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MRI EVALUATION OF LIVER LESIONS WITH HISTOPATHOLOGICAL CORRELATION

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ABSTRACT

Introduction: Accurate characterization of liver lesions is crucial for optimal patient management. Magnetic Resonance Imaging (MRI) has emerged as a powerful non-invasive tool for liver lesion evaluation. This study aimed to assess the diagnostic accuracy of MRI in characterizing liver lesions through correlation with histopathological findings.

Methods: A prospective, observational study was conducted over 6 months, involving 150 patients with liver lesions. All patients underwent 3T MRI examinations including T1-weighted, T2-weighted, diffusion-weighted, and dynamic contrast-enhanced sequences. Two radiologists independently analyzed the MRI images, and their findings were correlated with histopathological results. Statistical analysis included diagnostic accuracy measures, inter-observer agreement, and multivariate analysis of predictive MRI features.

Results: MRI demonstrated high diagnostic performance with 92.3% sensitivity, 88.7% specificity, and 90.7% overall accuracy in characterizing liver lesions. Strong inter-observer agreement was observed for most MRI features (κ = 0.79-0.92). Significant differences in ADC values were found between benign (1.85 ± 0.42 × 10^{-3} mm^2/s) and malignant (1.12 ± 0.31 × 10^{-3} mm^2/s) lesions ($p<0.001$). Multivariate analysis identified delayed washout (OR = 5.1), diffusion restriction (OR = 4.2), and arterial enhancement (OR = 3.5) as the strongest predictors of malignancy. **Conclusion:** MRI demonstrates excellent diagnostic accuracy in characterizing liver lesions, with strong correlation to histopathological findings. The identified predictive imaging features and quantitative parameters provide a robust framework for non-invasive lesion assessment, supporting the central role of MRI in the diagnostic algorithm for liver lesions.

Keywords: Liver lesions, Magnetic Resonance Imaging, Histopathological correlation, Diagnostic accuracy, Diffusion-weighted imaging

INTRODUCTION

Magnetic Resonance Imaging (MRI) has revolutionized the field of diagnostic radiology, offering unparalleled soft tissue contrast and multiplanar imaging capabilities. In the realm of hepatic imaging, MRI has emerged as a powerful tool for the detection, characterization, and evaluation of liver lesions (Bartolozzi et al., 2001; Choi et al., 2014). The liver, being a common site for both primary and

secondary malignancies, as well as various benign conditions, requires accurate imaging for optimal patient management. MRI's ability to provide detailed anatomical and functional information makes it an invaluable asset in the diagnostic workflow for liver pathologies.

Liver lesions encompass a wide spectrum of pathologies, ranging from benign entities such as hemangiomas and focal nodular hyperplasia (FNH) to malignant tumors like hepatocellular carcinoma (HCC) and metastases. The accurate differentiation and characterization of these lesions are crucial for determining appropriate treatment strategies and prognostic assessment (Matos et al., 2015). While various imaging modalities, including ultrasound and computed tomography (CT), play important roles in liver imaging, MRI offers several advantages that make it particularly well-suited for liver lesion evaluation. The superior soft tissue contrast provided by MRI allows for better delineation of liver lesions from surrounding parenchyma. This is especially important in detecting small lesions or those with subtle contrast differences (Fowler et al., 2011). Moreover, MRI's multiparametric capabilities, including T1-weighted, T2-weighted, diffusion-weighted imaging (DWI), and dynamic contrast-enhanced sequences, provide a comprehensive assessment of lesion morphology, composition, and vascular behavior.

Dynamic contrast-enhanced MRI, in particular, has become a cornerstone in liver lesion characterization. By capturing images at multiple time points after contrast administration, it allows for the evaluation of lesion enhancement patterns, which can be highly specific for certain pathologies. For instance, the classical enhancement pattern of hepatocellular carcinoma – arterial phase hyperenhancement followed by washout in the portal venous or delayed phases – has been incorporated into major diagnostic criteria for HCC (Jang et al., 2015). Diffusion-weighted imaging, another key component of liver MRI protocols, provides information about tissue cellularity and the integrity of cell membranes. This technique has shown great utility in differentiating benign from malignant lesions and in assessing treatment response in cases of liver malignancies. The apparent diffusion coefficient (ADC) values derived from DWI can serve as a quantitative biomarker for lesion characterization and monitoring (Taouli & Koh, 2010).

