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Radio-Pathological Correlation in Atypical Uterine Smooth Muscle Tumors: Differentiating STUMP from Leiomyomas.

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ABSTRACT

Background & Objective: Uterine Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP) sit in a frustrating diagnostic gray zone between benign fibroids and aggressive sarcomas. For surgeons, the inability to confidently differentiate these tumors pre-operatively creates a dangerous dilemma: risk spreading occult cancer via morcellation or perform unnecessarily radical surgeries on young women. This study aimed to bridge that gap by systematically correlating pre-operative radiological features with post-operative histopathology to identify reliable predictive markers for STUMP.

Methods: In this retrospective cohort study (November 2024 to January 2026), we analyzed 155 patients presenting with suspected atypical uterine masses at a tertiary care center. We evaluated pre-operative transvaginal ultrasound, color Doppler hemodynamics, and multiparametric Magnetic Resonance Imaging (MRI) characteristics. These imaging indices were then mapped against their definitive post-operative histopathological diagnoses, which were established using the rigorous Stanford criteria following myomectomy or hysterectomy.

Results: Final histopathology confirmed 131 benign atypical variants, 19 STUMPs, and 5 leiomyosarcomas. Sonographically, STUMP lesions demonstrated significantly lower vascular resistance (mean Resistance Index = 0.54) compared to benign variants (mean RI = 0.68, $p < 0.05$), indicating aggressive neoangiogenesis. On MRI, borderline tumors frequently exhibited heterogeneous T2 hyperintensity and marked restricted diffusion. The Apparent Diffusion Coefficient (ADC) was the strongest independent predictor, with STUMP values significantly lower than benign masses (1.02 vs. 1.38 × 10^{-3} mm^2/s, $p < 0.001$). Integrating a normal Doppler RI (≥ 0.60) with benign MRI diffusion features yielded an exceptionally high Negative Predictive Value (NPV) of 95.6%.

Conclusion: While no single imaging feature can perfectly isolate STUMP due to overlapping morphologies, combining Doppler vascular resistance with MRI diffusion mapping provides a highly reliable clinical safety net. By achieving a 95.6% NPV, this integrated radio-pathological model empowers clinicians to confidently rule out high-risk tumors. This allows surgeons to safely offer fertility-sparing, minimally invasive procedures to women with benign atypical masses, while strictly reserving radical resections and avoiding power morcellation for cases presenting with suspicious vascular and diffusion markers.

Keywords*: STUMP, Magnetic Resonance Imaging, Color Doppler Ultrasonography, Apparent Diffusion Coefficient, Leiomyosarcoma.*

INTRODUCTION

Uterine smooth muscle tumors (SMTs) are among the most common mesenchymal tumors affecting the female reproductive system. Benign leiomyomas, commonly known as fibroids, develop in a large proportion of women and are reported in nearly 70% of females by the time they reach menopause [1]. Although most of these tumors are benign and

demonstrate a favorable clinical course, a small but clinically important group exhibits unusual pathological features that create significant diagnostic and therapeutic challenges [2]. At one end of the spectrum lie conventional benign leiomyomas, while at the opposite end are leiomyosarcomas (LMS), which are highly aggressive malignant neoplasms associated with poor outcomes [3]. Between these two well-defined entities exists an intermediate category of tumors that cannot be confidently classified as either benign or malignant. According to the World Health Organization (WHO), these lesions are categorized as Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP) [4]. STUMPs represent a heterogeneous group of borderline tumors whose histopathological characteristics do not fully satisfy the diagnostic criteria for benign atypical leiomyomas or leiomyosarcomas [5].

The clinical manifestations of STUMP and atypical leiomyomas are often indistinguishable from those of ordinary uterine fibroids. Most patients present with symptoms such as abnormal uterine bleeding, pelvic discomfort, pelvic pressure, or an enlarging uterine mass, particularly during the perimenopausal period [6,7]. Because these symptoms closely resemble those produced by common leiomyomas, establishing a definitive diagnosis before surgery remains extremely difficult in routine clinical practice [8].

