**Supplementary Materials**

**eTable 1:** Summary of Search Strategies and Retrieved Records

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| Target Database | Summary of Search Strategy  | Retrieved Articles |
| PubMed | (nanomedicine[tiab] OR "nano medicine"[tiab] OR nanotechnolog\*[tiab] OR "nanoscale medicine"[tiab] OR Nanomedicine [Mesh] OR "Nanotechnology"[Mesh] OR "photothermal theranostic"[tiab] OR "Theranostic Nanomedicine"[Mesh] OR nanoparticle\*[tiab] OR nanomaterial\*[tiab] OR nanostructure\*[tiab] OR “nano particle\*” [tiab] OR “nano material\*” [tiab] OR “nano structure\*” [tiab] OR "Nanostructures"[Mesh])("machine learning"[tiab] OR "deep learning"[tiab] OR "hierarchical learning"[tiab] OR "large language model\*"[tiab] OR Deep Learning[Mesh] OR Machine Learning[Mesh] OR "reinforcement learning"[tiab:~2] OR "federated learning"[tiab] OR "neural network\*"[tiab] OR "Large Language Models"[Mesh] OR Artificial Intelligence[Mesh] OR “artificial intelligence”[tiab] OR “machine prediction”[tiab] OR “predictive learning model\*”[tiab] OR “sentiment analysis”[tiab] OR “natural language processing”[tiab] OR “machine pattern analysis”[tiab])("multiple sclerosis"[tiab] OR "Alzheimer s"[tiab] OR Alzheimer[tiab] OR Alzheimers[tiab] OR "Parkinson s disease"[tiab] OR "Parkinsons disease"[tiab] OR "Parkinson disease"[tiab] OR "brain cancer\*"[tiab] OR "brain neoplasm\*"[tiab] OR "brain tumor\*"[tiab] OR "Parkinson Disease"[Mesh] OR "Alzheimer Disease"[Mesh] OR "Brain Neoplasms"[Mesh] OR "Multiple Sclerosis"[Mesh] OR "brain carcinoma\*"[tiab] OR "brain malignan\*"[tiab] OR "chariot disease"[tiab:~0] OR "disseminated sclerosis"[tiab] OR "insular sclerosis"[tiab] OR "sclerosis multiplex"[tiab] OR "idiopathic parkinsonism"[tiab] OR "Parkinson dementia complex"[tiab] OR "primary parkinsonism"[tiab])English[lang] (2014:2024[pdat)The final search query was created by combining all search terms #1, #2, #3, #4, and #5 with the 'AND' operator. | 43 |
| Scopus | Title-Abs-Key (nanomedicine OR "nano medicine" OR nanotechnolog\* OR "nanoscale medicine” OR "photothermal theranostic" OR nanoparticle\* OR nanomaterial\* OR nanostructure\* OR "nano particle" OR "nano material" OR "nano structure" OR "nano particles" OR "nano materials" OR "nano structures”)Title-Abs-Key ("machine learning" OR “deep learning" OR "hierarchical learning" OR "large language model” OR "large language models" OR (reinforcement W/2 learning) OR "federated learning" OR "neural network" OR "neural networks" OR "artificial intelligence" OR "machine prediction" OR "predictive learning model" OR "predictive learning models" OR "sentiment analysis" OR "natural language processing" OR "machine pattern analysis")Title-Abs-Key ("multiple sclerosis" OR "Alzheimer s" OR Alzheimer OR Alzheimers OR "Parkinson s disease" OR "Parkinsons disease" OR "Parkinson disease" OR "brain cancer" OR "brain neoplasm" OR "brain tumor" OR "brain cancers" OR "brain neoplasms" OR "brain tumors" OR "brain tumour" OR "brain tumours" OR "brain carcinoma" OR "brain malignancy" OR "brain carcinomas" OR "brain malignancies" OR "chariot disease" OR "disseminated sclerosis" OR "insular sclerosis" OR "sclerosis multiplex" OR "idiopathic parkinsonism" OR "Parkinson dementia complex" OR "primary parkinsonism")(LIMIT-TO (LANGUAGE, “English”))( LIMIT-TO ( PUBYEAR , 2024 ) OR LIMIT-TO ( PUBYEAR ,2023 ) OR LIMIT-TO ( PUBYEAR , 2022 ) OR LIMIT-TO ( PUBYEAR , 2021 ) OR LIMIT-TO ( PUBYEAR , 2020 ) OR LIMIT-TO ( PUBYEAR , 2019 ) OR LIMIT-TO ( PUBYEAR , 2018 ) OR LIMIT-TO ( PUBYEAR , 2017 ) OR LIMIT-TO ( PUBYEAR , 2016 ) OR LIMIT-TO ( PUBYEAR , 2015 ) OR LIMIT-TO ( PUBYEAR , 2014 ) )The final search query was created by combining all search terms #1, #2, #3, #4, and #5 with the 'AND' operator. | 166 |
| Embase | ('nanomedicine':ti,ab,kw OR 'nano medicine':ti,ab,kw OR 'nanotechnolog\*':ti,ab,kw OR 'nanoscale medicine':ti,ab,kw OR 'nanomedicine'/exp OR 'nanotechnology'/exp OR 'photothermal theranostic':ti,ab,kw OR 'theranostic nanomedicine'/exp OR 'nanoparticle\*':ti,ab,kw OR 'nanomaterial\*':ti,ab,kw OR 'nanostructure\*':ti,ab,kw OR 'nano particle\*':ti,ab,kw OR 'nano material\*':ti,ab,kw OR 'nano structure\*':ti,ab,kw OR 'nanomaterial'/exp)('machine learning':ti,ab,kw OR 'deep learning':ti,ab,kw OR 'hierarchical learning':ti,ab,kw OR 'large language model\*':ti,ab,kw OR 'deep learning'/exp OR 'machine learning'/exp OR ('reinforcement' NEAR/3 'learning'):ti,ab,kw OR 'federated learning':ti,ab,kw OR 'neural network\*':ti,ab,kw OR 'large language model'/exp OR 'artificial intelligence'/exp OR 'artificial intelligence':ti,ab,kw OR 'machine prediction':ti,ab,kw OR 'predictive learning model\*':ti,ab,kw OR 'sentiment analysis':ti,ab,kw OR 'natural language processing':ti,ab,kw OR 'machine pattern analysis':ti,ab,kw)('multiple sclerosis':ti,ab,kw OR 'alzheimer s':ti,ab,kw OR 'alzheimer':ti,ab,kw OR 'alzheimers':ti,ab,kw OR 'parkinson s disease':ti,ab,kw OR 'parkinsons disease':ti,ab,kw OR 'parkinson disease':ti,ab,kw OR 'brain cancer\*':ti,ab,kw OR 'brain neoplasm\*':ti,ab,kw OR 'brain tumor\*':ti,ab,kw OR 'Parkinson disease'/exp OR 'Alzheimer disease'/exp OR 'brain tumor'/exp OR 'multiple sclerosis'/exp OR 'brain carcinoma\*':ti,ab,kw OR 'brain malignan\*':ti,ab,kw OR 'chariot disease':ti,ab,kw OR 'disseminated sclerosis':ti,ab,kw OR 'insular sclerosis':ti,ab,kw OR 'sclerosis multiplex':ti,ab,kw OR 'idiopathic parkinsonism':ti,ab,kw OR 'parkinson dementia complex':ti,ab,kw OR 'primary parkinsonism':ti,ab,kw)[english]/lim [embase]/lim [2014-2024]/pyThe final search query was created by combining all search terms #1, #2, #3, #4 #5 and #6 with the 'AND' operator. | 418 |
| Web of Science: Core Collection | TS= (nanomedicine OR "nano medicine" OR nanotechnolog\* OR "nanoscale medicine” OR "photothermal theranostic" OR nanoparticle\* OR nanomaterial\* OR nanostructure\* OR "nano particle" OR "nano material" OR "nano structure" OR "nano particles" OR "nano materials" OR "nano structures")TS= ("machine learning" OR “deep learning" OR "hierarchical learning" OR "large language model” OR "large language models" OR (reinforcement W/2 learning) OR "federated learning" OR "neural network" OR "neural networks" OR "artificial intelligence" OR "machine prediction" OR "predictive learning model" OR "predictive learning models" OR "sentiment analysis" OR "natural language processing" OR "machine pattern analysis")TS=("multiple sclerosis" OR "Alzheimer s" OR Alzheimer OR Alzheimers OR "Parkinson s disease" OR "Parkinsons disease" OR "Parkinson disease" OR "brain cancer" OR "brain neoplasm" OR "brain tumor" OR "brain cancers" OR "brain neoplasms" OR "brain tumors" OR "brain tumour" OR "brain tumours" OR "brain carcinoma" OR "brain malignancy" OR "brain carcinomas" OR "brain malignancies" OR "chariot disease" OR "disseminated sclerosis" OR "insular sclerosis" OR "sclerosis multiplex" OR "idiopathic parkinsonism" OR "Parkinson dementia complex" OR "primary parkinsonism")(LA=("ENGLISH"))PY= (2014-2024)The final search query was created by combining all search terms #1, #2, #3, #4, and #5 with the 'AND' operator. | 60 |

**eTable 2:** Information collected for the 39 studies. The collected information was sectioned into different columns to identify the different applications of nanomedicine, ML, and DL and to categorize the studies into diagnostic, prognostic, therapeutic, and computational development.