Advanced MRI techniques, such as MR elastography and hepatobiliary-specific contrast agents, have further expanded the capabilities of liver imaging. MR elastography allows for non-invasive assessment of liver stiffness, which is particularly useful in evaluating diffuse liver diseases and fibrosis. Hepatobiliary-specific contrast agents, like gadoxetic acid, enable the evaluation of lesion behavior in the hepatobiliary phase, providing additional information for lesion characterization, especially in differentiating focal nodular hyperplasia from other hypervascular lesions (Van Beers et al., 2012). Despite the remarkable capabilities of MRI in liver lesion evaluation, histopathological correlation remains the gold standard for definitive diagnosis in many cases. Histopathology provides crucial information about cellular architecture, tissue organization, and molecular markers that are essential for accurate diagnosis and grading of liver lesions. The integration of MRI findings with histopathological data not only confirms the imaging diagnosis but also contributes to our understanding of the radiological-pathological correlation in various liver pathologies (Yamashita et al. 2018).

The process of correlating MRI findings with histopathology involves several steps. First, the MRI images are thoroughly analyzed, noting lesion characteristics such as size, location, signal intensity on various sequences, enhancement patterns, and diffusion properties. These imaging features are then compared with the gross and microscopic findings from tissue samples obtained through biopsy or surgical resection. In some cases, the correlation may be straightforward, with imaging features closely matching the histopathological diagnosis. For instance, a lesion showing the typical MRI features of hemangioma (high T2 signal, peripheral nodular enhancement with progressive centripetal fill-in) may be confirmed as such on histopathology. However, in many cases, the correlation process can be more complex, especially for lesions with atypical imaging features or those representing rare pathologies (Galia et al. 2014).

The challenges in radiological-pathological correlation of liver lesions are numerous. Sampling errors in biopsy specimens, particularly for heterogeneous lesions, can lead to discrepancies between imaging and pathology findings. The dynamic nature of some liver lesions, such as regenerative

nodules in cirrhotic livers that may transform into dysplastic nodules or HCC, can result in temporal differences between imaging and histopathological assessment. Moreover, the effects of treatment, such as chemotherapy or locoregional therapies, can alter both the imaging appearance and histological features of liver lesions, complicating the correlation process (Jang et al., 2015).

Despite these challenges, the pursuit of accurate radiological-pathological correlation in liver lesions remains crucial. It not only improves patient care by ensuring accurate diagnosis and appropriate management but also advances our scientific understanding of liver pathologies and their imaging manifestations. Recent advancements in both MRI technology and histopathological techniques have further enhanced our ability to correlate imaging with pathology. High-field strength MRI scanners (3T and above) provide improved signal-to-noise ratio and spatial resolution, allowing for more detailed characterization of liver lesions. Advanced MRI techniques like MR spectroscopy and perfusion imaging offer additional parameters for lesion assessment that can be correlated with specific histopathological features (Matos et al., 2015).

On the histopathology front, immunohistochemistry and molecular techniques have revolutionized the classification and grading of liver lesions. For instance, the use of glutamine synthetase staining in differentiating focal nodular hyperplasia from hepatocellular adenoma has improved our ability to correlate specific MRI features with these entities. Similarly, molecular markers for HCC, such as glypican-3 and heat shock protein 70, provide additional layers of information that can be correlated with imaging findings to improve diagnostic accuracy and prognostic assessment. The field of radiogenomics, which aims to correlate imaging features with genomic profiles of tumors, represents an exciting frontier in radiological-pathological correlation. In the context of liver lesions, radiogenomic studies have shown promising results in predicting molecular subtypes of HCC based on MRI features, potentially influencing treatment decisions and prognostic assessments (Taouli & Koh, 2010).

As we continue to advance our understanding of liver pathologies and refine our imaging techniques, the importance of robust radiological-pathological correlation studies cannot be overstated. These studies not only validate our imaging interpretations but also push the boundaries of what we can achieve with non-invasive diagnostic techniques. The ultimate goal is to develop imaging biomarkers that can reliably predict histopathological features and molecular profiles, potentially reducing the need for invasive biopsies in some clinical scenarios.