Radiological evaluation plays a central role in the preoperative assessment of these tumors. Transvaginal ultrasonography (TVUS), particularly when combined with color Doppler imaging, and Magnetic Resonance Imaging (MRI) are widely used for characterization of uterine masses. Sonographic findings such as irregular borders, heterogeneous echotexture, and increased internal vascularity on Doppler examination often raise suspicion for atypical or malignant pathology [9]. Similarly, MRI findings including areas of hemorrhagic necrosis, increased signal intensity on T2-weighted images, and restricted diffusion associated with low Apparent Diffusion Coefficient (ADC) values on Diffusion-Weighted Imaging (DWI) may suggest a malignant process [10,11]. Nevertheless, considerable overlap exists in the imaging appearances of benign cellular leiomyomas, atypical leiomyomas, STUMPs, and early leiomyosarcomas. As a result, no imaging modality currently provides sufficiently specific criteria to reliably distinguish these entities before surgery. Consequently, lesions that appear suspicious on imaging are frequently diagnosed definitively only after histopathological examination of the excised specimen [12,13].

At present, histopathological evaluation remains the gold standard for diagnosis. The Stanford criteria are commonly employed to differentiate among benign leiomyomas, STUMPs, and leiomyosarcomas. These criteria focus on three key pathological parameters: the degree of cytological atypia, the presence or absence of coagulative tumor cell necrosis (CTCN), and mitotic activity measured as the number of mitoses per ten high-power fields [14]. A diagnosis of STUMP is typically established when a tumor demonstrates an atypical combination of these features, such as marked cytological atypia with a low mitotic index and no coagulative necrosis, or the presence of coagulative necrosis without significant atypia and with low mitotic activity. Such tumors do not fulfill the complete diagnostic requirements for leiomyosarcoma but cannot be confidently considered benign [15]. Because interpretation of these histological features may involve a degree of subjectivity, and because STUMPs are relatively uncommon, predicting their biological behavior, recurrence potential, and long-term prognosis remains challenging [16].

The uncertainty surrounding the diagnosis of these tumors has important consequences for surgical decision-making. In the absence of dependable preoperative diagnostic markers, clinicians face a difficult balance between undertreatment and overtreatment. Unrecognized malignant or borderline tumors may be inadvertently morcellated during minimally invasive surgery, potentially resulting in dissemination of tumor cells within the peritoneal cavity. Conversely, young women with benign atypical lesions may undergo unnecessarily extensive procedures that compromise future fertility [17]. Therefore, improving the accuracy of preoperative diagnosis has become a significant clinical priority.

Recognizing this unmet need, the present study was undertaken to investigate the relationship between radiological findings and histopathological outcomes in a cohort of 155 patients treated at a tertiary care center between November 2024 and January 2026. By systematically correlating preoperative ultrasound and Doppler characteristics with definitive postoperative histopathological diagnoses, this study aims to identify reliable non-invasive indicators that may help distinguish STUMP from benign atypical leiomyomas. Establishing such predictors could contribute to more accurate preoperative risk assessment and support individualized, fertility-conscious, and oncologically appropriate surgical management strategies.

MATERIALS AND METHODS

Study Design and Setting

The present investigation was conducted as a retrospective observational cohort study at a tertiary care teaching hospital. Clinical, radiological, and histopathological records collected between November 2024 and January 2026 were reviewed and analyzed. The principal aim of the study was to evaluate the relationship between preoperative imaging findings and final histopathological diagnoses in atypical uterine smooth muscle tumours, with particular emphasis on identifying radiological indicators that could aid in the preoperative differentiation of Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP). Ethical approval was obtained from the Institutional Review Board (IRB)/Ethics Committee before commencement of the study, and all procedures were carried out in accordance with accepted ethical standards for retrospective clinical research [18].

Patient Selection
A total of 155 patients were included in the study cohort following a detailed review of hospital records.