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| Covidence Number | Application | Study ID | Title | Aim of study | Study design | Target Disease | Machine learning/Deep learning | Type of Nanomedicine/Nanotechnology | Models used | Learning techniques | Classification/Prediction/Other | Metrics (values) | Cross-validation | Other information | Population description | Purpose of the study | Impact of the study |
| 80 | Diagnostic / Biomarker | Broza *et al,* 2017 | Exhaled Breath Markers for Nonimaging and Noninvasive Measures for Detection of Multiple Sclerosis | To develop a rapid, simple, non-invasive, and relatively inexpensive point-of-care test approach for diagnosing Multiple Sclerosis (MS). | Diagnostic test accuracy study | Multiple sclerosis | Machine Learning | To analyze sensor array data from nanomaterial-based breath analyzersGas-chromatography linked with mass-spectrometry (GC-MS) and nanomaterial-based sensors (termed, NA-NOSE). Sensor arrays | Multilayer perception type (MLP-type) artificial neural networks (ANNs) | Supervised Learning | Classification: discriminate between individuals with multiple sclerosis (MS) and healthy controls based on the analysis of volatile organic compounds (VOCs) in their breath using gas-chromatography mass-spectrometry (GC-MS) and a nanomaterial-based sensor array1. Blinded sets showed 95% positive predictive value (PPV) between MS- remission and control2. 100% sensitivity with 100% negative predictive value (NPV) between MS not-treated (NT) and control. 3. 86% NPV between relapse and control. | 1. sensitivity, specificity, accuracy, positive predictive value (PPV),and negative predictive value (NPV) for both training and validation set.2. blind set was categorized using ROC curve derived Youden's cutoff point. | 1. K-fold cross validation (K = 6) for evaluation of the generalization capability and applicability span of the model (2) different blind tests have been used.(MATLAB version 7.0.1.24704 (R14) is used for thedesigning and optimization of design of the MLPs.) | NA | Exhaled breath samples from 204 participants, including 146 multiple sclerosis (MS) patients and 58 healthy controls.Subgroups: remission (128 patients) and experiencing relapse (18 patients)Breath samples were collected at the Multiple Sclerosis Center, Carmel Medical Center, Haifa, Israelgas chromatography-mass spectrometry (GC-MS) + nanomaterial-based sensor array (NA-NOSE) -> to detect volatile organic compounds related to MS | Diagnostic | Nanotechnology-based sensors combined with an artificial neural network (ANN) for prediction models would be applicable for diagnosing or managing Multiple sclerosis conditions. |
| 109 | Diagnostic / Biomarker | Chung *et al,* 2021 | Plasma extracellular vesicles tau and ALPHA-amyloid as biomarkers of cognitive dysfunction of Parkinson's disease | To investigate the role of the plasma EV-borne tau and alpha-amyloid as biomarkers for cognitive dysfunction in PDby investigating subjects with mild to moderate stage of PD and non-PD controls | Case control study | Parkinson's disease | Machine Learning | To analyze plasma extracellular vesicles (EVs) containing tau and β-amyloidType of Nano: Plasma Extracellular vesicles (EVs) -borne tau. antibody functionalized magnetic nanoparticles | Artificial Neural Network | Supervised Learning | Classification: to identify cognitive dysfunction in Parkinson's disease (PD) patients using plasma extracellular vesicle (EV)-borne α-synuclein, tau, and β-amyloid 1-42 levels, along with age and gender, as predicting factors | AUC of 0.911 for the validation set. | 4-fold cross-validation | The neural network structure is poor, and it is only mentionedthat it was chosen empirically. With a logistic regression they would have obtained the same. | Number of patients: 162. Number of patients with PD: 116Number of control group: 46Ethnicity/race: NAAge: Control: 67.04 ± 7.04 PD: 69.66 ± 8.41Female: Control: 28 PD: 54MMSE: Control: 28.41 ± 1.24 PD: 24.17 ± 6Data collection method in the study: plasma EVs were isolated, and immunomagnetic reduction-based immunoassay was used to assess the levels of alpha-synuclein, tau, and ALPHA-amyloid 1-42 (beta1-42) within the EVs. | Biomarker Identification | Combining Artificial neural network (ANN) analysis with plasma EV biomarkers such as beta1-42 and tau, from patients enables the precise identification of cognitive dysfunction in Parkinson's disease |
| 114 | Diagnostic / Biomarker | Corbo *et al,* 2021 | Analysis of the Human Plasma Proteome Using Multi-Nanoparticle Protein Corona for Detection of Alzheimer's Disease | To develop noninvasive diagnostics for early detection of Alzheimer's Disease using multi-Nanoparticle Protein Corona | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | ML was used to analyze proteomic changes and identify disease-specific protein corona patterns.Type of Nano: 90–100 nm plain, amino-conjugated and carboxyl-conjugated silica nanoparticles and 90–100nm plain, amino-conjugated, and carboxyl-conjugated polystyrene nanoparticles | Random Forest Classifier | Supervised Learning | Classification: to develop a multi-nanoparticle protein corona nanoplatform to distinguish between Alzheimer's disease (AD), early-AD, and healthy individuals based on the protein corona composition formed on the nanoparticles when incubated in plasma | AUC non-cohort samples: 99.8%AUC Cohort samples: 99.47% | 1000 random replications of training and testing splits | Feature importance is to identify the most important protein-NP interactions | Plasma samples (11 AD samples and 8 healthy samples) were randomly stratified into two sets: A training set of 10 samples (6 AD and 4 healthy) and a test set of 9 samples (5 AD and 4healthy) | Diagnostic | The noninvasive nano-platform, which converts protein changes into disease identifiers, could enable early detection and intervention for Alzheimer's and other diseases. |
| 142 | Diagnostic / Biomarker | Eid *et al,* 2024 | Machine learning-powered lead-free piezoelectric nanoparticle-based deep brain stimulation: A paradigm shifts in Parkinson's disease diagnosis and evaluation. | To develop a new machine learning (ML)optimized lead-free piezoelectric nanoparticle-based deep brain stimulation (LF-PND-DBS) system for diagnosing and evaluating Parkinson's disease. | Other: Computational/Experimental study | Parkinson's disease | Deep Learning | The DL method processes EEG images by identifying relevant areas of neuronal activation associated with Parkinson's disease(attention maps?), thereby finding the optimal stimulation parameters (frequency, amplitude, duration).Type of Nano: lead-free piezoelectric nanoparticles | Transformer networks, hybrid Simulated Annealing-Particle Swarm Optimization (SA-PSO), and Federated Learning (FL) | Supervised and Federate Learning | Classification: to classify Parkinson’s disease severity and predicting the response to deep brain stimulation | Proposed model (TFA) Accuracy: 98.3 Precision: 98.2 Recall: 99.1 F1-Score: 99.2sensitivity of 99.1% and a specificity of 98.2% | The model was trained on several epochs, additionally Federated Learning was used, so it is likely to be difficult to make use of cross-validation. | NA | Clinical and electroencephalography (EEG) data from Parkinson’s patientsEEG dataset was sourced from Kaggle repositories | Diagnostic | Integration is a less invasive alternative to deep brain stimulation. It also allows customization of treatment as the Transformer model analyzes EEG to identify specific neural patterns in each patient. This increases the accuracy of diagnosis and progression of the disease by detecting early signs of Parkinson's disease. The integration allowsfor more precise and personalized stimulation, avoiding adverseeffects, i.e., other areas are unaffected, which generates behavioral or emotional changes. It incorporates an automatic and real-time adjustment of the stimulation parameters (Simulated Annealing and Particle Swarm Optimization). |
| 151 | Diagnostic / Biomarker | Etxebarria-Elezgarai *et al,* 2024 | Surface-Enhanced Raman Spectroscopy for Early Detection of Alzheimer's Disease | To develop an early detection method for Alzheimer's disease by analyzing cerebrospinal fluid samples using surface-enhanced Raman spectroscopy (SERS) with commercially available gold nanoparticle substrates. | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | The ML method used the spectral data to classify PD or healthy patients. The synergy between Nano and ML improves the classification of AD patients in early stages.Type of Nano: plasmonic nanoparticles | partial least squares discriminant analysis | Supervised Learning | Classification: to distinguish between patients with Alzheimer's disease (prodromal and preclinical stages) and healthy individuals using Surface-Enhanced Raman Spectroscopy (SERS) of cerebrospinal fluid (CSF) fractions and partial least squaresdiscriminant analysis (PLS-DA) | 100% accuracy in classifying AD patients85% for the healthy control group | They mentioned but they did not specified values | They selected 10 and 12 latent variables for the two different CSF fractions | 51 samples were analyzed for the cerebrospinal fluid-supernatant fraction (16 Prodromal stages, 15 Preclinical stages, 20 Healthy Individuals) and 45 samples for the cerebrospinal fluid-waste fraction (10 Prodromal stages, 15 Preclinical stages, 20 Healthy Individuals) | Diagnostic; Biomarker Identification | This study proposes the integration of ML with nanotechnology methods (gold nanoparticles in SERS) to improve the early detection of diseases such as Alzheimer's. In addition, biomarkers of different molecular weights can be detected using cerebrospinal fluid. |
