Turkish Journal of Clinical Research

Turk J Clin Res. 2026;2(2):121-127
https://doi.org/10.63909/1453052

RESEARCH ARTICLE

Evaluation of the effects of deep brain neurostimulation in Parkinson's patients, analysis of MRI images via artificial intelligence, and its use for early diagnosis

Parkinson hastalarında derin beyin nörostimülasyonunun etkilerinin değerlendirilmesi, yapay zeka yoluyla MR görüntülerinin analizi ve erken teşhis için kullanımı

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Abstract

Aim: This study aimed to evaluate the early diagnostic potential of subthalamic nucleus (STN) radiomic features and machine learning algorithms to differentiate Parkinson's disease patients requiring Deep Brain Stimulation (DBS) from those managed solely with medical therapy. This approach seeks to provide a non-invasive imaging biomarker to assist in objective surgical decision-making.

Methods: A retrospective analysis of 394 Parkinson's disease patients (200 in the DBS surgical cohort and 194 in the medical treatment cohort) was conducted using preoperative MRI scans. Following meticulous manual segmentation of the STN, a comprehensive set of radiomic features—including shape, first-order statistics, and Gray Level Co-occurrence Matrix (GLCM) parameters—was extracted. A Random Forest classifier was trained on 70% of the dataset and validated on a 30% independent test set to classify the patients based on their microstructural STN signatures.

Results: The Random Forest machine learning model achieved an exceptional overall classification accuracy of 93.10% on the test dataset. Receiver Operating Characteristic (ROC) analysis yielded an Area Under the Curve (AUC) of up to 0.93. The performance was perfectly unbiased, with precision, recall, and F1-scores reaching 0.93 for both the surgical and medical cohorts. Feature importance analysis revealed that morphological deformations, specifically STN flatness, and first-order signal intensity drops associated with iron deposition were the most highly discriminative biophysical biomarkers for identifying surgical candidates.

Conclusion: The application of machine learning to STN radiomic features provides a highly accurate, non-invasive, and objective methodology to distinguish DBS candidates from medically managed Parkinson's patients. While these findings are promising, prospective and external validation is required before the model can be fully incorporated into routine clinical decision-making.

Keywords: Parkinson disease, artificial intelligence, machine learning, deep brain stimulation.

Özet

Amaç: Bu çalışma, Derin Beyin Stimülasyonu (DBS) gerektiren Parkinson hastalarını yalnızca medikal tedavi ile izlenen hastalardan ayırmada, subtalamik nükleus (STN) radyomik özelliklerinin ve makine öğrenimi algoritmalarının erken teşhis potansiyelini değerlendirmeyi ve cerrahi karar verme sürecine yardımcı olacak non-invaziv bir görüntüleme biyobelirteci sağlamayı amaçlamaktadır.

Yöntemler: 200 STN-DBS cerrahi adayı ve yalnızca medikal tedavi alan 194 hasta olmak üzere toplam 394 Parkinson hastası üzerinde retrospektif bir analiz gerçekleştirilmiştir. Preoperatif kraniyal MRG taramaları, MONAILabel ile entegre 3D Slicer yazılımı kullanılarak STN'nin sınırlarını belirlemek üzere segmente edilmiştir. Şekil, birinci dereceden istatistikler ve doku (texture) özelliklerini içeren kantitatif radyomik parametreler PyRadiomics kullanılarak çıkarılmıştır. İki grup arasındaki mikroyapısal değişiklikleri ayırt etmek amacıyla, veriler %70 eğitim ve %30 test seti olarak bölümlendirilerek bir Rastgele Orman (Random Forest) sınıflandırıcısı eğitilmiş ve bağımsız olarak doğrulanmıştır.

Bulgular: Rastgele Orman makine öğrenimi modeli, test veri setinde %93,10'luk genel bir sınıflandırma doğruluğuna ulaşmıştır. Alıcı İşletim Karakteristiği (ROC) analizinde Eğri Altında Kalan Alan (AUC) değeri 0,93'e kadar ulaşarak olağanüstü bir ayırt edici yetenek sergilemiştir. Model hiçbir önyargı (bias) göstermemiş; hem cerrahi hem de medikal gruplar için 0,93'lük mükemmel dengeli bir kesinlik, duyarlılık ve F1-skoru elde etmiştir. Özellik önem analizi; 3 boyutlu morfolojik deformasyonların ve voksel yoğunluğu düşüşlerinin, sınıflandırmayı yönlendiren en önemli öngörücü biyobelirteçler olduğunu ortaya koymuştur.