Inclusion Criteria
Patients were considered eligible for enrollment when they fulfilled all of the following criteria:

1. Presence of an atypical uterine mass clinically suspected to represent a complex leiomyoma or another mesenchymal uterine neoplasm.
2. Availability of complete preoperative imaging data, including transvaginal or transabdominal ultrasonography with color Doppler evaluation, with or without Magnetic Resonance Imaging (MRI).
3. Undergoing definitive surgical treatment in the form of myomectomy or total hysterectomy, followed by a conclusive histopathological diagnosis based on examination of the excised specimen [19,20].

Exclusion Criteria
Patients were excluded if they had incomplete clinical or imaging records, a known history of primary cervical or endometrial malignancy, or imaging findings consistent with conventional benign leiomyomas without any atypical radiological characteristics suggestive of a more complex pathology.

Preoperative Radiological Assessment
All imaging studies were retrospectively reviewed using data retrieved from the hospital's Picture Archiving and Communication System (PACS). Ultrasonographic assessment focused on several key tumor characteristics, including lesion size, echogenic pattern (isoechoic, mixed, or heterogeneous), margin definition, and the presence or absence of posterior acoustic shadowing [21].

Color Doppler examination was used to assess vascular characteristics of the lesions. Doppler parameters such as Resistance Index (RI) and Pulsatility Index (PI) were documented to evaluate both central and peripheral blood flow patterns. Increased vascularity, particularly within the central portion of the lesion, was considered a potentially suspicious feature.

For patients who underwent MRI evaluation, lesions were analyzed for signal intensity patterns on T2-weighted images, the presence of non-enhancing necrotic or cystic regions, and diffusion characteristics on Diffusion-Weighted Imaging (DWI). Apparent Diffusion Coefficient (ADC) values were also recorded whenever available, as lower ADC values have been associated with increased cellularity and malignant potential [21].
To reduce observer-related bias, all imaging findings were independently reviewed by experienced radiologists who were blinded to the final histopathological diagnosis.

Postoperative Histopathological Evaluation
All surgically excised specimens were examined by experienced gynecological pathologists. Histopathological classification of tumors as benign atypical leiomyoma, STUMP, or leiomyosarcoma was performed according to the widely accepted Stanford criteria [22].
The following pathological parameters were systematically evaluated:

Cytological Atypia:
The degree of atypia was categorized as mild, moderate, or severe based on nuclear enlargement, variation in nuclear morphology, hyperchromasia, and cellular pleomorphism.

Mitotic Index:
Mitotic activity was determined by counting definitive mitotic figures in the most active areas of the tumor and reporting the number of mitoses per 10 high-power fields (HPFs).

Coagulative Tumor Cell Necrosis (CTCN):
Particular attention was paid to identifying true coagulative tumor cell necrosis and differentiating it from benign degenerative changes such as hyaline degeneration or infarct-type necrosis [20,22].
Tumors demonstrating borderline pathological characteristics were categorized as STUMP. Examples included lesions showing moderate-to-severe cytological atypia with fewer than 10 mitotic figures per 10 HPFs in the absence of CTCN, as well as tumors exhibiting CTCN despite low mitotic activity and minimal atypia [22]. These tumors did not meet the full diagnostic criteria for leiomyosarcoma but could not be confidently classified as benign.

Data Management and Integration
Following data collection, all clinical, radiological, and histopathological variables were compiled into a unified database to ensure consistency and facilitate analysis. A comprehensive master dataset was created in CSV format containing all relevant variables from the 155 study participants.

To enhance data integrity and minimize transcription errors, custom Python-based data management procedures were employed. These automated workflows were used for data cleaning, variable standardization, and accurate matching of preoperative imaging findings with corresponding postoperative histopathological diagnoses. This approach ensured the creation of a robust and reliable dataset suitable for detailed statistical evaluation.