| 153 | Diagnostic / Biomarker | Eyraud *et al,* 2023 | Plasma nanoDSF Denaturation Profile at Baseline Is Predictive of Glioblastoma EGFR Status | To determine if nanoDSF-derived protein denaturation profiles (PDPs), combined with artificial intelligence (AI), can accurately identify EGFR alterations in glioblastoma (GBM) brain tumors | Cohort study | Brain Cancer | Machine Learning | ML models were trained to analyze plasma denaturation profiles obtained via nanoDSF to distinguish molecular subtypes of GBM (EGFR amplification) and assess post-surgical changes.Type of Nano: nonoDsf technology | Classical Logistic Regression (LR), Support Vector Machine (SVM), andtwo Random Forest (RF) and Adaptive Boosting (AdaBoost). | Supervised Learning | Classification: classification of EGFR amplification and MGMT promoter methylation in GBM using plasma denaturation profiles | Accuracy ->AdaBoost: 81.5%SVM: 55.6%RF: 63.0%LR: 59.3% | Leave-one-out cross-validation | They used as confounder factor surgery-induced inflammatory response affected post-surgical PDPs.They did not perform hyperparameter tuning and model optimization because the small dataset limited.They used feature engineering by using the first derivatives of fluorescence and scattering measures to capture dynamic changes | Local prospective cohort of 38 adult patients (≥18 years) diagnosed with IDH wild-type glioblastoma (GBM) at Timone Hospital (Marseille, France) between June 2016 and October 2017Other variables: Age, gender, type of surgery, Karnofsky Performance Status (KPS), oncological treatment, clinical symptoms, steroid dosage, and MRI characteristicsMolecular profiling was performed using Next-Generation Sequencing (NGS) for EGFR amplification and pyrosequencing for MGMT promoter methylation | Screening | GBM-specific baseline plasma PDP signatures offer potential for predicting the molecular profile of these tumors. |
| 304 | Diagnostic / Biomarker | Kim *et al,* 2024.1 | Distinct plasma phosphorylated-tau proteins profiling for the differential diagnosis of mild cognitive impairment and Alzheimer's disease by plasmonic asymmetric nanobridge-based biosensor | To develop a plasmonic asymmetric nanobridge (PAN) biosensor for quantitative p-tau profiling in plasma, allowing for the differentiation of MCI and AD and the determination of its correlation with AD progression. | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | They used a SVM model to analyze and classify diagnostic dataderived from the Plasmonic Asymmetric Nanobridge-based biosensorType of Nano: Plasmonic asymmetric nanobridge (PAN)-based biosensor | Support vector machine (SVM) | Supervised Learning | Classification: to profile distinct plasma phosphorylated-tau (p-tau) proteins using a plasmonic asymmetric nanobridge-based biosensor and support vector machine (SVM) classifier | 1. AUC (MCI patients Vs HCs) =0.9659, AUC (MCI Vs AD patients) = 0.90632. Coefficient of determination R2 > 0.950 | Train-test split (60% training, 40% testing) | Quantitative profiling of p-tau expression levels (input feature) -> SVM model | Plasma samples from AD patients = 20MCI patients = 16 Human controls (HCs) =11 | Diagnostic | The PAN-based plasmonic biosensor shows significant clinical potential for predicting asymptomatic Alzheimer's disease (AD) progression. |
| 297 | Diagnostic / Biomarker | Kim *et al,* 2024.2 | Surface-functionalized SERS platform for deep learning-assisted diagnosis of Alzheimer's disease | To establish a deep learning-assisted SERS platform for separate blood amyloid beta(1-42) and metabolite analysis, for Alzheimer's disease diagnosis | Diagnostic test accuracy study | Alzheimer's disease | Deep Learning | They used DL to distinguish spectral features of AD-relatedblood biomarkers from the interfering components in biofluidsType of Nano: Surface-functionalized SERS platform ( Au nanowire arrays) | Feed-forward neural network | Supervised Learning | Classification: classification of SERS spectra into Alzheimer's Disease vs. Healthy Control categories. Differentiation of different stages of beta42 oligomerization in AD diagnosis | Oligomerization classification 96-100% accuracyBlood plasma classification, sensitivity: 82.9%, and specificity: 92.2% | model trained on 10 epochs | ANN structure: Three hidden layers with sizes 2500, 1000, and 100 neurons. ReLU activation function. | human blood plasma samples from two groups: 20 healthy controls (HC) and 20 Alzheimer's disease (AD) patientsHC -> Biobank of Chungnam National University HospitalAD -> Biobank of Pusan National University HospitalPlasma sample was analyzed using Surface-enhanced Raman spectroscopy (SERS) | Diagnostic | This study demonstrates the potential of antibody immobilized and SAM-coated substrates, combined with deep learning, to revolutionize AD diagnosis through rapid and non-invasive blood plasma analysis. |
| 333 | Diagnostic / Biomarker | Li *et al,* 2024 | Candidate biomarkers of EV-microRNA in detecting REM sleep behavior disorder and Parkinson's disease | To identify reliable, minimally invasive, plasma extracellular vesicle (EV)-derived microRNA (miRNA) biomarkers for the early detection and monitoring of Parkinson's disease (PD) and idiopathic REM sleep behavior disorder (iRBD). | Diagnostic test accuracy study | Parkinson's disease | Machine Learning | They used ML models analyze EV-associated miRNA signatures to differentiate between normal, iRBD, and PD patientsType of Nano: EV-microRNA | SVM | Supervised Learning | Classification: identification of diagnostic miRNA signatures for distinguishing REM Sleep Behavior Disorder vs. Healthy individuals, PD vs. Healthy individuals, PD vs. REM Sleep Behavior Disorder patients | iRBD vs. Healthy: AUC: 0.969PD vs. Healthy: AUC: 0.916PD vs. iRBD: AUC: 0.929 | 5-fold cross-validation | Selection of differentially expressed miRNAsThey used EV-small sequencing for optimizing library construction for small RNA inputs | No. of Participants: 169(Three groups: 56 iRBD patients, 53 PD patients, and 60 healthy people)Age: 63.5 ± 9.0 (healthy) 64.0 ± 7.3 (iRBD) and 63.0 ±9.0 (PD)Sex(M/F): 32/25 (healthy), 34/22 (iRBD), 25/28 (PD). | Biomarker Identification | This study identifies plasma EV-derived miRNA biomarkers for the early detection and monitoring of Parkinson's disease (PD) and prodromal PD (iRBD). Also, highly accurate diagnostic signatures using optimized sequencing and machine learning, enabling differentiation between healthy, iRBD, and PD states and tracking iRBD conversion. This offers a minimally invasive tool for improved diagnosis, monitoring, and drug development. |
| 365 | Diagnostic / Biomarker | Meehan *et al,* 2024 | A reproducible approach for the use of aptamer libraries for the identification of Aptamarkers for brain amyloid deposition based on plasma analysis | To develop a blood-based diagnostic test for brain amyloid deposition (a risk factor for Alzheimer's disease) using aptamer library | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | They used ML models to evaluate the predictive capability of aptamer-based biomarkers (Aptamarkers) for detecting brain amyloid depositionType of Nano: Aptamer library | Extra Trees ClassifierRandom Forest ClassifierGradient BoostingLogistic RegressionDecision TreesSupport Vector Machines (SVM)Gaussian Naive BayesMulti-Layer Perceptron (MLP)XGBoostRidge Classifier | Supervised Learning | Classification: predicting high vs. low brain amyloid deposition based on aptamer qPCR signals and clinical variablesIdentifying the most relevant aptamers for distinguishing between amyloid-positive and amyloid-negative samples | Best Model (Extra Trees Classifier) -> AUROC: 0.79Model including ApoE genetic status (Random Forest) -> AUROC: 0.81 | 4-fold cross-validation | Features included normalized qPCR aptamer signals and selected clinical variablesClinical variables considered: Age, sex, cognitive status | Plasma samples from 390 individuals obtained from the Australian Imaging, Biomarkers, and Lifestyle (AIBL) study | Diagnostic | Aptamarkers advance disease diagnosis with non-invasive tests, exemplified by Alzheimer's detection, promising earlier intervention and improved outcomes. |
| 480 | Diagnostic / Biomarker | Rani *et al,* 2021 | Nanoscale imaging technique for accurate identification of brain tumor contour using the NBDS method | To develop a fast, accurate brain tumor detection and classification system in MRI images using advanced image processing, nanotechnology-based segmentation, and deep neural networks. | Diagnostic test accuracy study | Brain Cancer | Deep Learning | The Nanotechnology-based detection scheme system enhances segmentation accuracy by identifying tumor seed pixels at the nanoscale. Deep learning classification is used for the final tumor categorization.Type of Nano: Nanotechnology-Based Detection Scheme (MATLAB). The article talks about nanoscale detection. | Deep-neural network | Supervised Learning | Classification: the model classifies tumors into benign or malignant categories using extracted features | Accuracy: 97.3%Sensitivity: 96.7%Specificity: 95.6%Precision: 98.4% | NA | Extracted features included mean, variance, skewness, mutual information, and statistical measures of tumor shape and texture. | Kaggle Brain MRI Database -> 432 healthy brain images and1,018 brain tumor images.The International Cancer Center Neyyoor (ICCN) -> 175 healthy brain images and 205 brain tumor images | Diagnostic | This study develops a fast, accurate (97.3%) AI system for brain tumor diagnosis from MRIs, enabling earlier detection and improved patient care through advanced image processing and nanotechnology-inspired segmentation. |
