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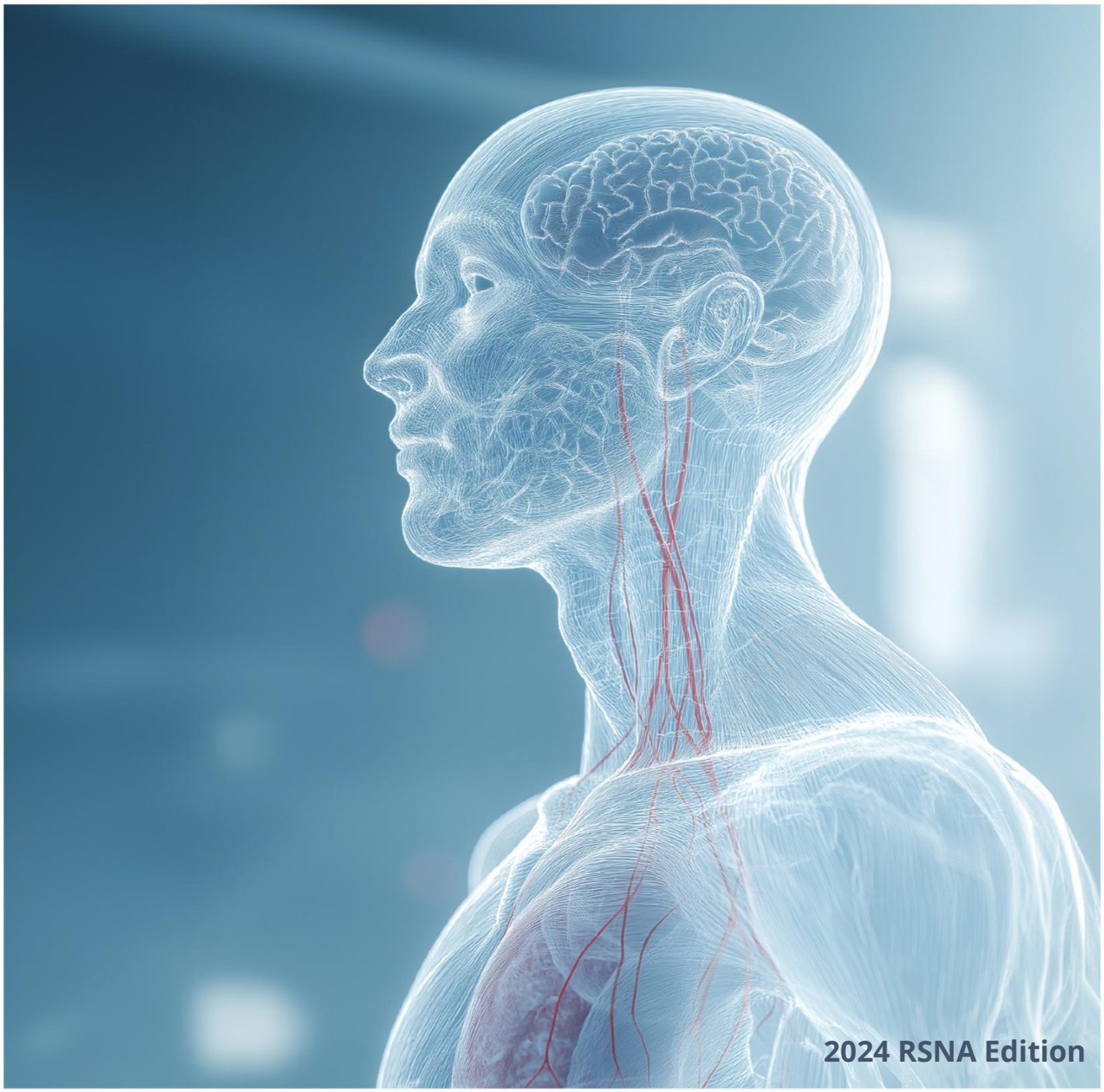

Issue Highlights

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Role of MULTIPLEX MRI in the characterization of brain tissues

Anand H.K.[a] , Ramachandra C.R.[a], Lohith H.P. [a], Pooja B. P.[a], Harshith G. [a], Arjun Raju[a]
[a]Tenet Diagnostic Centre, Bengaluru, India

1. Introduction

Brain tumors present a significant diagnostic and therapeutic challenge due to their heterogeneity, variability in progression, and response to treatment (1). Accurately distinguishing between control brain tissue and tumor regions, as well as characterizing the grade and type of tumors, is crucial for optimizing treatment strategies (2).