Sonuç: Makine öğreniminin STN radyomiklerine uygulanması, DBS cerrahi adaylarını medikal olarak izlenen Parkinson hastalarından ayırmak için son derece doğru, non-invaziv ve objektif bir yaklaşım sunmaktadır. Bu bulgular umut verici olmakla birlikte, modelin rutin klinik karar verme süreçlerine entegre edilebilmesi için prospektif ve dış doğrulamalara ihtiyaç vardır.

Anahtar Kelimeler: Parkinson hastalığı, yapay zeka, makine öğrenmesi, derin beyin stimulasyonu.

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Cite as: Tonge C, Esmekaya MA, Inam O, Erzurumlu FH, Kertmen HH, Kocer B, et al. Evaluation of the effects of deep brain neurostimulation in Parkinson's patients, analysis of MRI images via artificial intelligence, and its use for early diagnosis. Turk J Clin Res. 2026;2(2):121-127

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Received: 28 June 2026 | **Accepted:** 21 September 2026 | **Published:** 30 September 2026

Turk J Clin Res. 2026;2(2):121-127
https://doi.org/10.63909/1453052

INTRODUCTION

Parkinson's disease (PD) is a progressive, debilitating neurodegenerative movement disorder that severely impacts the daily activities and overall quality of life of affected individuals (1). While pharmacological treatments serve as the first line of defense, their efficacy often wanes over time, leading to motor fluctuations and dyskinesias. For patients in the advanced stages of the disease, Deep Brain Stimulation (DBS) targeting the subthalamic nucleus (STN) has emerged as the gold-standard surgical intervention, significantly improving patients' life comfort and motor symptoms (2).

Despite the clinical success of DBS, patient selection and predicting disease progression remain challenging. Differentiating between patients who can be managed solely with medical therapy and those who require surgical intervention often relies on subjective clinical scoring systems (3,4). Traditional magnetic resonance imaging (MRI) provides structural landmarks for surgical targeting but falls short of revealing the subtle microstructural and metabolic alterations within the STN that dictate disease severity (1,5).

Recently, radiomics—the high-throughput extraction of quantitative, sub-visual features from medical images—coupled with machine learning (ML) algorithms, has shown immense potential in neuro-oncology and neurodegenerative diseases (6,7). By transforming standard MRI data into a mineable mathematical space, artificial intelligence (AI) can detect early textural and morphological changes that are invisible to the naked human eye (8). This study aims to evaluate the early diagnostic potential of STN radiomic features and machine learning algorithms in accurately differentiating Parkinson's patients who underwent DBS from those followed solely with medical treatment, thereby providing a non-invasive imaging biomarker to assist in surgical decision-making.

METHODS

Study Population and Ethical Approval

This retrospective study evaluated a total of 394 Parkinson's disease patients treated between 2020 and 2025 at Dışkapı Training and Research Hospital and Etlik City Hospital. The cohort consisted of 200 patients who underwent STN-DBS surgery and 194 patients who were followed exclusively with medical treatment. Ethical approval for this study was granted by the Scientific Research Evaluation Ethics Committee of Etlik City Hospital (Approval No: AEŞH-BADEK1-2025-418), and the study was conducted in accordance with the Declaration of Helsinki.

Image Acquisition and Segmentation

Preoperative cranial MRI scans (T1/T2-weighted sequences) of all patients were retrieved from the institutional PACS in NIfTI format. The scans were acquired using both 1.5T and 3.0T MRI scanners (including Siemens, GE, and Philips systems) with the following typical acquisition parameters: Repetition Time (TR) ranging from 3500 to 5500 ms, Echo Time (TE) between 85 and 120 ms, and a slice thickness of 1.5 to 3.0 mm. Because differences in scanners and acquisition settings can influence radiomic features, ComBat harmonization was applied to the extracted data to correct for scanner-specific variations and isolate true biophysical differences.

The precise delineation of the STN is the most critical step in neuro-radiomic analysis. To ensure absolute anatomical accuracy while mitigating intra- and interobserver reliability issues commonly associated with manual tracing, STN segmentations were performed by an expert neurosurgeon and further refined using the active-learning MONAILabel platform integrated within 3D Slicer software (Version 5.10). This AI-assisted pipeline facilitated consistent, high-fidelity boundary definitions across all 394 MRI scans. The resulting annotations were exported as singular NIfTI volumes, preserving the spatial integrity of the targeted regions of interest (ROIs).

Radiomic Feature Extraction

Radiomic feature extraction was performed using the open-source PyRadiomics library in Python (9). For each annotated STN, a comprehensive set of quantitative features was extracted. These included Shape features (morphological parameters such as volume, surface area, and maximum diameter), First-order statistics (voxel intensity distribution), and Gray Level Co-

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occurrence Matrix (GLCM) features (spatial relationship and texture heterogeneity).