| 486 | Diagnostic / Biomarker | Resmi *et al,* 2024 | Ultrasensitive Detection of Blood-Based Alzheimer's Disease Biomarkers: A Comprehensive SERS-Immunoassay Platform Enhanced by Machine Learning | To introduce a SERS-based, machine-learning-driven method for the ultrasensitive detection of multiple AD biomarkers | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | Machine learning was used to process and classify SERS spectral data, distinguishing between different clinical groups (AD, MCI, and healthy controls)Type of Nano: Cs-AuNPs on Al Surface (SERS -immunoassay Platform) | Multilayer Perceptron (MLP)Radial Basis Function (RBF)Support Vector Machine (SVM)Linear Discriminant Analysis (LDA) | Supervised Learning | Classification: classification of control vs MCI, control vs AD, and MCI vs AD.Classification: differentiation of disease progression stages using spectral features.Classification: identifying significant biomarkers (beta42, beta40, p-tau, t-tau). | Linear Discriminant Analysis: Sensitivity: 40-100% (Control vs. MCI), 46-100% (Control vs. AD), 40-88% (MCI vs. AD); Specificity: 56-100% (Control vs. MCI), 60-100% (Control vs. AD), 63-88% (MCI vs. AD) | 70% training, 30% testing | For feature engineering: Spectral data normalizationPCA for dimensionality reductionSelection of spectroscopically significant bands | Blood plasma samples from 75 individuals recruited from the Neurology Department of the Sree Chitra Tirunal Institutefor Medical Sciences and Technology (SCTIMST).Three groups: 25 individuals diagnosed with Alzheimer's disease, 25 with mild cognitive impairment (MCI), and 25 healthy controls. The control group consisted of age-matched volunteers with no neurological or psychiatric disorders | Biomarker Identification | A novel SERS-based platform, combined with machine learning, enables ultrasensitive, non-invasive detection of AD biomarkers in blood, offering potential for early diagnosis and improved management. |
| 508 | Diagnostic / Biomarker | Ryzhikova *et al,* 2019 | Multivariate Statistical Analysis of Surface Enhanced Raman Spectra of Human Serum for Alzheimer's Disease Diagnosis | To develop a rapid, accurate, and minimally invasive blood test for Alzheimer's disease (AD) diagnosis using surface-enhanced Raman spectroscopy (SERS) coupled with multivariate statistical analysis and artificial neural networks (ANNs) | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | DL models (ANNs) analyze SERS spectral data to differentiate between AD, OD, and HC samplesType of Nano: Silver colloidal nanoparticle (AgNPs) | Artificial Neural Networks | Supervised Learning | Classification: Binary classification: Differentiating AD vs. HC. Tertiary classification: Differentiating mild AD, moderate AD, and HC.Another tertiary model: Differentiating HC, AD, and OD. | Genetic Algorithm + Artificial Neural Networks:Binary Model (AD vs. HC): Accuracy: 96.47%Tertiary Model (Mild AD, Moderate AD, HC): Accuracy: 94.84%Tertiary Model (AD, HC, OD): Accuracy: 98.31% | Bootstrap Latin Partition (BLP) Cross-Validation | Genetic Algorithm (GA) was used for feature selection,optimizing spectral regions for classification. | Samples were obtained from neurological clinics at Albany Medical Center, blood serum samples from a total of 48 individuals, Three groups: Alzheimer’s disease patients (n = 20), patients with other neurodegenerative dementias (OD) (n = 18), and healthy controls (HC) (n = 10). The AD group included 10 mild and 10 moderate cases, while the OD group comprised individuals diagnosed with Lewy body dementia (n = 5), Parkinson’s disease dementia (n = 10), and frontotemporal dementia (FTD) (n = 3). The dataset: 480 Raman spectra (10 spectra per sample) -> analyzed using Surface Enhanced Raman Spectroscopy | Diagnostic | SERS-based blood test shows promise for rapid, accurate, and non-invasive Alzheimer's diagnosis, enabling earlier detection and improved patient care. |
| 569 | Diagnostic / Biomarker | Sun *et al,* 2024 | A radiometric SERS strategy for the prediction of cancer cell proportion and guidance of glioma surgical resection | To develop a rapid, label-free SERS strategy for intraoperative glioma cell quantification | Diagnostic test accuracy study | Brain Cancer | Deep Learning | To analyze radiometric SERS signals from silver nanoparticles, enabling precise quantification of glioma cell proportions forintraoperative tumor boundary detection.Type of Nano: Silver Nanoparticles (AgNPs) | Artificial Neural Network & Polynomial Regression Model | Supervised Learning | Regression: quantification of glioma cells using spectral peaks at 655 cm-1 and 717 cm-1. Classification: delineation of tumor margins during intraoperative surgical resection.Classification: detection of residual tumor burden in frozen samples using AI models. | ANN Model: R2 = 0.83, RMSE = 0.26Polynomial Regression: R2 = 0.85, RMSE = 0.19 | Internal validation was performed using 20% of the dataset in the ANN model | Baseline correction, normalization, and featureselection was performed on Raman spectra.PCA and Partial Least Squares Discriminant Analysis (PLS-DA) were used to separate glioma cells from normal brain tissuebased on spectral patterns. | Simulated samples were prepared by homogenizing normal brain tissue and patient-derived glioma cells (PDC-4, PDC-21, and PDC-63) in varying proportions.31 frozen tumor samples from 20 glioma patients, obtained during surgical resectionsThe dataset included RNA sequencing data | Diagnostic | This research developed a rapid, label-free SERS method for quantifying glioma cells during surgery. The method improves tumor margin detection and promises better surgical outcomes and broader cancer diagnostic applications. |
| 633 | Diagnostic / Biomarker | Wang *et al,* 2023 | Ultra-sensitive SERS detection of beta 1-42 for Alzheimer's disease using graphene oxide/gold nanohybrids | To develop a highly sensitive SERS method using GO/Au NPs to detect beta1-42 for early Alzheimer's diagnosis | Diagnostic test accuracy study | Alzheimer's disease | Deep Learning | DL models were used to classify and quantify different fibrillation stages of the Alzheimer's biomarker (beta1-42) based on SERS spectral dataType of Nano: Graphene Oxide/ Gold Nanoparticles (GO/Au NPs) | Support Vector Machine (SVM)One-Dimensional Convolutional Neural Network (1DCNN) (based on ResNet) | Supervised Learning | Classification of different fibril states of beta1-42 (0-120 hours of incubation). | SVM Accuracy: 88.33%1DCNN Accuracy: 98.9% | 1DCNN optimized with Adam optimizer and cross-entropy loss function | They extracted Raman spectral features(e.g., peak intensities) as input for classification. | Solutions of Aβ 1–42 (ranging from 0.1 to 1 ng/mL) obtained from Sigma-Aldrich + fetal bovine serum (FBS) | Diagnostic | This study introduces a highly sensitive SERS method using GO/Au nanohybrids to detect low levels of beta1-42, enabling earlier Alzheimer's diagnosis. This method offers improved sensitivity for AD biomarker detection, broader neurodegenerative disease research potential, and the possibility of developing portable, noninvasive diagnostic tools. |
| 636 | Diagnostic / Biomarker | Wang *et al,* 2024.1 | Integrated Ultrasound-Enrichment and Machine Learning in Colorimetric Lateral Flow Assay for Accurate and Sensitive Clinical Alzheimer's Biomarker Diagnosis | To develop a machine learning-optimized lateral flow assay (LFA)with ultrasound enrichment for highly sensitive and accurate detection of tau proteins in Alzheimer's disease diagnosis. | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | Integration of ultrasound-enriched colloidal gold nanoparticles (AuNPs) in a lateral flow assay (LFA)type of Nano: colloidal gold nanoparticle | K-nearest neighbor (KNN) and Gaussian process regression (GPR) | Supervised and Unsupervised Learning | Classification: k-nearest neighbor (KNN) for classification of samples based on distance in concentration classes. Regression: Gaussian process regression (GPR) for quantification (regression) of low abundance detectors | KNN algorithm as a classifier and the GPR algorithm as a quantifier, achieving 98.11% accuracy in differentiation and 99.99% accuracy in quantification against undiluted samples. | 5-fold cross-validation | NA | Clinical samples were obtained from Longgang District Central Hospital of Shenzhen. Six clinical plasma samples for validation. | Biomarker Identification | ML and Nano leverage ultrasound-enriched colloidal gold nanoparticles to enhance the signal. KNN and GPR process and quantify colorimetric data, resulting in highly sensitive and accurate tau protein detection for Alzheimer's diagnosis. |
| 629 | Diagnostic / Biomarker | Wang *et al,* 2024.2 | A distinction of gliomas at cellular and tissue level by surface-enhanced Raman scattering spectroscopy | To develop SERS-based methods, combined with machine learning, for rapid and accurate detection and characterization of glioblastoma multiforme (GBM) at both cellular and tissue levels, including tumor grading and IDH mutation identification, for potential intraoperative diagnosis. | Other: Methodological Development | Brain Cancer | Machine Learning | Machine learning algorithms were used to analyze and classify SERS spectral data to differentiate glioma from trauma tissues and to distinguish tumor grades and IDH mutationsType of Nano: Gold nanoshell (SiO2@Au) & Gold nanoisland (AuNI) | Support Vector Machine (SVM) with a linear kernel.Orthogonal Partial Least Squares Discriminant Analysis (OPLS-DA). | Supervised Learning | Classification: Differentiation of glioma cells from normal astrocytes and non-CNS tumor cells. Classification of glioma vs. trauma tissues. Distinguishing tumor grades and identifying IDH mutations. | OPLS-DA model: sensitivity of 100%, specificity of 87.50%, and an overall accuracy of 97.50%. ROC AUC Values: Over 0.99 for all classification tasks. | 7-fold Cross-Validation | SERS spectral data were preprocessed, and specific Raman peak intensities were used as features. | SERS spectra from tissue samples of 64 glioma patients and 16 brain trauma patientsFour different cell types: normal human astrocytes (HA1800), human glioma cell lines (U87 and U251), and a human myeloma cell line (U266) | Diagnostic | This study demonstrates that SERS combined with machine learning offers rapid, accurate glioma detection and characterization at cellular and tissue levels, enabling improved diagnostics, surgical guidance, and treatment decisions. |