Advances in magnetic resonance imaging (MRI) technology have significantly enhanced the ability to non-invasively characterize brain tissues, providing critical information for diagnosing and understanding neurological disorders. Brain tumors are routinely evaluated using T1-weighted pre- and post-gadolinium contrast (T1w and T1wGd), T2-weighted (T2w), fluid-attenuated inversion recovery (T2w FLAIR), perfusion, and diffusion-weighted MRI sequences (3). The lengthy acquisition times (~30 min) of conventional quantitative MR techniques hinder their clinical adoption. Currently, MRI-based diagnosis primarily relies on visual inspection and interpretation, as the analysis of complex multi-parametric and multimodal data continues to be challenging (4, 5).

To overcome these limitations, advanced multi-parametric MRI techniques are being developed, which can simultaneously offer T1 mapping, T2/T2* mapping, quantitative susceptibility mapping (QSM), and proton density (PD) mapping etc. These techniques offer quantitative data and improve the objective assessment of brain tumors, showing potential to differentiate between tumor types, grades, and other pathological conditions with greater precision (5-7).

Pirkl CM et al. (5) investigated accelerated 3D imaging techniques for mapping T1, T2, and PD in glioma patients, assessing the feasibility of these fast protocols for clinical use. Deistung A et al. (8) emphasized the importance of integrating QSM into routine MRI protocols for glioblastoma, which could enhance diagnosis and treatment strategies. Quantitative MRI measurements, including T1, T2, T2*, PD, and QSM, provide valuable insights into the microstructural changes associated with Parkinson's disease (9-10).

Acquiring multiple quantitative MR parameters in a single, shorter scan would enhance patient comfort and reduce the risk of misalignment of critical anatomical details between imaging sequences taken at different times. Among the most promising developments in this field is MULTIPLEX (MTP)[1] MRI (11), a single-scan, multi-parametric 3D high-resolution MRI technique that offers detailed anatomical and quantitative information across multiple imaging modalities. By capturing high resolution (e.g. 1 mm isotropic voxels or less) images, MTP MRI generates 14 distinct sets of images, including T1W, PD, T2*-weighted, and susceptibility-weighted images (SWI), as well as quantitative maps of T1, T2*, PD, and QSM. It utilizes a design featuring dual repetition times (TR), dual flip angles (FA), and multi-echo gradient echo (GRE), combined with advanced image processing techniques such as multi-dimensional integration and cutting-edge algorithms (11). This approach provides comprehensive structural, functional, and biochemical information about brain tissues within a single scan lasting approximately 7.5 minutes (11).
On the other hand, machine learning (ML) has demonstrated significant potential in medical imaging, particularly for the automated classification of brain tumors (12). With the potential of quantitative MR mapping in brain tumor diagnosis, we aim to investigate machine learning models for brain tissue classification using multi-parametric (MTP) data. The objective of this study was to assess the role of T1, T2*, PD, and QSM mapping obtained from MTP MRI in the characterization of control and malignant brain tissues using ML algorithms.

2. Materials and Methods

[1] This product is not available for sale in the U.S. for clinical uses and also may not be available for such sales in other countries.