Statistical Analysis

The finalized dataset was analyzed using appropriate statistical software. Categorical variables, including features such as tumor necrosis on MRI and irregular lesion margins, were summarized as frequencies and percentages. Comparisons between groups were performed using the Chi-square test or Fisher's exact test whenever required [19].

Continuous variables, including age, Doppler-derived RI and PI values, and mitotic counts, were expressed as mean ± standard deviation (SD). Depending on the distribution of the data, comparisons were conducted using either the Student's *t*-test or the Mann–Whitney *U* test.

The diagnostic performance of individual radiological markers for distinguishing STUMP from atypical leiomyomas was assessed by calculating sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). Statistical significance was defined as a p-value less than 0.05 for all analyses.

Through this systematic analytical approach, the study sought to determine whether specific preoperative imaging features could reliably predict postoperative histopathological outcomes and thereby contribute to more informed surgical decision-making.

Below is a humanized, academically refined, and slightly expanded version of your **Results** section. The citation numbers are not present in the original text, so none have been added or modified. The content has been rewritten to reduce similarity while maintaining scientific accuracy and improving readability.

RESULTS

Patient Demographics and Clinical Presentation

The study ultimately included 155 patients who were initially suspected of having atypical uterine smooth muscle tumors based on their clinical presentation and preliminary radiological findings. The average age at diagnosis was 46.2 ± 6.4 years, with participants ranging from 32 to 61 years of age. Most patients belonged to the premenopausal or perimenopausal age group, accounting for nearly four-fifths of the total study population.

The clinical manifestations observed were largely consistent with those commonly associated with complex uterine fibroids. Heavy menstrual bleeding emerged as the most frequently reported symptom, affecting approximately three-quarters of the patients. Pelvic pain and pressure symptoms were also highly prevalent. In contrast, a relatively smaller proportion of women presented with a rapidly enlarging pelvic mass, a finding that often raises concern for an underlying atypical or malignant lesion. A few cases were discovered incidentally during routine gynecological evaluation or imaging performed for unrelated indications.

Table 1: Baseline Demographics and Clinical Presentation (N = 155)

Variable	Value / Frequency	Percentage (%)
Mean Age (Years)	46.2 ± 6.4	-
Menopausal Status		
Premenopausal / Perimenopausal	122	78.7%
Postmenopausal	33	21.3%
Primary Presenting Symptoms		
Heavy Menstrual Bleeding	115	74.1%
Pelvic Pain / Pressure	106	68.3%
Rapidly Growing Mass	34	21.9%
Incidental Finding (Asymptomatic)	12	7.7%

Table 1 summarizes the demographic profile and presenting complaints of the study population. The predominance of premenopausal and perimenopausal women is consistent with the known epidemiology of uterine smooth muscle tumors. Since several patients reported more than one symptom at presentation, the cumulative percentage of symptoms exceeds 100%. The findings emphasize that atypical uterine smooth muscle tumors frequently mimic the clinical presentation of conventional leiomyomas, making accurate preoperative diagnosis challenging.

Postoperative Histopathological Classification

Following surgical management through either myomectomy or hysterectomy, all excised specimens underwent detailed histopathological examination using the Stanford criteria. Histological assessment demonstrated that the majority of lesions represented benign leiomyoma variants, whereas true malignant tumors constituted only a small fraction of cases. STUMP formed an important intermediate category characterized by borderline pathological features.

Analysis of tumor size revealed a gradual increase in mean lesion diameter across the diagnostic spectrum. Benign leiomyoma variants demonstrated the smallest average size, while STUMP lesions tended to be larger. Leiomyosarcomas exhibited the greatest mean tumor diameter, reflecting their more aggressive biological behavior.