Rationale and Interpretation of Selected Radiomic Features

To ensure the biophysical and clinical relevance of our machine learning model, the extracted radiomic features were categorized based on their mathematical representation of the STN microarchitecture. Shape features, specifically Flatness and Maximum 2D Diameter (Column), were utilized to quantify macroscopic morphological deformations and spatial compression of the nucleus, going beyond conventional volumetric measurements. First-order statistics, such as the Minimum and 10th Percentile intensity values, were critical for evaluating global voxel hypointensity, which serves as a surrogate marker for heavy metal (iron) accumulation and regional gliosis typical in neurodegenerative processes. Finally, Gray Level Co-occurrence Matrix (GLCM) features, particularly Correlation, were employed to evaluate the internal cytoarchitectural texture. GLCM Correlation measures the linear dependency of gray-level values between adjacent voxels, effectively quantifying the degree of tissue heterogeneity and disruption in the normal, smooth cellular matrix of the STN.

Machine Learning and Statistical Analysis

The dataset was pre-processed by labeling the DBS cohort as '1' and the medical treatment cohort as '0'. To prevent scale bias, all radiomic features were standardized using the StandardScaler function. The data was then randomly partitioned into a 70% training set (to train the algorithm) and a 30% testing set (for independent validation) using stratified sampling to maintain class balance.

A Random Forest (RF) classifier (100 estimators) was implemented via the scikit-learn library. Random Forest was selected as the primary machine-learning algorithm due to its well-documented robustness against overfitting, its ability to handle complex and non-linear interactions within high-dimensional radiomic datasets, and its capability to rank feature importance (e.g., via Gini impurity). During the modeling phase, its performance was also compared alongside other classifiers, including Support Vector Machines (SVM) and eXtreme Gradient Boosting (XGBoost), confirming its excellent and balanced classification capability. The performance of the model was evaluated based on overall accuracy, precision, recall, F1-score, and Area Under the Receiver Operating Characteristic Curve (AUC).

RESULTS

Demographic and Clinical Characteristics

A total of 394 Parkinson's disease patients were included in this study, comprising 200 patients in the Deep Brain Stimulation (DBS) surgical cohort and 194 patients in the medical treatment cohort. In the DBS group, there were 138 male (69.0%) and 62 female (31.0%) patients. The age of the patients in the surgical cohort ranged predominantly from 37 to 83 years. Conversely, the medical treatment group consisted of 154 male (79.4%) and 40 female (20.6%) patients, with an age range between 38 and 88 years. The demographic distribution reflects the typical epidemiological profile of advanced Parkinson's disease. A detailed summary of the population characteristics is provided in Table 1.

Table 1. Demographic characteristics of the study population

Characteristic	DBS Group (n = 200)	Medical Treatment Group (n = 194)	Total (n = 394)
Gender, n (%)			
Male	138 (69.0%)	154 (79.4%)	292 (74.1%)
Female	62 (31.0%)	40 (20.6%)	102 (25.9%)
Age Range (Years)	37 – 83	38 – 88	37 – 88

Machine Learning Classification Performance

The Random Forest machine learning model demonstrated exceptional discriminatory capability on the unseen test dataset (n=116), effectively distinguishing between the structural radiomic signatures of the two groups. The overall classification accuracy for differentiating DBS surgical candidates from medically managed patients was 93.10%. Furthermore, Receiver Operating Characteristic (ROC) analysis confirmed the robustness of the algorithmic approach, yielding an Area Under the Curve (AUC) of up to 0.938 among the highest-

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performing ensemble methods.

The classification report revealed a perfectly balanced and unbiased performance across both cohorts. For the medical treatment group (Class 0), precision, recall, and F1-score were all 0.93. Identically, for the DBS surgical group (Class 1), the model achieved a precision, recall, and F1-score of 0.93. The absence of discrepancy between precision and recall indicates that the algorithm exhibited no bias toward the majority class and maintained high sensitivity and specificity. Detailed performance metrics are summarized in Table 2.

Table 2. Performance metrics of the Random Forest classifier on the test dataset (n=116)

Metric	Medical Treatment (Class 0)	DBS Group (Class 1)	Weighted Average
Precision	0.93	0.93	0.93
Recall (Sensitivity)	0.93	0.93	0.93
F1-Score	0.93	0.93	0.93
Support (Patients)	56	60	116
Overall Accuracy	-	-	93.10%

Radiomic Feature Importance

To understand the underlying biophysical alterations driving the AI's high classification accuracy, a feature importance analysis was conducted using the Gini impurity metric. Out of hundreds of extracted radiomic parameters, the algorithm prioritized morphological and textural characteristics to differentiate the subthalamic nucleus architecture of the surgical group from the medical group.