2.1 MRI data

This prospective study used an MRI dataset of 14 subjects (age: 45 ± 10 years) who were suspected of having brain diseases. Scanning was performed on a 3T MR scanner (uMR 780, United Imaging Healthcare Co., Ltd., Shanghai, China) at Tenet Diagnostics, Bengaluru, India from April 2024 to June 2024. All patients underwent MRI as part of their routine clinical care, and written informed consent was obtained from all participants. The MTP was acquired using a 3D GRE sequence with the following parameters: dual flip angles of 4° and 16°, repetition times (TR1/TR2) of 7.21 ms and 28.29 ms, seven echoes with echo times (TE) ranging from 3.05 ms to 22.97 ms, a bandwidth of 260 Hz/px, a matrix size of 218 × 256, 36 slices, and a 3D voxel size of 1.03 × 0.82 × 2 mm^3.. Without additional scan time, the MTP sequence produced T1, T2*, PD and susceptibility-weighted images together with their corresponding quantitative maps. All reconstructed T1, T2*, PD, and QSM maps were aligned in the same spatial coordinates.

2.2 Data processing

MRI data in DICOM format were transferred to a workstation and processed using MATLAB (v. 2022; MathWorks, Natick, MA, USA). An elliptical region of interest (ROI) was utilized to measure the quantitative parameter values in the T1, T2*, PD, and QSM maps for both healthy and malignant brain tissues. Figure 1 provides an illustration of the maps generated from MTP, along with ROI markings displayed on the quantitative maps.

2.2.1 Diagnostic performance of the maps derived from MTP

Parameters derived from MTP, such as T1, T2*, PD, and QSM values are used as input features for ML algorithms. Linear support-vector machine (SVM), Gaussian SVM and k-nearest neighbor (KNN) were employed to evaluate the diagnostic accuracy of the proposed framework by classification of control (n =14) and malignant (n =14) tissues using stratified 5-fold cross-validation. Figure 2 illustrates the workflow of the proposed methodology.

2.2.2 Statistical analysis

The performance of the classification model was evaluated by calculating key metrics such as sensitivity, specificity, accuracy, and the area under the receiver-operating characteristic curve (AUROC). To further analyze the differences in T1, T2*, PD, and QSM values between the two groups, a paired t-test was conducted. Additionally, boxplots were used to visually represent the distribution and variability of these quantitative parameters,

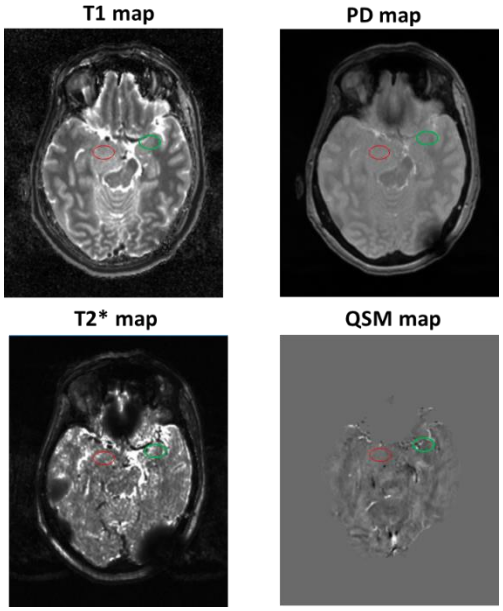

Figure 1: Example of the T1, T2*, PD and QSM maps derived from MTP MRI., Red ROI represents the malignant lesion and green ROI represents the healthy tissues

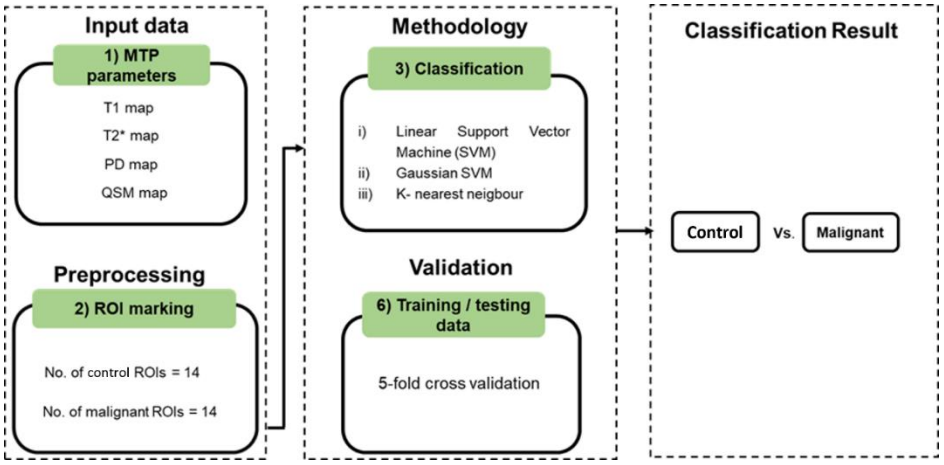

Figure 2: Overview of the proposed framework for classification using parameters derived by MTP