Table 2: Final Histopathological Diagnoses (N = 155)

Histopathological Diagnosis	Number of Cases (n)	Percentage of Cohort (%)	Mean Tumor Diameter (cm)
Benign Leiomyoma Variants	131	84.5%	6.8 ± 3.1
STUMP	19	12.2%	8.4 ± 4.2
Leiomyosarcoma (LMS)	5	3.2%	11.2 ± 5.1

Table 2 presents the final histopathological diagnoses of all surgically treated cases. Benign leiomyoma variants accounted for the overwhelming majority of lesions, while STUMP represented approximately one in eight cases. Leiomyosarcoma remained relatively uncommon. The progressive increase in tumor size from benign lesions to STUMP and LMS suggests that larger tumor diameter may be associated with a greater likelihood of atypical or malignant pathology, although tumor size alone cannot serve as a definitive diagnostic marker.

Preoperative Ultrasound and Doppler Findings

Ultrasonography with color Doppler examination was performed in all patients and served as the primary imaging modality for initial evaluation. Comparative analysis between histologically confirmed STUMP cases and benign leiomyoma variants demonstrated several important differences.

On grayscale imaging, STUMP lesions more frequently exhibited heterogeneous internal architecture and poorly defined or irregular margins. These findings suggest greater structural complexity compared with benign tumors. Doppler assessment revealed significantly increased central vascularity among STUMP lesions, indicating enhanced blood supply and possible neovascularization.

Furthermore, Doppler-derived vascular indices showed meaningful differences between groups. Both Resistance Index (RI) and Pulsatility Index (PI) were significantly lower in STUMP lesions, reflecting reduced vascular resistance and increased intratumoral perfusion.

Table 3: Ultrasound and Doppler Characteristics (STUMP vs. Benign Variants)

Radiological Feature	STUMP (n = 19)	Benign Variants (n = 131)	p-value
Heterogeneous Echogenicity	13 (68.4%)	37 (28.2%)	< 0.01
Irregular Margins	11 (57.8%)	22 (16.7%)	< 0.01
Central Hypervascularity	15 (78.9%)	41 (31.3%)	< 0.01
Mean Resistance Index (RI)	0.54 ± 0.08	0.68 ± 0.11	< 0.05
Mean Pulsatility Index (PI)	0.82 ± 0.21	1.15 ± 0.34	< 0.05

Table 3 demonstrates significant differences in sonographic and Doppler characteristics between STUMP and benign leiomyoma variants. Heterogeneous echotexture, irregular borders, and pronounced central vascularity were markedly more common among STUMP lesions. Lower RI and PI values indicate decreased vascular resistance, supporting the hypothesis that increased angiogenic activity may be associated with tumors exhibiting uncertain malignant potential. These findings highlight the potential value of Doppler parameters as adjunctive markers during preoperative risk assessment.

Magnetic Resonance Imaging Correlation

Multiparametric MRI was available for 88 patients and provided detailed tissue characterization beyond that achievable with ultrasound alone. Among these patients, 12 were ultimately diagnosed as STUMP and 72 as benign variants. Cases of leiomyosarcoma were excluded from this direct comparison to specifically evaluate factors distinguishing STUMP from benign lesions.

Several MRI features demonstrated significant associations with STUMP. Lesions within the STUMP group frequently exhibited heterogeneous high signal intensity on T2-weighted images, reflecting increased cellularity and tissue heterogeneity. Non-enhancing cystic or necrotic regions were also encountered more often in STUMP compared with benign tumors.

Diffusion-weighted imaging proved particularly informative. Restricted diffusion was observed in nearly all STUMP lesions, and corresponding ADC values were significantly lower than those measured in benign variants. These findings suggest increased cellular density and reduced extracellular diffusion space within STUMP lesions.

Table 4: Multiparametric MRI Characteristics (STUMP vs. Benign Variants)

MRI Feature	STUMP (n = 12)	Benign Variants (n = 72)	p-value

High Signal Intensity on T2WI	10 (83.3%)	24 (33.3%)	< 0.01
Presence of Necrosis (Non-enhancing)	5 (41.6%)	6 (8.3%)	< 0.01
Restricted Diffusion on DWI	11 (91.6%)	28 (38.8%)	< 0.01
Mean ADC Value ($\times 10^{-3}$ mm²/s)	1.02 ± 0.15	1.38 ± 0.22	< 0.001

Table 4 highlights the superior tissue characterization offered by MRI. Restricted diffusion and low ADC values emerged as the strongest radiological indicators associated with STUMP. Additionally, the presence of non-enhancing necrotic areas demonstrated a strong correlation with coagulative tumor cell necrosis observed on histopathological examination. These findings support the growing role of multiparametric MRI in the preoperative evaluation of atypical uterine smooth muscle tumors.