| 645 | Diagnostic / Biomarker | Xu *et al,* 2022 | Machine Learning-Assisted Sensor Array Based on Poly(amidoamine) (PAMAM) Dendrimers for Diagnosing Alzheimer's Disease | To develop a fluorescent sensor array composed of three modified polyamidoamine dendrimers | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | They used ML models to process fluorescence pattern datafrom the sensor array, allowing classification of different aggregation states of beta40/beta42 proteinsType of Nano: Fluorescent sensor (pyrenemodified G5 PAMAM dendrimers) | Linear Discriminant Analysis (LDA)Decision Tree (DT)Support Vector Machine (SVM)Logistic Regression (LR) | Supervised Learning | Classification: differentiation of beta40 and beta42 aggregates in different structural states (monomer, oligomer, fibril). Identification of beta biomarkers in various biological fluids, including serum and cerebrospinal fluid.Regression: Testing of the sensor array's performance under interference from metal ions and other proteins. | LDA classification accuracy: 100% for protein discrimination.Prediction accuracy in serum samples: 88.9%.AUROC for distinguishing beta40 and beta42 in cerebrospinal fluid: 96.6% | leave-one-out cross-validation | For feature engineering, fluorescence intensity changes at different pH levels (5.0, 7.4, 9.0) were used to optimize signal differentiation | Amyloid-β (Aβ) protein aggregates (Aβ40 and Aβ42) in different aggregation states (monomer, oligomer, and fibril). Also, real-world data -> serum and cerebrospinal fluid (CSF) | Diagnostic | This study introduces a highly accurate fluorescent sensor array, demonstrating 100% accuracy in general protein discrimination and detection of Alzheimer's disease biomarkers, beta40 and beta42 aggregates, even within complex biological samples. |
| 653 | Diagnostic / Biomarker | Xu *et al,* 2023.1 | Machine Learning-Assisted Nanoenzyme/Bioenzyme Dual-Coupled Array for Rapid Detection of Amyloids | To develop a fluorescent sensor array integrating AuNPs and horseradish peroxidase for amyloid detection | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | They used ML models to optimize sensor element selection, reducing redundant features while maintaining high prediction accuracy.Type of Nano: Fluorescent Sensor (Gold Nanoparticles(AuNPs) & Bioenzyme (Horseradish Peroxidase) | Linear Discriminant Analysis (LDA)K-Nearest Neighbors (KNN) | Supervised Learning | Classification: to classify different amyloid species, including monomers, oligomers, and fibrils, which correspond to different Alzheimer's disease stages | k-nearest neighbors classifier, best model: 100% accuracy in classifying amyloid-beta aggregation states. AUROC between AD vs. Healthy Mice: 1 | 10-fold cross-validation | Feature selection was performed using the K-best model with ANOVA F-values | Synthetic amyloid peptide samples and blood plasma samples 'from AD model mice and healthy mice | Diagnostic | Developed a highly sensitive nanoenzyme-amplified sensor array, coupled with machine learning, for accurate amyloid-beta (beta) peptide discrimination. It enables ultralow detection and differentiation of beta aggregates, offering potential for improved Alzheimer's diagnosis and large-scale biomolecule screening. |
| 650 | Diagnostic / Biomarker | Xu *et al,* 2023.2 | Diagnosis of Parkinson's Disease via the Metabolic Fingerprint in Saliva by Deep Learning | To develop a noninvasive, high-throughput, and highly reproducible diagnostic platform for Parkinson's disease using saliva metabolic fingerprinting. | Diagnostic test accuracy study | Parkinson's disease | Machine Learning / Deep Learning | They integrated nanoparticle-enhanced LDI-MS for high-throughput saliva metabolic fingerprinting with deep learning modelType of Nano: ferric particles | Least Absolute Shrinkage and Selection OperatorXGBoostSupport Vector MachinesRandom ForestAdaptive BoostingStroke Network | Supervised Learning | Classification: Parkinson's Disease (PD) patients and healthy controls | Stroke Network (SN), best model: training cohort,AUC of 0.8009, sensitivity of 81.01%, and specificity of 80.18%. validation cohort, AUC of 0.8496, sensitivity of 88.01%, and specificity of 79.18% | 10-fold-CV | NA | 312 participants: 187 Parkinson's Disease (PD) patients, 125 Healthy Controls (HC) | Diagnostic; Biomarker Identification | Combining both methodologies allows an automated, scalable, and high-accuracy metabolic data interpretation method. On the other hand, it is noninvasive and early detection, which improves the accuracy of detection, as it can be used for detecting PD in asymptomatic or early-stage patients. It allowed the identification of biomarkers; for example, the study highlighted the molecules 7-hydroxyprogesterone, creatinine, creatine, and ADP. |
| 663 | Diagnostic / Biomarker | Yu *et al,* 2022 | The Feasibility of Early Alzheimer's Disease Diagnosis Using a Neural Network Hybrid Platform | To develop a high-sensitivity and high-specificity diagnostic tool by detecting biochemical changes in cerebrospinal fluid (CSF) associated with AD using a neural network hybrid platform that combines surface-enhanced Raman spectroscopy (SERS) and convolutional neural networks (CNNs) | Diagnostic test accuracy study | Alzheimer's disease | Deep Learning | They used deep learning to interpret nanoparticle-enhanced mass spectrometry for disease biomarker discoveryType of Nano: nanopores (specifically α-hemolysin nanopores and the engineered MspA-N91H nanopore) | 1D-Convolutional Neural Network | Supervised Learning | Classification: hierarchical cluster analysis (HCA) to group samples based on their SERS spectra, achieving concordancewith sample provenance, and to distinguish between clinicallyevident AD and pre-clinical AD (FAD samples) | overall accuracy of 92%, with 100% accuracyfor normal individuals and 88.9% accuracy for AD patients | leave-one-group-out cross-validation | Structure of the CNN:Convolutional LayersMax-Pooling LayersFully Connected (Dense) LayersThey used data augmentationRandom shifting of spectra by 1-2 wavenumbers.Addition of random noise.Generation of linear combinations of spectra from the same sample. | 30 cerebrospinal fluid (CSF) samples were obtainedfrom patients at the University of California, Irvine (UCI) Institute for Memory Impairment and Neurological Disorders (ADRC). | Diagnostic; Biomarker Identification | This study delves into improving the early and accurate detection of Alzheimer's disease. It achieved much better detection than conventional methods. It has become a non-invasive and cost-effective diagnostic test. It reduces human intervention in interpreting the results of SERS spectra. |
| 312 | Methodological / Computational Development | Kostrikov *et al,* 2021 | Optical tissue clearing and machine learning can precisely characterize extravasation and blood vessel architecture in brain tumors | To develop two machine learning-based workflows for semi-automated image analysis, enabling detailed quantification of compound extravasation and tumor angioarchitecture in large 3D cleared tissue datasets | Other: Methodological Development | Brain Cancer | Deep Learning | They used ML to segment and analyze tumor vasculature and compound extravasation patternsType of Nano: Tramethylrhodamine (TRITC)-labeled dextran (hydrodynamic radius ~27 nm) | Deep convolutionalneural network (VGG-19) and random forest | Supervised Learning | Classification: the model classified and segmented different vascular structures, categorized regions based on the degree of transcardial perfusion, and identified extravasation spots of injected compounds | They compared human annotators vs model,the metrics are related to the accuracy and precision of extravasation and vasculature analysis.Machine learning workflow provided larger spot counts compared to manual annotation. | They compared model's segmentation results with manual annotations | Blind deconvolution to reduce out-of-focus light and improve segmentation accuracy | Orthotopic xenograft models of glioblastoma (GBM) in NMRI-nude micesyngeneic colorectal cancer models in BALB/c and C57BL/6 mice | Other: Methodological development | The methodology enables precise and comprehensive analysis of extravasation in brain tumors, facilitating the correlation of extravasation patterns with specific features of the heterogeneous tumor vasculature |