3 Results

3.1 T1, T2*, PD and QSM values

The mean values of T1, T2*, and QSM in malignant tissues were observed to be 1357.50 ± 99.70 ms, 67.08 ± 14.53 ms, and 0.061 ± 0.003 ppm, respectively. In comparison, healthy tissues exhibited mean values of 918.08 ± 101.23 ms for T1, 42.08 ± 15 ms for T2*, and 0.014 ± 0.007 ppm for QSM. The differences in T1, T2*, and QSM values between malignant and healthy tissues were statistically significant, with a *p*-value of less than 0.05. However, there were no significant differences in the PD values between the two groups. Boxplots illustrating the quantitative parameter values for both groups are shown in Figure 3.

3.2 Diagnostic performance using machine learn learning methods

The performance of the proposed classification model was evaluated using individual parametric maps (T1, T2*, PD, and QSM) as well as their combinations, such as combination of T1/T2* and T1/T2*/QSM. The combination of T1 and T2* parameters achieved a sensitivity of 74.23 ± 2.06%, a specificity of 78.56 ± 1.50%, an accuracy of 81.50 ± 1.10%, and an AUC of 0.80 when using a Gaussian SVM classifier. Additionally, the classification performance of PD alone was assessed, but it demonstrated poor accuracy, suggesting that this parameter has limited utility in the current pathological context. In contrast, the highest classification performance was achieved using the combination of T1, T2*, and QSM values. The Gaussian SVM classifier demonstrated a sensitivity of 82.10 ± 1.10%, a specificity of 84.34 ± 2.10%, an accuracy of 84.18 ± 1.10%, and an AUC of 0.83 for two-class classification. Figure 4 presents the ROC curves for the two-class classifications using three different classifiers. The results indicate that combining T1, T2*, and QSM parameters yields superior classification accuracy compared to using individual parameters.

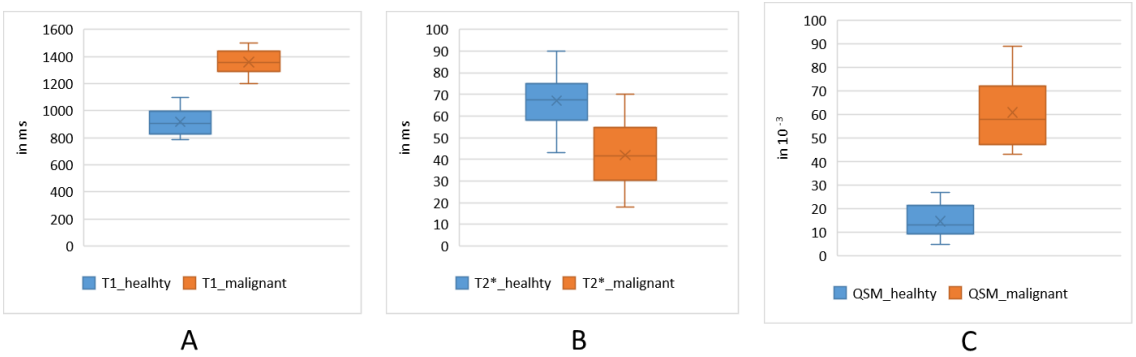

Figure 3: Boxplots for the comparison for A) T1, B) T2* and C) QSM values between healthy and malignant tissues