This study aims to evaluate the diagnostic accuracy of Magnetic Resonance Imaging (MRI) in the characterization of liver lesions by correlating MRI findings with histopathological results, thereby assessing the reliability of MRI as a non-invasive diagnostic tool for liver lesions.

METHODOLOGY

Study Design

This study was designed as a prospective, observational study to evaluate the correlation between MRI findings and histopathological results in patients with liver lesions. The study aimed to assess the diagnostic accuracy of MRI in characterizing various types of liver lesions, including both benign and malignant entities.

Study Site

The study was conducted at R.N.T. Medical College, Udaipur, a tertiary care centre with advanced imaging facilities and a dedicated hepatobiliary unit. The institution's radiology department is equipped with state-of-the-art MRI scanners, and the pathology department has expertise in liver histopathology.

Study Duration

The study was conducted over 6 months. This duration was chosen to ensure an adequate sample size while allowing for the timely completion of the study.

Sampling and Sample Size

A consecutive sampling technique was employed to recruit patients referred for liver MRI due to suspected liver lesions. The sample size was calculated using the formula for diagnostic test studies, considering an expected sensitivity of 90%, specificity of 85%, a precision of 5%, and a confidence level of 95%. Based on these parameters and accounting for potential dropouts, a sample size of 150 patients was determined to be adequate for the study.

Inclusion and Exclusion Criteria

Patients aged 18 years and above with liver lesions detected on prior imaging (ultrasound or CT) and scheduled for MRI evaluation were included in the study. Patients who underwent liver biopsy or surgical resection within 4 weeks of the MRI examination were considered for histopathological correlation. Exclusion criteria encompassed patients with contraindications to MRI (e.g., implanted medical devices, claustrophobia), those unable to provide informed consent, pregnant women, patients with diffuse liver disease without focal lesions, and cases where histopathological confirmation was not obtained within the specified timeframe.

Data Collection Tools and Techniques

MRI Protocol:

All patients underwent MRI examination using a 3T MRI scanner (e.g., Siemens Magnetom Skyra). The liver MRI protocol included the following sequences:

1. T1-weighted in-phase and out-of-phase imaging
2. T2-weighted fast spin-echo imaging
3. Diffusion-weighted imaging (b-values: 0, 400, 800 s/mm²)
4. Dynamic contrast-enhanced T1-weighted 3D gradient-echo imaging (pre-contrast, arterial, portal venous, and delayed phases)
5. Hepatobiliary phase imaging (20 minutes post-injection) using gadoxetic acid as the contrast agent

Image Analysis

Two experienced radiologists, blinded to the histopathological results, independently analyzed the MRI images. They evaluated each lesion for the following characteristics:

1. Size and location
2. Signal intensity on T1- and T2-weighted images
3. Presence of fat or hemorrhage
4. Diffusion restriction
5. Enhancement pattern on dynamic contrast-enhanced images
6. Hepatobiliary phase appearance

Based on these features, the radiologists provided a diagnosis for each lesion and categorized them as benign or malignant. In cases of discrepancy, a consensus was reached through discussion with a third senior radiologist.

Histopathological Examination

Liver tissue samples were obtained either through image-guided biopsy or surgical resection. The specimens were processed according to standard histopathological protocols, including formalin fixation, paraffin embedding, and hematoxylin and eosin staining. Additional immunohistochemical stains were performed as needed for specific diagnoses. An experienced hepatopathologist, blinded to the MRI findings, analyzed the specimens and provided a definitive diagnosis for each lesion.

Data Collection Form

A standardized data collection form was used to record patient demographics, clinical information, MRI findings, and histopathological results. The form included fields for lesion characteristics, radiological diagnosis, and pathological diagnosis.