| 339 | Methodological / Computational Development | Liu *et al,* 2015 | Probing enzyme -nanoparticle interactions using combinatorial gold nanoparticle libraries | To elucidate the complex relationships between nanoparticle surface chemistry and their binding interactions with proteins, specifically acetylcholinesterase (AChE), using a combinatorial approach. | Other: Methodological Development | Alzheimer's disease | Machine Learning | The ML models predicted the nanoparticle-enzyme interactions,helping to identify specific nanoparticle surface chemistries that strongly influence AChE inhibition and bindingType of Nano: Gold nanoparticle | Bayesian Regularized Artificial Neural NetworkMultiple Linear Regression with Expectation Maximization | Supervised Learning | Regression: prediction of AChE inhibition levels based on nanoparticle surface chemistry | Linear Model: r2 (train) = 0.91, r2 (test) = 0.81Bayesian Neural Network: r2 (train) = 0.87, r2 (test) = 0.81 | Train-Test Split (80% training, 20% testing) | Several features were extracted from the nanoparticle surface chemistry:Spatial moments of electronegativities (DISPe)Molecular shape indices (G2v, WHIM descriptors)Radial distribution functions (RDF140m)Autocorrelation functions (R3m+, R2u+)Lipophilicity (LogP)Functional group counts (e.g., hydroxyl, carboxyl groups) | A combinatorial library of 47 surface-modified gold nanoparticles (f-GNPs)It contains measurements of AChE binding, enzyme inhibition, and fluorescence quenching, collected through Western blot analysis, enzymatic activity assays, and fluorescence spectroscopy | Other: Methodological development | Study provides a more detailed understanding of the complex relationships between nanoparticle surface chemistry and protein binding, specifically with acetylcholinesterase (AChE). Also, the models created can be used to predict potentially harmful interactions, therefore advancing nanotoxicology studies. |
| 443 | Methodological / Computational Development | Parker *et al,* 2023 | Targeting intra-tumoral heterogeneity of human brain tumors with in vivo imaging: A roadmap for imaging genomics from multiparametric MR signals | To develop in vivo brain tumor cellular and molecular mapping for optimized cancer treatment strategies | Other: Roadmap Review Study | Brain Cancer | Machine Learning / Deep Learning | They used ML models to enhance MRI capabilities by mappingcellular and molecular tumor features at a microscopic scaleType of Nano: Nanoscale Intra-Tumoral Heterogeneity (ITH) | Generalized Additive Models (GAM)Convolutional Neural Networks (CNNs)Generative Adversarial Networks (GANs)Adaptive Boosting (AdaBoost)Support Vector Machines (SVMs)Random Forests | Supervised, Unsupervised and Semi-supervised Learning | Classification: classification of tumor heterogeneity based on MR imaging.Regression: prediction of tumor recurrence risk and treatment response.Classification: segmentation of tumor regions in MRI scans.Classification: estimation of cellular and molecular properties from MRI features. | RMSE for predicting cell density: 1.06 × 10³ cells/mm² (GAM model).Voxel-wise classification accuracy (CNN): >95% | NA | NA | Multiparametric MRI (mpMR) imagingGenomic and histopathological information | Other: Methodological Development | 1. This roadmap could significantly advance brain tumor research and clinical management, leading to more effective and personalized treatments.2. It sets a framework for future research that integrates cutting-edge technologies to address the challenges of tumor heterogeneity and treatment resistance. |
| 677 | Methodological / Computational Development | Zhang *et al,* 2024 | Real-time detection of 20 amino acids and discrimination of pathologically relevant peptides with functionalized nanopore | To build a copper(II)-functionalized Mycobacterium smegmatis porin A (MspA) nanopore with the N91H substitution, whichenables direct identification of all 20 proteinogenic amino acids when combined with a machine-learning algorithm. | Other: Computational/Experimental study | Parkinson's disease | Machine Learning | After detecting the amino acid signals, ML is used to classify an amino acid. This opens the possibility of sequencing proteins without the need for mass spectrometry.Type of Nano: nanopores (specifically α-hemolysin nanopores and the engineered MspA-N91H nanopore) | Random ForestNaive BayesNeural Networkk-Nearest NeighborsBagged CARTAdaBoost | Supervised Learning | Classification: to identify amino acids based on signals obtained from nanopore translocation events | Random Forest: 0.996 (training), 0.993 (testing), and 0.989 (validation)Accuracy of the model reached 99.1% when using 30.9% of the signalsLimit of Detection (LOD) for Glycine was <100 nM | 10-fold-CV |  | The data sample consists of electrophysiology recordings from experiments that detect and classify 20 proteinogenic amino acids, two post-translationally modified (PTM) amino acids, and one unnatural amino acid | Other: Molecular sequencing | The biomedical applications are interesting in the sense that it can sequence the 20 proteinogenic amino acids and their post-translational modifications. No replication or amplification of the sequences is required to obtain a good signal. It allowsthe identification of proteoforms; for example, alpha-amyloid mutant peptides were differentiated. The incorporation of ML increased the accuracy of detection. |
| 95 | Monitoring / Prognosis | Chan *et al,* 2022 | Monitoring Amyloidogenesis with a 3D Deep-Learning-Guided Biolaser Imaging Array | To develop a peptide-encapsulated droplet microlaser to monitor the amyloidogenesis process and evaluate the efficacy of anti-amyloid drugs. | Diagnostic test accuracy study | Alzheimer's disease; Parkinson's disease | Deep Learning | Detection of amyloid peptide and nanostructure conformation using protein-based microdroplet laser array.Type of Nano: two PAH (Polycyclic Aromatic Hydrocarbon) sensors | Multimodal learning (MML) comprised of five 2D convolutional layers, five 1D convolutional layers, and two fully connected layers | Supervised Learning | Classification: in this study a 3D deep-learning strategy is developed to classify laser images from peptide-encapsulated droplet microlasers to monitor the progression of the amyloidogenesis process and evaluate the efficacy of anti-amyloid drugs | Confusion Metrics for all data sets including training, validation and Test set (accuracy for all dataset is over 95%) | k-fold cross-validation (k=10) was used to test the CNN model | NA | Laser emission images from microdroplets containing native insulin.The dataset included images collected at different time intervals to monitor protein aggregation stages | Screening; Diagnostic | The integration of these biosensors with deep learning offers high-throughput drug screening platforms that may help scientist to develop therapeutics and diagnostic devices for neurodegenerative diseases, such as Alzheimer's and Parkinson's. |
| 118 | Monitoring / Prognosis | Crimi *et al,* 2014 | Predictive Value of Imaging Markers at Multiple Sclerosis Disease Onset Based on Gadolinium- and USPIO-Enhanced MRI and Machine Learning | Characterize patients with clinically Isolated Syndrome from spatio-temporal lesion imaging to improve prognosis and better treatment in the early stages of multiple sclerosis. | Non-randomized experimental study | Multiple sclerosis | Machine Learning | To classify spatio-temporal lesion patterns in Multiple Sclerosis patients using USPIO-enhanced MRI (a nanotechnology-based contrast agent that highlights macrophage activity)Type of Nano: Ultrasmall Super Paramagnetic Iron Oxide (USPIO) and Gadolinium | Regression Model | Supervised Learning | Classification: to identify a pattern of multiple sclerosis lesions using contrast agents and spectral clustering. Regression: to relate the volume of chronic hypointense lesions to patient classification | R2 score of 0:90. | NA | NA | 25 Clinically Isolated Syndrome (CIS) patients (17 women and 8 men) aged 32.9 ± 8.6 years, recruited from multiple French centers between July 2009 and April 2011 | Other: Early Prognosis | This approach offers a potential refinement of MS lesion classification beyond traditional measures, which helps to improve patient stratification for clinical trials focused on preventing or delaying disease progression and disability. |
| 227 | Monitoring / Prognosis | Hozhabr *et al,* 2024 | Machine Learning-Empowered Multicolor Detection and Discrimination of Dopaminergic Agents: Utilizing Gold Nanorods for Generating Rainbow Signals | To create an improved method for rapid and sensitive multianalyte detection of dopaminergic agents to accurately assess Parkinson's disease progression. | Diagnostic test accuracy study | Parkinson's disease | Machine Learning | Machine learning helped analyze spectral data and differentiate between L-DOPA, Carbidopa, and Benserazide by recognizing color variations and plasmonic shifts due to chemical interactions.Type of nano: Gold nanorods | Linear discriminant analysis (LDA) for pattern recognitionand partial least-squares regression (PLSR) for regression analysis | Supervised Learning | Classification: to discriminate between different dopaminergic agents (L-DOPA, Carbi, and Benz) and their mixtures using a multicolorimetric sensor based on the inhibition etching of gold nanorods (AuNRs) and linear discriminant analysis (LDA). Regression: quantitative assessment of individual analytes and their mixtures using partial least squares regression (PLSR) | L-DOPA: R2 = 0.9993, Limit of Detection = 0.9 μmol/LCarbidopa: R2 = 0.9702, Limit of Detection = 0.9 μmol/LBenserazide: R2 = 0.9767, Limit of Detection = 0.4 μmol/LAccuracy = 1, Sensitivity = 1, and Selectivity = 1, for all classes (L-DOPA, Carbi, Benz, and their binary and ternary mixtures) | Leave-One-Out Cross-Validation for LDAVenetian Blind Cross-Validation and test-set validation for PLSR | For feature Engineering, they used PCA for LDA. | Spectroscopic and colorimetric responses of gold nanorods (AuNRs) subjected to etching inhibition by dopaminergic agents—levodopa (L-DOPA), carbidopa (Carbi), and benserazide (Benz).The dataset includes UV–vis absorption spectra (350–950 nm) and corresponding color variationsreal sample analysis using pharmaceutical tablets(Norstor and Parkin-C Fort) | Diagnostic | This study allows for the rapid and accurate detection of dopaminergic agents using machine learning-assisted, color-based sensors using etched gold nanorods. Also, it performed excellently in pharmaceutical quality control and demonstrates potential for portable, on-site use. |