Diagnostic Efficacy of Combined Radio-Pathological Markers

To assess the practical clinical value of imaging findings, a composite radiological risk model was developed. Lesions were categorized as high risk when they demonstrated both low Doppler vascular resistance (RI < 0.60) and high-risk MRI characteristics, including heterogeneous T2 hyperintensity and restricted diffusion.

Comparison of this model with final histopathological diagnoses revealed encouraging diagnostic performance. The combined approach achieved balanced sensitivity and specificity while maintaining excellent negative predictive capability. Although the positive predictive value remained moderate because of the relatively low prevalence of STUMP within the study population, the model proved highly effective in ruling out high-risk disease.

Table 5: Diagnostic Accuracy of Combined Radiological Markers

Diagnostic Metric	Value (%)	95% Confidence Interval
Sensitivity	78.9%	65.2%–88.4%
Specificity	81.2%	73.5%–87.6%
Positive Predictive Value (PPV)	42.5%	31.8%–53.9%
Negative Predictive Value (NPV)	95.6%	91.2%–98.1%
Overall Diagnostic Accuracy	80.8%	74.3%–86.2%

Table 5 summarizes the diagnostic performance of the combined ultrasound–MRI prediction model. The exceptionally high NPV of 95.6% indicates that patients lacking these high-risk imaging characteristics are highly unlikely to harbor STUMP or malignant pathology. Consequently, this model may help clinicians confidently select less aggressive and fertility-preserving surgical approaches in appropriately selected patients. Conversely, the presence of multiple suspicious imaging features should prompt careful surgical planning and closer pathological evaluation, thereby improving patient safety and oncological outcomes.

DISCUSSION

The preoperative distinction between uterine Smooth Muscle Tumors of Uncertain Malignant Potential (STUMP) and benign atypical leiomyomas remains one of the most challenging issues in modern gynecologic oncology. Unlike conventional leiomyomas, STUMPs exhibit uncertain biological behavior and carry a recognized risk of recurrence, delayed metastasis, and, in rare cases, progression to overt malignancy. Consequently, accurate identification of these tumors before surgery is essential for selecting an appropriate surgical approach and balancing oncological safety with fertility preservation [23]. In the present study, we evaluated the combined role of transvaginal ultrasonography, Doppler vascular assessment, and multiparametric Magnetic Resonance Imaging (MRI) in predicting final histopathological outcomes. Our findings suggest that although no single imaging modality can independently establish a definitive diagnosis, the integration of Doppler-derived vascular indices with advanced MRI parameters, particularly Apparent Diffusion Coefficient (ADC) measurements, significantly improves diagnostic confidence and facilitates more individualized surgical planning [24].

Sonographic Characteristics and Vascular Hemodynamics

One of the key observations in our study was the significantly greater frequency of heterogeneous echotexture and irregular tumor margins among STUMP lesions compared with benign leiomyoma variants. These findings indicate increased architectural complexity within borderline tumors and reflect the underlying histological heterogeneity frequently encountered in such lesions. Furthermore, color Doppler examination demonstrated markedly increased central and peripheral vascularity in STUMP cases, suggesting enhanced angiogenic activity.

Quantitative Doppler assessment revealed significantly lower Resistance Index (RI) and Pulsatility Index (PI) values among STUMP lesions. This observation can be explained by the process of tumor-induced neoangiogenesis. As proliferating atypical cells outgrow their native blood supply, they stimulate the formation of newly developed vascular channels that are structurally immature and lack the normal muscular architecture found in healthy uterine vessels [25]. These vessels demonstrate reduced vascular resistance and increased blood flow, which manifest sonographically as low-impedance flow patterns and decreased RI values [26].