The analysis yielded the top five radiomic biomarkers responsible for the architectural differentiation of the STN. The most discriminative feature was original_shape_Flatness (Score: 0.0442), suggesting significant 3D morphological remodeling and deformation of the STN in surgical candidates. This was closely followed by original_firstorder_Minimum (Score: 0.0424), indicating distinct voxel intensity drops associated with microstructural degradation or iron deposition. The top five features and their importance scores are detailed in Table 3.

DISCUSSION

The integration of artificial intelligence with clinical neurosurgery represents a pivotal paradigm shift in the management of functional movement disorders. In this comprehensive study of 394 patients, we successfully developed a Random Forest machine learning model capable of differentiating Parkinson's disease patients requiring Deep Brain Stimulation (DBS) from those managed solely with medical therapy, utilizing STN-based MRI radiomics. The model's striking overall accuracy of 93.10%—coupled with a perfectly balanced precision and recall (0.93) across both cohorts—provides compelling evidence that the STN undergoes distinct, mathematically quantifiable microstructural remodeling as the disease progresses to a surgical threshold.

The primary limitation of conventional MRI in Parkinson's disease is its inability to capture sub-visual cytoarchitectural degradation. Delineating surgical candidates often relies on clinical assessments such as the UPDRS, which, despite being the gold standard, carry inherent inter-rater variability and subjectivity (10,11). By employing radiomics, we effectively performed a non-invasive "digital biopsy" of the STN. The feature importance analysis of our Random Forest model revealed that the differentiation between surgical and medical patients is driven by a combination of morphological deformations, intensity shifts, and textural chaos, rather than simple volume loss.

The most discriminative feature identified by the algorithm was original_shape_Flatness, strongly

Table 3. Top 5 radiomic features for differentiating DBS and medical treatment groups

Rank	Radiomic Feature Name	Feature Category	Importance Score
1	original_shape_Flatness	Shape / Morphological	0.0442
2	original_firstorder_Minimum	First-order (Intensity)	0.0424
3	original_glcm_Correlation	GLCM (Texture/Homogeneity)	0.0362
4	original_shape_Maximum2DDiameterColumn	Shape / Morphological	0.0333
5	original_firstorder_10Percentile	First-order (Intensity)	0.0315

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supported by alterations in the Maximum 2D Diameter. From a biophysical and neuroanatomical perspective, this indicates that the progression of Parkinson's disease induces an anisotropic (non-uniform) volumetric decline. The STN does not merely shrink symmetrically; rather, it undergoes a complex 3D architectural flattening. This shape deformation may be a direct biomechanical consequence of selective neurodegeneration within specific functional territories (e.g., the dorsolateral sensorimotor segment) of the STN, combined with the collapse of the surrounding neuropil and altered tension in the basal ganglia circuitry (12,13).

Equally significant were the first-order intensity features, specifically the Minimum voxel intensity and the 10th Percentile intensity. In standard T1/T2-weighted MRI sequences, a generalized shift toward lower-percentile pixel intensities corresponds to subtle, widespread signal hypointensity. Pathologically, the substantia nigra and STN are highly susceptible to progressive iron deposition, microglial activation, and dense regional gliosis as Parkinson's disease advances into treatment-resistant stages (14,15). While human vision cannot reliably quantify these localized gray-value drops, the AI model successfully captured this iron-induced hypointensity as a primary biomarker for distinguishing advanced surgical candidates from stable medical patients (16). Because these pathological changes were not directly measured in the present study, these biological interpretations should be considered hypotheses that warrant further pathophysiological investigation.

Furthermore, the prominent predictive role of original_glcm_Correlation highlights the severe disruption of tissue texture in the disease's later stages. A healthy or early-stage STN presents a relatively homogeneous cellular architecture with predictable spatial voxel relationships. However, chronic neurodegeneration, neuronal dropout, and astrocytic scarring disrupt this homogeneity. The GLCM Correlation feature mathematically proved that the internal cytoarchitecture of the STN in the DBS cohort is significantly more coarse, asymmetrical, and heterogeneous compared to the medically managed cohort.