| 296 | Monitoring / Prognosis | Kim *et al,* 2021 | Stretchable and self-healable catechol-chitosan-diatom hydrogel for triboelectric generator and self-powered tremor sensor targeting at Parkinson disease | To develop a stretchable, ionically conductive CCDHG and a self-powered tremor sensor for Parkinson's disease monitoring | Other: Computational/Experimental study | Parkinson's disease | Machine Learning | A 3D AuNW substrate fabricated from gold nanowire arrays forSERS-based biomarker analysisType of Nano: stretchable and self-healable catechol-chitosan-diatom hydrogel (CCDHG)-based triboelectric nanogenerator (TENG) | Support Vector Machine (SVM) and K-Nearest Neighbor (KNN) | Supervised Learning | Classification: to classify Parkinson’s disease tremor severity using a machine learning model based on voltage signals from a self-powered tremor sensor | Accuracy achieved by the linear SVM model was 100% | 5-fold cross-validation | For feature engineering, they extracted:maximum peak frequency, root mean square of peak frequencies,maximum power spectral density, and integral of power spectral density | Fabrication and testing of the CCDHG using biomaterials such as catechol, chitosan, and diatom frustules, followed by mechanical, electrical, and adhesion strength evaluations -> detects low-frequency vibrations | Other: Monitoring Disease Progression | The study pioneered catechol-chitosan-diatom hydrogel (CCDHG) as a stretchable electrode in triboelectric nanogenerators (TENGs). The CCDHG's mussel-inspired catechol chemistry enabled strong adhesion to hydrophobic polymers, and the resulting tremor sensor, analyzed with machine learning, effectively identified Parkinson's disease patient conditions. |
| 309 | Monitoring / Prognosis | Komoto *et al,* 2020 | Time-resolved detection of neurotransmitters in mouse brain tissue for PD diagnostics | To develop a method for high temporal resolution mapping of neurotransmitter distribution in the brain | Diagnostic test accuracy study | Parkinson's disease | Machine Learning | They used ML to enhance the discrimination of neurotransmitter signals by analyzing current waveformsType of Nano: Nanogap electrodes | XGBoost classifierRandom Forest classifier | Supervised Learning | Classification: to classify dopamine (DA), serotonin (5-HT), and norepinephrine (NE) from single-molecule conductance signals | F1-score = 0.52 vs random classification F1-score of 0.33Accuracy of classification improved with signal accumulation -> 80% for 20 signals, 90% for 40 signals, and 99% for 110 signals | Tenfold cross-validation | Noise signals from electrode migration and non-target molecules were removed. | Dopamine (DA), serotonin (5-HT), and norepinephrine (NE)in aqueous solutions -> mouse brain tissue samples.Brain tissue was obtained from a 10-week-old female C57BL/6J mouse ->mounted on a mechanically controllable break junction (MCBJ) substrate for electrical measurements | Diagnostic | This study provides a powerful new tool for investigating neurotransmitter dynamics in the brain, which might help develop new diagnostic tools and therapeutic strategies for neurological disease. |
| 386 | Monitoring / Prognosis | Morris *et al,* 2020 | Engineered immunological niches to monitor disease activity and treatment efficacy in relapsing multiple sclerosis | To develop and validate a novel, minimally invasive, biomaterial-based immunological niche system in a mouse model of multiple sclerosis (MS) to serve as a platform for real-time monitoring of immune activity within target tissues. | Diagnostic test accuracy study | Multiple sclerosis | Machine Learning | They used ML models to analyze the gene expression changes induced by nanoparticle treatments, distinguishing effective from ineffective therapies and monitoring disease progression.Type of Nano: Antigen encapsulating PLG nanoparticles | Singular Value DecompositionBootstrap Aggregated Decision Tree Ensemble | Supervised and Unsupervised Learning | Classification: classification of healthy vs. diseased mice based on gene expression data. Prediction of disease onset and severity using gene signature scores. | AUC: 0.97-1 (95% CI: 0.89-1.06) | Leave-One-Out Cross-Validation | Gene selection was optimized using elastic net regularizationto extract the most relevant predictors of disease state | Mouse model of multiple sclerosis (experimental autoimmune encephalomyelitis (EAE) model).gene expression profiles from subcutaneousINs implanted in SJL/J miceimmune cell populations in the INs, blood, and spleen -> assessed via flow cytometry | Diagnostic; Other: Prognosis | Engineered niche technology enables early MS relapse detection, guides targeted therapy, reveals hidden immune dysfunction, and improves autoimmune disease management. |
| 395 | Monitoring / Prognosis | Muraoka *et al,* 2021 | Proteomic Profiling of Extracellular Vesicles Separated from Plasma of Former National Football League Players at Risk for Chronic Traumatic Encephalopathy | To investigate the potential of plasma extracellular vesicle (EV) protein profiles as diagnostic biomarkers for Chronic TraumaticEncephalopathy (CTE) in former National Football League (NFL)players | Diagnostic test accuracy study | Alzheimer's disease | Machine Learning | They used ML models to analyze proteomic profiles of Plasma Extracellular vesicles (Evs) and identify potential biomarkers for Chronic Traumatic EncephalopathyType of Nano: Size-exclusion chromatography -> separateEvs and nanoparticle tracking analysis -> characterize Evs | Linear Discriminant Analysis (LDA)Naive BayesSupport Vector Machine (SVM) | Supervised Learning | Classification: machine learning model classified former National Football League players at risk of CTE versus control individuals based on proteomic signatures in EVs | The ensemble classifier achieved 85% accuracy.AUC values (proteins):COL6A3 alone: 0.74COL6A3 + RELN: 0.83COL6A3 + RELN + COL6A1: 0.85 | Train/test user-blinded test set | Confounding factors: body mass index (BMI), age,and neuropsychological factors | Plasma samples were available for 26 participants, including 14 symptomatic former NFL players (mean age: 56.7 years, range 46-67) and 12 asymptomatic controls (mean age: 55.1, range 48-65) for proteomics, and 27 symptomatic former NFL players (mean age: 56.6, range 40-68) and 25 asymptomatic controls (mean age: 57.0, range 45-68) for ultrasensitive immunoassay for t-tau and p-tau. | Biomarker Identification | The identification of specific protein biomarkers (t-tau, p-tau181, COL6A3, RELN, COL6A1) in plasma EVs offers the possibility of developing a non-invasive blood test for CTE. This would be a major advancement, as CTE diagnosis currently relies on post-mortem brain examination. |
| 519 | Monitoring / Prognosis | Sandler *et al,* 2023 | Multiplexed Digital Characterization of Misfolded Protein Oligomers via Solid-State Nanopores | To develop a high-throughput, single-molecule method using nanopores and DNA barcoding to accurately detect and quantify misfolded protein oligomers, aiding in neurodegenerative disease diagnostics and therapeutics. | Diagnostic test accuracy study | Parkinson's disease | Machine Learning | Machine learning was used in a parallel study to optimize small-molecule inhibitors that block alpha-synuclein secondarynucleation, which in turn affects oligomer detection in nanopore assaysType of Nano: DNA nanostructure | Active learning-based docking simulations | Supervised Learning | Regression: the ML model predicted the efficacy of small molecules in inhibiting alpha-synuclein oligomerization by modeling their interactions with fibril surfaces | Percentage of events with an oligomer bound to the DNA barcode: I3.08 (inhibitor): 14.4%, Anle-138b (inhibitor): 41.8%, DMSO (control): 29.8% | Comparison with an alternative technique (micro free flow electrophoresis, ŒºFFE) | Digital DNA barcoding was employed to label oligomer populations for identification in multiplexed samples. | monomeric and oligomeric α-synuclein (αS) oligomers samples + αS aggregation kinetics data | Diagnostic; Other: Therapeutic | This study offers a high-throughput, single-molecule nanopore method for detecting elusive protein oligomers, which has been demonstrated for Parkinson's drug discovery. The method surpasses existing techniques in throughput, enables in vivo oligomer quantification via click chemistry, and holds broad potential for protein misfolding and drug discovery research. |
| 578 | Monitoring / Prognosis | Tahirbegi *et al,* 2022 | Toward high-throughput oligomer detection and classification for early-stage aggregation of amyloidogenic protein | To develop a high-throughput, single-molecule photobleaching method with machine learning to analyze the early-stage aggregation kinetics of beta-amyloid and alpha-synuclein. | Other: Methodological Development | Alzheimer's disease; Parkinson's disease | Machine Learning | ML was used to classify fluorescence signals correspondingto different oligomeric states of proteinsType of Nano: Gold nanoparticles | Support Vector Machines (SVM)Multilayer Perceptron (MLP) Artificial Neural Networks | Supervised Learning | Classification: Classification of single-molecule fluorescence signals to determine oligomer size. Differentiation between monomeric and oligomeric protein states. | Multilayer Perceptron model, best model: accuracy of 83.5% on simulated photobleaching traces up to 19-mers | NA | Features such as initial intensity, integrated intensity, standard deviation, kurtosis, and bleaching gradient were used. | Single-molecule photobleaching measurements obtained through high-throughput fluorescence microscopy | Diagnostic | This study demonstrates a high-throughput single-molecule method, coupled with Machine learning, for analyzing early protein aggregation. It reveals insights into the mechanisms of Alzheimer's and Parkinson's diseases and paves the way for targeted therapies. |