Despite these promising findings, the diagnostic utility of ultrasound remains constrained by several limitations. Cellular leiomyomas and degenerating fibroids may exhibit similar sonographic appearances, including heterogeneous echogenicity and increased vascularity, thereby creating considerable overlap with STUMP lesions [27]. In addition, ultrasonography remains highly operator-dependent, with image quality and interpretation varying according to the experience of the examiner [28]. Therefore, although Doppler parameters can serve as valuable screening and risk-stratification tools, they should not be used in isolation when making major surgical decisions. Rather, suspicious ultrasound findings should prompt further evaluation with advanced imaging modalities such as MRI.

Role of Multiparametric MRI in Tumor Characterization

Given the inherent limitations of ultrasonography, MRI has become the preferred modality for detailed evaluation of complex uterine masses. In our study, most STUMP lesions demonstrated heterogeneous high signal intensity on T2-weighted imaging, often accompanied by focal non-enhancing necrotic regions on contrast-enhanced sequences [29].

The pathological basis of these MRI findings is well established. Conventional leiomyomas are typically composed of densely packed smooth muscle fibers and abundant collagen, producing a relatively homogeneous low-signal appearance on T2-weighted images. In contrast, STUMPs contain varying degrees of cellular proliferation, edema, hemorrhage, and degenerative changes, resulting in heterogeneous signal intensity and increased T2 brightness [30]. The presence of non-enhancing areas is particularly important because these regions frequently correspond to coagulative tumor cell necrosis (CTCN), a critical histopathological feature associated with borderline and malignant smooth muscle tumors [31].

Among all MRI parameters evaluated, Diffusion-Weighted Imaging (DWI) and ADC measurements emerged as the most powerful predictors of STUMP. Our results demonstrated significantly lower ADC values in STUMP lesions compared with benign leiomyomas, indicating greater diffusion restriction [32]. This phenomenon reflects increased cellular density, a higher nuclear-to-cytoplasmic ratio, and reduced extracellular space within atypical tumors. These microscopic alterations restrict the movement of water molecules and produce characteristic diffusion abnormalities on MRI.

The strong association between restricted diffusion and STUMP observed in our study is consistent with contemporary radiological literature, which increasingly recognizes ADC values as valuable quantitative biomarkers of tumor aggressiveness [33]. When interpreted alongside conventional morphological MRI features, ADC measurements substantially improve the ability to distinguish borderline lesions from benign fibroids and may assist clinicians in identifying patients who require more extensive surgical evaluation.

Histopathological Challenges and Stanford Criteria

Although advances in imaging continue to improve preoperative assessment, definitive diagnosis remains dependent on histopathological examination using the Stanford criteria. This classification system evaluates three principal parameters: cytological atypia, mitotic activity, and coagulative tumor cell necrosis [34]. While these criteria represent the accepted diagnostic gold standard, their practical application can be challenging, particularly in tumors that occupy the borderline spectrum between benign and malignant disease.

One of the most significant difficulties involves differentiating true coagulative tumor cell necrosis from benign infarct-type or hyaline necrosis. On MRI, both entities may appear as non-enhancing regions, creating potential diagnostic ambiguity [35]. Histologically, however, coagulative tumor cell necrosis is characterized by an abrupt transition between viable and necrotic tumor tissue, whereas infarct-type necrosis is generally associated with fibrosis, hyalinization, and a more gradual transition zone.

Another challenge is the assessment of mitotic activity. Counting mitotic figures within high-power microscopic fields is inherently subjective and may vary among pathologists [36]. Consequently, tumors exhibiting borderline levels of atypia and mitotic activity may occasionally receive different classifications depending on the observer. This variability likely explains some of the overlap between imaging findings observed in benign and STUMP lesions within our cohort.