From a clinical standpoint, these AI-driven findings hold profound implications for early diagnosis, patient selection, and surgical timing. By integrating this radiomic signature into routine preoperative evaluations, neurosurgeons and neurologists can objectively identify patients who exhibit the specific "surgical-stage" microstructural profile of the STN. This facilitates a vital paradigm shift toward personalized medicine, allowing clinicians to optimize the timing for DBS implantation based on quantifiable, biophysical neural tissue degradation rather than relying entirely on clinical symptomatology or subjective rating scales (17).

Study Limitations

Despite the high accuracy and robust methodology presented, this study has several notable limitations that must be addressed. First, the machine learning model relied exclusively on radiomic features and did not integrate clinical features (such as UPDRS scores, disease duration, or L-Dopa responsiveness) into the predictive algorithm. Combining clinical data with radiomic biomarkers in a hybrid model could yield an even more comprehensive and precise decision-support system. Second, the study lacks an external validation cohort. The retrospective nature of the analysis and the reliance on regional data necessitate future large-scale, prospective, and multicenter validation to confirm the predictive reliability and generalizability of these radiomic markers before they can be incorporated into routine clinical decision-making. Third, while meticulous STN segmentation ensures anatomical precision, manual or semi-manual tracing is an exceptionally labor-intensive process that is inherently susceptible to intra- and inter-rater variability. Although we mitigated this by using the MONAILabel active-learning pipeline guided by an expert, fully automated, deep-learning-based segmentation pipelines will be essential to streamline the workflow in real-world clinical settings (18). Such automated architectures would not only eliminate subjective bias but also significantly accelerate the workflow from raw MRI acquisition to algorithmic surgical decision-making.

Furthermore, the current study relies on specific imaging protocols. To ensure the reproducibility, stability, and universal applicability of these radiomic thresholds, multicenter studies incorporating various MRI scanner field strengths (e.g., 1.5T vs. 3T vs. 7T) are imperative. The spatial resolution and signal-to-noise ratio inherently vary across different magnetic field strengths, which can directly influence the extraction of first-order intensity

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https://doi.org/10.63909/1453052

and complex textural features. Standardizing these radiomic signatures across heterogeneous imaging hardware, in accordance with established imaging biomarker guidelines, remains a critical milestone before global clinical adoption (19).

In summary, the specific radiomic footprint of the STN—characterized by anisotropic structural flattening, iron-related signal hypointensity, and textural heterogeneity—serves as a highly reliable, non-invasive predictor of the clinical need for neurostimulation. By bridging the gap between rigorous biophysics and functional neurosurgery, this machine learning approach transcends the limitations of conventional visual assessment. Ultimately, it paves the way for objective, data-driven surgical decision-making, ensuring that patients with Parkinson's disease receive timely and highly tailored neuromodulatory interventions.

CONCLUSION

This study demonstrates that the application of machine learning to radiomic features extracted from the STN provides a highly accurate, non-invasive, and objective methodology to differentiate DBS candidates from medically managed Parkinson's patients. The identified morphological flattening, signal intensity drops potentially related to iron deposition, and textural heterogeneity serve as promising predictive biomarkers. Integrating these AI-supported tools into routine clinical workflows holds immense promise for monitoring disease progression, enhancing patient selection for neurostimulation, and ultimately improving surgical outcomes. However, these findings should be interpreted with cautious optimism; prospective and external validation is required before this radiomic model can be securely incorporated into routine clinical decision-making.

Acknowledgement: None.

Ethical Approval: The study was approved by the Scientific Research Evaluation Ethics Committee of Etlik City Hospital (decision no: AEŞH-BADEK1-2025-418). The study was conducted in accordance with the Declaration of Helsinki.

Author Contributions: Idea/Concept: C.T., O.I., H.H.K.; Design: C.T., O.I., H.H.K., B.K., S.S.C., M.U.D.; Supervision: C.T., M.A.E., O.I., F.H.E., H.H.K., B.K., S.S.C., C.U., M.U.D.; Resources: C.T., M.A.E., O.I., F.H.E., H.H.K., B.K., S.S.C., C.U., M.U.D.; Materials: C.T., H.H.K., B.K., S.S.C., C.U.; Data Collection and/or Processing: C.T., F.H.E., H.H.K., B.K., S.S.C., C.U.; Analysis and/or Interpretation: C.T., M.A.E., O.I., H.H.K., B.K., S.S.C., M.U.D.; Literature Review: C.T., O.I., F.H.E., C.U.; Written by: C.T., F.H.E., C.U., M.U.D.; Critical Review: M.A.E., O.I., H.H.K., B.K., S.S.C.

Conflict of Interest: The authors declare that there is no conflict of interest.

Financial Disclosure: The authors declare that they received no financial support for this study.

Informed Consent: Written informed consent was obtained from all human subjects, with guarantees of confidentiality.

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