this context, the novel detection model GravityNet [18] has been employed to address the inherent complexity of cytological images, demonstrating strong capabilities in detecting nuclei under challenging conditions such as dense cellularity, overlapping structures, and significant morphological variability [19]. By reliably identifying diagnostically relevant features, GravityNet contributes to the development of robust and scalable AI pipelines for cervical cancer screening.

3. Movement Analysis

Gait Analysis (GAn) is an objective assessment of an individual's walking abilities and stands as an essential component of comprehensive motor assessment. It empowers healthcare professionals to make informed clinical decisions and devise targeted rehabilitation strategies aimed at enhancing gait functions. In standard clinical practice, GAn is typically performed by healthcare professionals through a combination of standardised questionnaires, functional tests, and direct visual observation of the patient's walking pattern. The identification of gait irregularities often relies on the subjective quantification of spatio-temporal parameters, alongside detailed kinematic and kinetic evaluations. The advent of various advanced technologies has fundamentally transformed the objective analysis of human motion. Among these, optical motion capture systems are recognised for their superior accuracy and precision in assessing joint kinematics, establishing them as the "gold standard" within laboratory environments. Such systems facilitate the precise acquisition of motion data through reflective markers placed at strategic anatomical locations, which are then tracked by multiple cameras. However, the deployment of these technologies is largely confined to specialised gait laboratories and research settings. This limitation stems from several factors, including their substantial cost, the need for specialised technical expertise, and the extensive time required for setup, all of which hinder their widespread adoption in routine clinical practice.

3.1. The Emergence and Advancement of Markerless Motion Analysis

Markerless Motion Analysis (MMA) addresses the limitations of marker-based systems by eliminating the need for physical markers, significantly reducing preparation time and enabling GAn outside traditional lab settings. This makes MMA valuable for biomechanical evaluations in diverse environments, from sports to assessing patients with neuromotor impairments. Machine learning (ML) approaches, especially Convolutional Neural Networks (CNNs), are central to MMA for precise human pose estimation. Our work, Poseidon, exemplifies this by using a Vision Transformer (ViT)-based architecture for enhanced multi-frame pose estimation, bridging the gap between rigorous lab analysis and practical everyday assessment[20].

3.2. Clinical Applications and Future Directions

MMA's practical utility spans various clinical areas. In knee osteoarthritis, our research demonstrated its effectiveness for gait classification using MMA-extracted spatio-temporal and kinematic features[21]. For Parkinson's Disease (PD), MMA provides crucial insights into how the disease affects mobility, aiding diagnosis and monitoring. ML algorithms classify disease presence or stage based on gait features, with a focus on explainability to build trust in clinical interpretation. MMA systems facilitate continuous, real-time monitoring of PD patients, enabling personalised rehabilitation. Current research aims to enhance the biomechanical interpretability of MMA data by accurately mapping 3D pose estimations to anatomical landmarks, transitioning from joint centre estimations to a deeper understanding of segmental kinematics and kinetics. This progress is vital for refining clinical assessments, developing targeted interventions, and improving patient outcomes and athletic performance.

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Declaration on Generative AI

During the preparation of this work the authors used ChatGPT in order to improve language and readability. After using this tool/service, the authors reviewed and edited the content as needed and take full responsibility for the content of the publication.

References

[1] C. Vicidomini, F. Fontanella, T. D'Alessandro, G. N. Roviello, C. De Stefano, F. Stocchi, M. Quarantelli, M. F. De Pandis, Resting-state functional mri metrics to detect freezing of gait in parkinson's disease: a machine learning approach, Computers in Biology and Medicine 192 (2025) 110244.

[2] T. D'Alessandro, C. De Stefano, F. Fontanella, O. Pustovalova, Advancements and challenges in artificial intelligence for lewy body disease research: A brief survey, in: S. Palaiahnakote, S. Schuckers, J.-M. Ogier, P. Bhattacharya, U. Pal, S. Bhattacharya (Eds.), Pattern Recognition. ICPR 2024 International Workshops and Challenges, Springer Nature Switzerland, Cham, 2025.

[3] N. Cilia, C. De Stefano, F. Fontanella, A. Scotto di Freca, An experimental protocol to support cognitive impairment diagnosis by using handwriting analysis, Procedia Computer Science 141 (2018) 466 – 471.

[4] N. Dalia Cilia, T. D'Alessandro, C. De Stefano, F. Fontanella, Offline handwriting image analysis to predict alzheimer's disease via deep learning, in: 2022 26th International Conference on Pattern Recognition (ICPR), 2022, pp. 2807–2813.

[5] N. D. Cilia, T. D'Alessandro, C. De Stefano, F. Fontanella, Deep transfer learning algorithms applied to synthetic drawing images as a tool for supporting alzheimer's disease prediction, Machine Vision and Applications 33 (2022) 49.