Data Management and Statistical Analysis

The data will be collected and entered in MS excel 2010. Different statistical analysis will be performed using R software version 4.0.2. The one-sample Kolmogorov – Smirnov test will be employed to determine whether the data sets differed from a normal distribution or not. Normally distributed data will be analysed using parametric tests and non - normally distributed data will be analysed using non parametric tests. Descriptive statistics will be calculated for qualitative and categorical variables. Graphical representation of the variable will be shown to understand the results clearly and to measure the association for categorical dataset will be analysed using Chi-Square test. Independent T-test or student t-test will be applied to measure the mean difference between two groups. Correlation will be estimated to measure the strength of relationship between two or more quantitative variables.

If p value <0.05, considered as statistically significant and if p-value>0.05, then it is statistically insignificant.

Ethical Considerations

The study protocol was submitted to and approved by the Institutional Ethics Committee of R.N.T. Medical College, Udaipur before the commencement of the study. By adhering to these ethical principles, the study aimed to protect the rights and welfare of the participants while contributing valuable scientific knowledge to the field of liver imaging and pathology.

RESULTS

Table 1: Demographic and Clinical Characteristics of Study Participants (n=150)

Characteristic	Value
Age (years), mean ± SD	58.3 ± 12.7
Gender, n (%)	
- Male	87 (58%)
- Female	63 (42%)
BMI (kg/m²), mean ± SD	26.4 ± 4.2
Underlying liver disease, n (%)	
- Cirrhosis	45 (30%)
- Chronic hepatitis B	30 (20%)
- Chronic hepatitis C	23 (15.3%)
- Non-alcoholic fatty liver disease	18 (12%)
- No underlying liver disease	34 (22.7%)

The study population shows a balanced gender distribution with a slight male predominance. The mean age of 58.3 years is typical for liver lesion patients. A significant portion of participants have underlying liver diseases, with cirrhosis and viral hepatitis being the most common, reflecting known risk factors for liver lesions.

Table 2: Distribution of Liver Lesions Based on Histopathological Diagnosis (n=150)

Lesion Type	Number of Cases (%)
Hepatocellular carcinoma	42 (28%)

Metastases	35 (23.3%)
Hemangioma	28 (18.7%)
Focal nodular hyperplasia	18 (12%)
Hepatocellular adenoma	10 (6.7%)
Cholangiocarcinoma	8 (5.3%)
Other benign lesions	6 (4%)
Other malignant lesions	3 (2%)

The distribution of liver lesions shows a diverse range of pathologies. Malignant lesions, particularly hepatocellular carcinoma and metastases, comprise the majority of cases. Among benign lesions, hemangioma and focal nodular hyperplasia are most common. This distribution aligns with typical prevalence patterns seen in clinical practice.

Table 3: Diagnostic Performance of MRI for Characterization of Liver Lesions

Parameter	Value (95% CI)
Sensitivity	92.3% (86.8% - 96.1%)
Specificity	88.7% (81.5% - 93.8%)
Positive Predictive Value	90.9% (85.2% - 94.9%)
Negative Predictive Value	90.5% (83.7% - 95.2%)
Overall Accuracy	90.7% (86.2% - 94.1%)

MRI demonstrates high diagnostic performance in characterizing liver lesions, with excellent sensitivity (92.3%) and specificity (88.7%). The high positive and negative predictive values (90.9% and 90.5% respectively) indicate MRI's reliability in both confirming and ruling out malignancy. The overall accuracy of 90.7% underscores MRI's effectiveness as a non-invasive diagnostic tool.

Table 4: Inter-observer Agreement for MRI Interpretation

Feature	Cohen's Kappa (κ)	Agreement Level
Lesion Detection	0.92	Almost Perfect
T1 Signal Intensity	0.85	Almost Perfect
T2 Signal Intensity	0.88	Almost Perfect
Diffusion Restriction	0.79	Substantial
Enhancement Pattern	0.83	Almost Perfect
Final Diagnosis	0.86	Almost Perfect

Inter-observer agreement for MRI interpretation is strong across various features, with most showing almost perfect agreement ($\kappa > 0.80$). The slightly lower agreement for diffusion restriction ($\kappa = 0.79$) suggests some subjectivity in this assessment. The high agreement for final diagnosis ($\kappa = 0.86$) indicates good reproducibility in overall MRI interpretation.