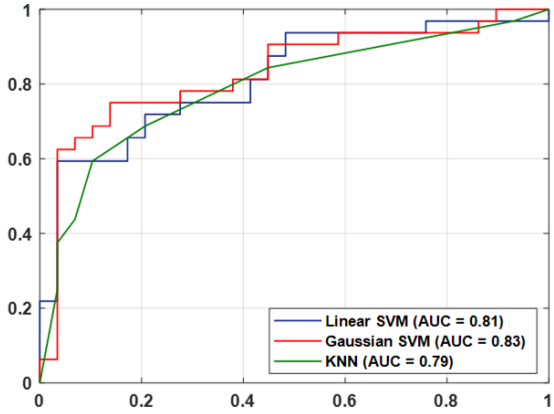

Figure 4: ROC graphs for the two-class classification using the combination of T1, T2*, and QSM maps

4. Discussions

The integration of MTP MRI and ML techniques for the characterization of healthy and malignant brain tissues offers significant advantages over conventional imaging methods. This study demonstrates that combining quantitative MTP parameters, such as T1, T2*, and QSM, can improve the diagnostic accuracy and differentiation between normal and tumor tissues.

One of the primary strengths of MTP MRI (11) is its ability to acquire multiple imaging parameters in a single scan, thus reducing scan time and minimizing patient discomfort. Traditional MRI sequences often require multiple scans, increasing the likelihood of patient movement and image misregistration. The ability to extract several quantitative maps in one session enhances diagnostic efficiency and allows for a more comprehensive evaluation of tissue microstructure. These quantitative maps provide objective, reproducible measurements that overcome the subjectivity associated with conventional MRI interpretation.

This study highlights the performance of ML algorithms, particularly linear SVM, Gaussian SVMs and KNN. These algorithms were selected based on the previous literature (13-14). Notably, the combination of T1, T2*, and QSM parameters achieved higher classification accuracy, with AUC of 0.83, significantly outperforming the use of single parameters. These results emphasize the importance of combining multiple parameters to capture the full spectrum of tissue characteristics, especially in complex tumor environments where individual parameters may provide limited information.

The study reinforces the critical role of QSM and T2* maps in tissue characterization. Both parameters have proven sensitive to microstructural changes in the tumor environment. While the results of this pilot study are promising, few limitations must be acknowledged. First, the dataset was small. Larger, multi-center datasets are needed to validate the generalizability of these findings across diverse populations and tumor types. Future research should focus on external validation to assess model performance in real-world clinical settings.

Additionally, despite the strong performance of T1, T2*, and QSM combinations, other potentially valuable parameters—such as DWI and perfusion-weighted imaging were not explored in this study. These modalities could provide complementary information about tumor cellularity and vascularity, further enhancing the ML models' ability to distinguish between different tumor types and grades. Future studies could investigate the inclusion of these parameters to develop even more robust, multi-modal ML models.

5. Conclusion

This study highlights the advantages of MTP MRI for brain tissue characterization, offering multiple quantitative parameters, such as T1, T2*, PD and QSM, in a single and fast scan. The ability to acquire high-resolution, multi-parametric data significantly improves diagnostic accuracy when combined with ML techniques. By reducing scan time and minimizing misregistration, MTP MRI provides a more efficient, comprehensive, and objective evaluation of brain tissues, enhancing its potential for use in clinical practice and personalized treatment planning.

6. Image/Figure Courtesy

All images are the courtesy of Tenet Diagnostic, Bengaluru India.

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Author Biographies

Dr. Anand H.K.
Chief of Medical Services and CEO,
Tenet Diagnostics,
Ex-President of Indian Radiological and Imaging Association (IRIA), Karnataka
Bengaluru, India

Dr. Anand H. K. is an experienced Radiology and Imaging expert with over 22 years in the field. He is the Chief of Medical Services and CEO at Tenet Diagnostics in Bengaluru. He completed his MBBS in 1996 and earned an MD in Radiology with a Gold Medal in 2000 from Kasturba Medical College, Manipal, India. Dr. Anand co-founded Clumax Diagnostics and has worked as a Consultant Radiologist at various healthcare institutions. He also served as an Assistant Professor at Kasturba Medical College and is an accomplished researcher in areas like Neuro Radiology, Body and Musculoskeletal Imaging, and Cardiac Imaging. He received multiple Radiologists Fellowships for CT Coronary Angiography and has presented and published research at national and international conferences. His contributions demonstrate his dedication to advancing the field of Radiology.

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