[6] T. D'Alessandro, C. Carmona-Duarte, C. De Stefano, M. Diaz, M. A. Ferrer, F. Fontanella, A machine learning approach to analyze the effects of alzheimer's disease on handwriting through lognormal features, in: A. Parziale, M. Diaz, F. Melo (Eds.), Graphonomics in Human Body Movement. Bridging Research and Practice from Motor Control to Handwriting Analysis and Recognition, Springer Nature Switzerland, Cham, 2023, pp. 103–121.

[7] T. D'Alessandro, C. De Stefano, F. Fontanella, E. Nardone, C. D. Pace, From handwriting analysis to alzheimer's disease prediction: An experimental comparison of classifier combination methods, in: E. H. Barney Smith, M. Liwicki, L. Peng (Eds.), Document Analysis and Recognition - ICDAR 2024, Springer Nature Switzerland, Cham, 2024, pp. 334–351.

[8] G. Lozupone, E. Nardone, C. D. Pace, T. D'Alessandro, Transformers and cnns in neurodiagnostics: Handwriting analysis for alzheimer's diagnosis, in: A. Antonacopoulos, S. Chaudhuri, R. Chellappa, C.-L. Liu, S. Bhattacharya, U. Pal (Eds.), Pattern Recognition, Springer Nature Switzerland, Cham, 2025, pp. 447–463.

[9] E. Nardone, T. D'Alessandro, C. De Stefano, F. Fontanella, A. Scotto di Freca, A bayesian network combiner for multimodal handwriting analysis in alzheimer's disease detection, Pattern Recognition Letters 190 (2025) 177–184.

[10] E. Nardone, C. De Stefano, N. D. Cilia, F. Fontanella, Handwriting strokes as biomarkers for alzheimer's disease prediction: A novel machine learning approach, Computers in Biology and Medicine 190 (2025) 110039.

[11] G. Lozupone, A. Bria, F. Fontanella, F. J. Meijer, C. De Stefano, Axial: Attention-based explainability for interpretable alzheimer's localized diagnosis using 2d cnns on 3d mri brain scans, arXiv preprint arXiv:2407.02418 (2024).

[12] G. Lozupone, A. Bria, F. Fontanella, F. J. Meijer, C. De Stefano, H. Huisman, Latent diffusion autoencoders: Toward efficient and meaningful unsupervised representation learning in medical imaging, arXiv preprint arXiv:2504.08635 (2025).

[13] M. Cantone, C. Marrocco, F. Tortorella, A. Bria, Convolutional networks and transformers for mammography classification: an experimental study, Sensors 23 (2023) 1229.

[14] M. Cantone, C. Marrocco, F. Tortorella, A. Bria, Learnable dog convolutional filters for microcalcification detection, Artificial Intelligence in Medicine 143 (2023) 102629.

[15] A. S. Betancourt Tarifa, C. Marrocco, M. Molinara, F. Tortorella, A. Bria, Transformer-based mass detection in digital mammograms, Journal of Ambient Intelligence and Humanized Computing 14 (2023) 2723–2737.

[16] M. Ryspayeva, A. Bria, C. Marrocco, F. Tortorella, M. Molinara, Transfer learning in breast mass detection and classification, Journal of Ambient Intelligence and Humanized Computing 15 (2024) 3587–3602.

[17] M. Cantone, C. Marrocco, F. Tortorella, A. Bria, Transformer models for enhanced calcifications detection in mammography, in: International Conference on Pattern Recognition, Springer, 2024, pp. 17–33.

[18] C. Russo, A. Bria, C. Marrocco, GravityNet for end-to-end small lesion detection, Artificial Intelligence in Medicine (2024) 102842.

[19] C. Russo, Y. B. Tanriverdi, A. Bria, C. Marrocco, A pixel-based anchor approach for nuclei detection in cervical cytology imaging, in: S. Palaiahnakote, S. Schuckers, J.-M. Ogier, P. Bhattacharya, U. Pal, S. Bhattacharya (Eds.), Pattern Recognition. ICPR 2024 International Workshops and Challenges, Springer Nature Switzerland, 2025, p. 268–278.

[20] C. D. Pace, A. M. De Nunzio, C. De Stefano, F. Fontanella, M. Molinara, Poseidon: A vit-based architecture for multi-frame pose estimation with adaptive frame weighting and multi-scale feature fusion, arXiv preprint arXiv:2501.08446 (2025).

[21] C. D. Pace, A. M. De Nunzio, C. De Stefrano, F. Fontanella, M. Molinara, Markerless machine learning approach for gait classification in knee osteoarthritis, in: International Conference on Pattern Recognition, Springer, 2024, pp. 116–128.