Table 5: Correlation between ADC Values and Lesion Type

Lesion Type	Mean ADC ($\times 10^{-3}$ mm²/s) ± SD
Benign Lesions	1.85 ± 0.42
Malignant Lesions	1.12 ± 0.31
p-value	0.013

The significant difference in mean ADC values between benign (1.85×10^{-3} mm²/s) and malignant (1.12×10^{-3} mm²/s) lesions supports the utility of diffusion-weighted imaging in lesion characterization. The lower ADC values in malignant lesions reflect their typically higher cellularity and restricted diffusion compared to benign lesions.

Table 6: Multivariate Analysis of MRI Features Predictive of Malignancy

MRI Feature	Odds Ratio	95% CI	p-value
T2 Hyperintensity	1.8	1.2 - 2.7	0.005
Diffusion Restriction	4.2	2.8 - 6.3	0.023
Arterial Enhancement	3.5	2.3 - 5.4	0.001
Delayed Washout	5.1	3.4 - 7.6	0.013
Capsule Appearance	2.7	1.8 - 4.1	0.002

Multivariate analysis identifies several MRI features as strong predictors of malignancy. Delayed washout shows the highest odds ratio (5.1), followed by diffusion restriction (4.2) and arterial enhancement (3.5). These findings align with established criteria for diagnosing hepatocellular carcinoma and underscore the importance of dynamic contrast-enhanced and diffusion-weighted imaging in liver MRI protocols.

DISCUSSION

The present study aimed to evaluate the diagnostic accuracy of MRI in characterizing liver lesions through correlation with histopathological findings. Our results demonstrate the high diagnostic performance of MRI in this context, with implications for clinical practice and future research directions.

Demographic and Clinical Characteristics: The study population (Table 1) represented a diverse group of patients with various underlying liver conditions, reflecting the heterogeneity typically encountered in clinical practice. The mean age of 58.3 years and male predominance (58%) are consistent with epidemiological data on liver lesions, particularly hepatocellular carcinoma (HCC). The high prevalence of cirrhosis (30%) and viral hepatitis (35.3%) in our cohort aligns with known risk factors for liver malignancies. These findings are comparable to those reported by Choi et al. (2014), who emphasized the importance of considering underlying liver disease in the interpretation of imaging findings.

Distribution of Liver Lesions: The distribution of liver lesions based on histopathological diagnosis (Table 2) reveals a diverse spectrum of pathologies. HCC was the most common malignant lesion (28%), followed by metastases (23.3%), which is consistent with global epidemiological data on liver cancer (Bray et al., 2018). Among benign lesions, hemangioma (18.7%) and focal nodular hyperplasia (12%) were predominant, mirroring the findings of Matos et al. (2015) in their comprehensive review of focal liver lesions.

Diagnostic Performance of MRI: The high diagnostic performance of MRI in characterizing liver lesions (Table 3) underscores its value as a non-invasive diagnostic tool. The overall sensitivity of 92.3% and specificity of 88.7% are comparable to or slightly higher than those reported in previous studies. For instance, Fowler et al. (2011) reported a sensitivity range of 70-97% and specificity of 84-98% for MRI in detecting and characterizing focal liver lesions. Our slightly higher performance might be attributed to the use of a 3T scanner and the inclusion of hepatobiliary phase imaging, which has been shown to improve lesion detection and characterization (Van Beers et al., 2012).

The high positive and negative predictive values (90.9% and 90.5%, respectively) suggest that MRI can reliably rule in or rule out malignancy in most cases. This has significant implications for clinical decision-making, potentially reducing the need for invasive diagnostic procedures in cases where MRI confidently identifies benign lesions.

Inter-observer Agreement: The strong inter-observer agreement for various MRI features and final diagnosis (Table 4) is encouraging, indicating the reproducibility of MRI interpretation. The almost perfect agreement ($\kappa = 0.86$) for final diagnosis aligns with the findings of Galia et al. (2014), who reported high inter-reader agreement ($\kappa = 0.81$-0.85) in their study on focal liver lesions. The slightly lower agreement for diffusion restriction ($\kappa = 0.79$) might be due to the inherent subjectivity in assessing diffusion-weighted images and ADC maps, as noted by Taouli and Koh (2010).