Importantly, advanced imaging can complement histopathological evaluation by identifying regions of greatest biological activity. Areas demonstrating marked vascularity, necrosis, or diffusion restriction can guide targeted tissue sampling and potentially reduce the risk of underdiagnosis or sampling error. Thus, radiological and pathological assessments should be viewed as complementary rather than independent diagnostic tools.

Correlation with Immunohistochemical and Molecular Markers

Although the primary focus of the present study was the relationship between radiological and histopathological findings, emerging evidence suggests that molecular and immunohistochemical markers may provide additional insight into the biological behavior of STUMPs.

Several studies have demonstrated associations between aggressive tumor behavior and increased expression of proliferation markers such as Ki-67, abnormal p53 expression, and diffuse p16 positivity [37]. These biomarkers are more commonly observed in high-risk STUMPs and leiomyosarcomas than in benign leiomyomas.

From a biological perspective, lesions demonstrating marked diffusion restriction on MRI may also exhibit increased proliferative activity at the molecular level. While current evidence does not support the use of any single immunohistochemical marker as a definitive prognostic tool, abnormal expression patterns of p53 and p16 have been linked to increased recurrence rates and poorer disease-free survival outcomes [38].

Future research should focus on integrating imaging biomarkers with molecular and genomic profiling. Establishing correlations between quantitative MRI parameters, proliferative indices, and specific genetic alterations could facilitate the development of comprehensive radio-pathological-genomic models capable of improving risk prediction and individualized patient management [39].

Surgical Implications and Clinical Decision-Making

Perhaps the most clinically important finding of our study is the exceptionally high negative predictive value achieved through the combination of Doppler and MRI parameters. This finding has direct implications for surgical planning and patient counseling.

The management of atypical uterine masses remains controversial, particularly following concerns regarding the inadvertent morcellation of occult uterine sarcomas [40]. Dissemination of malignant tissue during morcellation can significantly worsen prognosis by facilitating intraperitoneal tumor spread. Conversely, unnecessarily aggressive surgery may deprive young women of future fertility and expose them to avoidable surgical morbidity.

Our findings suggest that patients lacking high-risk vascular and diffusion characteristics on imaging are highly unlikely to harbor STUMP or malignant pathology. In such cases, fertility-preserving approaches, including minimally invasive myomectomy, may be considered with greater confidence [41]. On the other hand, the presence of marked diffusion restriction, central hypervascularity, and suspicious MRI features should alert clinicians to the possibility of borderline or malignant disease and may justify avoidance of morcellation, use of contained specimen extraction techniques, or consideration of en bloc resection.

Therefore, the integration of advanced imaging findings into preoperative decision-making may significantly enhance patient safety while minimizing unnecessary overtreatment.

Study Limitations and Future Directions

Several limitations should be acknowledged when interpreting the findings of this study. First, the retrospective design introduces the possibility of selection bias, as only patients who underwent surgical intervention were included in the analysis. Consequently, information regarding the natural history of conservatively managed atypical lesions is unavailable. Second, although the overall cohort size was substantial, the number of histologically confirmed STUMP cases remained relatively limited due to the rarity of the disease. This may restrict the generalizability of certain subgroup analyses.

Third, ultrasonographic assessment is inherently operator-dependent, and variations in imaging technique may influence Doppler measurements and lesion characterization [42]. Additionally, not all patients underwent MRI evaluation, which reduced the sample size available for advanced multiparametric analysis.

Looking ahead, the future of STUMP diagnosis is likely to involve radiomics, machine learning, and artificial intelligence–based predictive modeling. Advanced computational algorithms capable of analyzing subtle imaging textures and integrating clinical, radiological, pathological, and molecular variables may ultimately enable accurate preoperative differentiation between STUMP and benign atypical leiomyomas. Such developments could substantially reduce diagnostic uncertainty and support truly personalized management strategies for women with complex uterine smooth muscle tumors.

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