| 96 | Therapy / Drug Delivery | ChandraKaushik *et al,* 2019 | Evaluation of anti-EGFR-iRGD recombinant protein with GOLD nanoparticles: synergistic effect on antitumor efficiency using optimized deep neural networks | To Investigate the frequency and prognostic significance of EGFR alterations in glioma and develop a novel in silicodeep neural network approach for screening potential EGFR inhibitors. | Other: Computational/Experimental study | Brain Cancer | Deep Learning | To analyze plasma extracellular vesicle (EV) biomarkers (tau and β-amyloid) for predicting cognitive dysfunction in Parkinson’s diseaseNanoparticle library.Type of Nano: gold nanoparticles (NPs) | Differentiable neural networks | Supervised Learning | Regression: to predict the inhibitory potential of gold nanoparticles (AuNPs) against the EGFR receptor using an optimized deep neural network approach. | Validation set: AUC of 0.911, accuracy of 91.3%, precision of 90.0%, sensitivity of 100%, and specificity of 60.0% | Cross validation with previous literature | NA | The Cancer Genome Atlas (TCGA) and cBioPortal to retrieve mutational, copy number variation, and expression data for EGFR across different cancer typesglioma and glioblastoma (GBM), combining Low-Grade Glioma (LGG) and GBM cohortsPubChem's chemical compound library was used to screen potential nanoparticles (NPs) | Screening; Other: EGFR can be used asan independent prognostic indicator for glioma patients | 1. In silico optimized deep neural network approach could efficiently screen a nanoparticle (NP) library for EGFR inhibition.2. This study confirmed the potential of the combined anti-EGFR-iRGD protein and gold nanoparticles (AuNP) strategy for inhibiting tumors driven by EGFR overexpression. |
| 259 | Therapy / Drug Delivery | Kakulade *et al,* 2024 | Development, characterization and pharmacokinetic evaluation of selegiline HCl loaded cubosomal thermoreversible mucoadhesive gel for nose to brain delivery | To formulate and evaluate SGH-loaded intranasal thermoreversible cubosomal gel to enhance its bioavailability and ensure efficient brain targeting. | Other: Computational/Experimental study | Alzheimer's disease; Multiple sclerosis; Parkinson's disease | Machine Learning | To enhance nanoparticle formulation, drug delivery systems, and material characterizationType of Nano: cubosomal thermoreversible mucoadhesive gel | Artificial Neural Network | Supervised Learning | Regression: to optimize the formulation of a cubosomal gel for intranasal drug delivery using an artificial neural network to predict particle size, entrapment efficiency, and drug release. | Best-performing formulation parameters: particle size, entrapment efficiency, drug release, and pharmacokinetic parameters.Particle Size: 166.8 ± 3.12 nmPolydispersity Index: 0.163 ± 0.031Zeta Potential: −20.8 ± 1.21 mVEntrapment Efficiency: 72.85 ± 1.50%In vitro Drug Release at 6 hours: 89.15 ± 1.04%Pharmacokinetic parameters in vivo:Cmax in brain: 77 ± 0.32 ng/mLarea under the curve for drug concentration over time: 36.92 ± 0.41 ng.min/mL | 71.4% for training dataset28.6% for validation dataset | They explored the use of ANN to optimize the formulation of SGH loaded intranasal thermoreversible cubosomal gel. However, finding a larger error than the Response Surface Methodology model, they pursued the optimization of the gel formulation with the latter. | one receiving intranasal administration of selegiline HCl drug solution (1 mg/kg) and the other receiving intranasal administrationof selegiline HCl-loaded cubosomal gel (1 mg/kg)Two groups: one receiving intranasal administration of selegiline HCl drug solution (1 mg/kg) and the other receiving intranasal administration of selegiline HCl-loaded cubosomal gel (1 mg/kg)Blood samples: via cardiac puncture at different time intervals (30, 120, 240, and 360 minutes) + brain tissue samples14 experimental formulations of cubosomes loaded with Selegiline HCl | Other: Drug delivery | Although ANNs were not used to optimize gel formulation, this data-poor ML method showed competitive results to the Response Surface Methodology (RSM). The ANN model can find more complex nonlinear relationships with more data than the proposed RSM method. |
| 269 | Therapy / Drug Delivery | Karthik *et al,* 2024 | Improving brain tumor treatment with better imaging and real-time therapy using quantum dots | To introduce a comprehensive methodology merging Quantum Dots (QDs) and Real-Time Imaging-Guided Therapeutics (RIGT) to refine the precision of brain tumor radiotherapy. | Non-randomized experimental study | Brain Cancer | Deep Learning | They combine DL and nanotechnology by combining QuantumDots (QDs) with a Real-Time Imaging-Guided Therapeutics system,integrating CNN-GAN model to improve the treatment of brain tumors.Type of Nano: near-infrared quantum dots | Hybrid Convolutional Neural Networks-Generative Adversarial Networks.CNN used: convLayer + MaxPool + convLayer + FullyConnectedLayerCNN compared: ResNet50, VGG19, AlexNet | Supervised Learning | Classification: classification for segmentation of tumor and Regression to predict tumor size and volume (measured in mm≥ or cm-1). | IoU (Intersection over Union): 0.89Dice Coefficient: 0.95F1-score: 0.94Structural Similarity Index (SSI): 0.91 | Not used | Medical data of the patient were incorporated, to predictthe evolution of the tumor and possible responses to treatment. | The distribution of the population is not precise. Still, the following groups were used: patients who received radiotherapy,patients with brain tumors who did not receive radiotherapy, control group without brain tumors. | Other: Treatment improvement | This study makes a breakthrough in personalized medicine by employing nanotechnology and AI methods. This is achieved with nanotechnology to be more accurate in identifying brain tumors in deep regions. Additionally, incorporating AI methods increases tumor segmentation compared to traditional CNN models. Incorporating these two methods allows real-time radiotherapy to be performed while minimizing exposure to healthy tissue. |
| 393 | Therapy / Drug Delivery | Munteanu *et al,* 2021 | Prediction of Anti-Glioblastoma Drug-Decorated Nanoparticle Delivery Systems Using Molecular Descriptors and Machine Learning | To develop a computational model for predicting the formation of drug-decorated nanoparticle delivery systems with anti-glioblastoma activity using molecular descriptors and machine learning techniques | Other: Computational/Experimental study | Brain Cancer | Machine Learning | The ML were trained to predict the likelihood of nanoparticle-drugcomplexes forming with anti-glioblastoma propertiesType of Nano: Drug-decorated nanoparticles (DDNPs) | Bagging ClassifierDecision Tree ClassifierRandom Forest ClassifierXGBoost ClassifierGradient Boosting ClassifierK-Nearest NeighborsGaussian Naive BayesLogistic RegressionLinear Discriminant AnalysisAdaBoost Classifier | Supervised Learning | Classification: predicting whether a drug-nanoparticle complex has anti-glioblastoma properties. Identifying key molecular descriptors affecting prediction performance | For the best model - Bagging Classifier:F1-Score: 0.87AUROC: 0.96 | 75% training, 25% test | Feature selection reduced 104 molecular descriptors to 41 important featuresMolecular descriptors were transformed based on perturbation theory to improve predictive power | 855,129 drug-nanoparticle complexes (combination of nanoparticle experimental data with drug assay data from the ChEMBL database and literature sources)molecular descriptors of both drugs and nanoparticlestheir perturbations under various experimental conditionsFor Drug, Polar Surface Area (PSA) and logPFor Nanoparticle, surface area, Van der Waals volume, and coating properties | Other: Therapeutics | The PTML model provides a powerful tool for the virtual screening of drug-nanoparticle combinations, significantly speeding up the identification of promising candidates for glioblastoma treatment. |
| 570 | Therapy / Drug Delivery | Sun *et al,* 2021 | Bionanoscale Recognition Underlies Cell Fate and Therapy | Quantify and compare the bionanoscale recognition of 1T-MoS2 (octahedral coordination) and 2H-MoS2 (triangular prism coordination) with fibronectin and liposomes | Other: Computational/Experimental study | Parkinson's disease | Machine Learning | Machine learning models, particularly Random Forest (RF) and Structural Equation Models (SEMs), are used to analyze the influence of nanostructured architectures on cell viability, adhesion, and differentiation.These models help identify key morphological features affecting cell healthType of Nano: 1T-MoS2 (octahedral coordination) and 2H-MoS2 (triangular prism coordination) nanostructures | Random Forest ModelStructural Equation Model | Supervised Learning | Classification: RF Model: Classifies cell health based on morphological features like neurite length and cell area.Regression: SEM Model: Quantifies how specific nanostructured architectures enhance cell viability. | Accuracy of RF Model: 89.2%AUC of RF Model: 0.893 | NA | Feature extraction was performed on sevenmorphological metrics related to neurite outgrowth and cell health. | in vitro experiments using PC12 cells, a neuronal cell line Parkinson’s disease (PD) model mouse | Other: Cell-based Therapeutics | This study demonstrates that octahedral coordination in nanomaterials, specifically 1T-MoS2, significantly enhances bio-nanoscale recognition, improving cell fate control and therapeutic potential. This discovery enables the rational design of biomaterials for targeted drug delivery, cell therapy, and neurodegenerative disease treatment, particularly Parkinson's disease, by modulating interactions with key biomolecules like fibronectin, liposomes, and alpha-synuclein. |