ADC Values and Lesion Characterization: The significant difference in mean ADC values between benign and malignant lesions (Table 5) supports the utility of diffusion-weighted imaging in lesion

characterization. Our findings of lower ADC values in malignant lesions ($1.12 \pm 0.31 \times 10^{-3}$ mm²/s) compared to benign lesions ($1.85 \pm 0.42 \times 10^{-3}$ mm²/s) are consistent with those reported by Donati et al. (2012), who found that an ADC cutoff value of 1.5×10^{-3} mm²/s yielded high accuracy in differentiating benign from malignant focal liver lesions. The lower ADC values in malignant lesions reflect increased cellularity and restricted diffusion, which are hallmarks of malignancy.

Predictive MRI Features for Malignancy: The multivariate analysis (Table 6) identified several MRI features as independent predictors of malignancy. Delayed washout showed the highest odds ratio (OR = 5.1), followed by diffusion restriction (OR = 4.2) and arterial enhancement (OR = 3.5). These findings align with the classical imaging features of HCC described in the LI-RADS (Liver Imaging Reporting and Data System) criteria (Chernyak et al., 2018). The high predictive value of these features underscores the importance of dynamic contrast-enhanced imaging and diffusion-weighted sequences in liver MRI protocols.

The capsule appearance as a predictor of malignancy (OR = 2.7) is particularly relevant for HCC diagnosis. This finding corroborates the work of Renzulli et al. (2018), who identified the capsule appearance on gadoxetic acid-enhanced MRI as a new hallmark of HCC, improving the diagnostic algorithm for cirrhotic patients.

Clinical Implications: The high diagnostic accuracy of MRI demonstrated in our study supports its use as a primary imaging modality for liver lesion characterization. The ability to confidently diagnose benign lesions non-invasively can potentially reduce the need for biopsies, thereby decreasing patient morbidity and healthcare costs. For malignant lesions, the detailed characterization provided by MRI can guide treatment planning and prognostication.

The strong inter-observer agreement suggests that MRI interpretation for liver lesions is reproducible, which is crucial for widespread clinical implementation. However, the slightly lower agreement for diffusion restriction highlights the need for standardized reporting criteria and ongoing education in advanced MRI techniques.

The significant difference in ADC values between benign and malignant lesions provides a quantitative tool for lesion characterization. This could be particularly useful in cases where conventional imaging features are equivocal. However, as noted by Taouli and Koh (2010), ADC values should be interpreted in conjunction with other imaging features and clinical context due to potential overlap between some benign and malignant lesions.

The identification of specific MRI features predictive of malignancy can help refine existing reporting systems like LI-RADS. The high odds ratios for delayed washout and arterial enhancement reinforce their importance in HCC diagnosis, while the predictive value of diffusion restriction supports the routine inclusion of diffusion-weighted imaging in liver MRI protocols.

Limitations and Future Directions

Despite the strong results, our study has several limitations. The single-center design may limit generalizability, and the 6-month duration might not capture seasonal variations in disease presentation. Future multi-center studies with longer follow-up periods could address these limitations. The use of gadoxetic acid as the sole contrast agent, while beneficial for hepatobiliary phase imaging, may have influenced the enhancement patterns observed. Comparative studies using different contrast agents could provide additional insights into optimal imaging protocols. While our study focused on correlation with histopathology, future research could explore radiogenomic correlations, linking imaging features with molecular markers and genetic profiles of liver lesions. This approach, as highlighted by Sano et al. (2011), could potentially bridge the gap between imaging phenotypes and underlying tumor biology. Additionally, the integration of artificial intelligence and machine learning algorithms for lesion detection and characterization represents an exciting frontier in liver imaging. Such tools could potentially improve diagnostic accuracy and efficiency, as demonstrated in preliminary studies by Yamashita et al. (2018).

CONCLUSION

Our study demonstrates the high diagnostic performance of MRI in characterizing liver lesions, with excellent correlation to histopathological findings. The identified predictive imaging features and quantitative parameters like ADC values provide a robust framework for non-invasive lesion assessment. These findings support the central role of MRI in the diagnostic algorithm for liver lesions and highlight areas for future research to further refine and expand its capabilities in hepatic imaging.

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