OPINION PAPER

DOI: 10.52054/FVVO.2025.248
Facts Views Vis Obgyn

A proposed MRI classification of junctional zone morphology based on reproductive performance: the JZ-MRI ReproClass

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ABSTRACT

We propose the junctional zone- magnetic resonance imaging (JZ-MRI) ReproClass, a four-tiered MRI-based classification for describing JZ morphology, developed from more than a decade of clinical experience in women with recurrent implantation failure or pregnancy loss despite normal embryo quality. The system characterises the spectrum of JZ appearances -from normal architecture to complete loss of differentiation- and is particularly informative when ultrasound and hysteroscopy appear normal. By standardising MRI assessment of the JZ, the ReproClass may help identify morphological patterns associated with impaired reproductive performance and support more individualised diagnostic reasoning. It provides a foundation for future research into the role of JZ architecture in fertility outcomes.

Keywords: Fertility, infertility, MRI, magnetic resonance imaging, pregnancy, women

Introduction

The inner myometrium is increasingly recognised as a critical structure in reproductive medicine.[1] Functionally distinct from the outer myometrium, it originates embryologically from the Müllerian ducts and plays a key role in sperm transport, embryo implantation, and placentation through its hormone-responsive peristaltic activity.[2,3,4]

With the advent of magnetic resonance imaging (MRI), our understanding of uterine architecture has deepened significantly. MRI allows for a clear visualisation of three distinct uterine layers: the endometrium, the inner myometrium, and the outer myometrium. During the 1980s, T2-weighted MRI revealed a distinct low-signal intensity band between the endometrium and the outer myometrium, which was subsequently defined as the junctional zone (JZ).[5] Importantly, the JZ is not a discrete histological entity and cannot be clearly delineated from the outer myometrium using conventional light microscopy. Similarly, the JZ visualised on ultrasound -as described in the MUSA (Morphological Uterus Sonographic Assessment) criteria[6]- does not correspond to the JZ seen on MRI. Harmsen et al.[7] recently emphasised the poor agreement between MRI, ultrasound, and histology in evaluating the JZ, highlighting that each modality assesses fundamentally different structural or functional features. On MRI, the JZ is characterised by its distinct tissue composition: higher smooth muscle cell density, reduced extracellular matrix, lower water content, higher iron concentrations, and concentric fibre orientation; features that collectively give rise to its low signal intensity on T2-weighted images.[8,9]

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Received: 25.09.2025 **Accepted:** 07.12.2025 **Epub:** 17.02.2026

Cite this article as: Campo R, Gordts S, Van Kerrebroeck H, Gillet E. A proposed MRI classification of junctional zone morphology based on reproductive performance: the JZ-MRI ReproClass. Facts Views Vis Obgyn. [Epub Ahead of Print].

Despite this improved anatomical delineation, several questions remain unresolved. What constitutes a normal JZ on MRI? What degree of variation is physiological, and how do hormonal fluctuations influence its appearance?[9-13] While numerous studies have investigated JZ thickness and its association with adverse reproductive outcomes[14-17] -particularly in assisted reproduction- no standardised classification system currently exists to characterise JZ morphology on MRI. This lack of a unified approach creates inconsistency in clinical interpretation, limits cross-study comparisons, and hampers prospective validation of JZ-related risk factors.

Over the past decade, we have systematically incorporated pelvic MRI into the evaluation of all women entering our egg donation program.[17] This accumulated clinical and imaging experience suggests that variations in JZ morphology -ranging from subtle irregularities to complete loss of differentiation- may be associated with impaired implantation and differences in reproductive performance, even when ultrasound and hysteroscopy are unremarkable. Although the aetiology of these abnormalities is likely multifactorial, proposed contributing factors include chronic inflammation, hormonal dysregulation (e.g., prolonged oestrogen exposure), prior uterine trauma, and early or subclinical adenomyosis.[18] These mechanisms may disrupt the normal contractile and receptive functions of the JZ, thereby compromising implantation and placentation.

Our observation has highlighted a critical diagnostic gap: while the JZ can be visualised reliably on MRI, we currently lack a universally accepted classification system to define what is normal, borderline, or pathological in the context of reproduction. To move the field forward, a reproducible, intuitive, and clinically meaningful framework is urgently needed -one that can help stratify reproductive risk and guide future prospective studies.

The JZ-MRI ReproClass: Toward A Standardised Framework for JZ Morphology

The proposed classification emerged from the cumulative interpretation of hundreds of high-quality T2-weighted MRI scans, each reviewed in parallel with detailed ultrasound and hysteroscopic assessments. Although it is not derived from a prospective dataset, the JZ-MRI ReproClass represents a structured synthesis of reproducible morphological patterns -ranging from normal JZ architecture to complete loss of differentiation between the JZ and outer myometrium- that appear to correlate with reproductive performance. Its development is rooted in extensive clinical experience within a high-performance egg donation program, where subtle deviations in JZ morphology aligned with implantation outcomes.

The primary goal of this framework is to facilitate more consistent communication between radiologists, gynaecologists, and fertility specialists, particularly in cases of unexplained infertility, recurrent implantation failure, or pregnancy loss in which conventional imaging fails to identify a clear abnormality. By offering a standardised language to describe JZ morphology, the JZ-MRI ReproClass may help bridge the diagnostic gap between structural appearance and reproductive function.

The JZ-MRI ReproClass includes four distinct categories: (A) Normal, (B) Subtle changes, (C) Focal pathology, and (D) Advanced or global disruption.

Class A: Normal

Class A is defined by a well-delineated JZ, clearly distinct from the outer myometrium. The JZ occupies no more than one-third of the total myometrial thickness and shows a smooth, continuous contour without interruption (Figure 1). This morphology is considered physiologically normal and reflects an intact, well-organised inner myometrium. Clinical experience consistently shows that a normal JZ is associated with optimal uterine function, without features suggestive of impaired implantation or reduced receptivity. Overall, Class A morphology appears to be a highly favourable marker of endometrial receptivity and uterine competence.

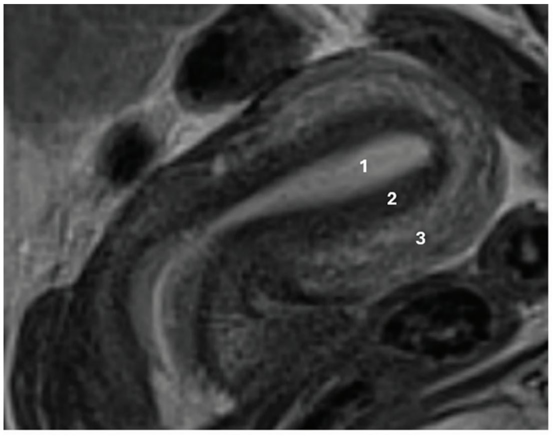

Figure 1. Example of JZ-MRI ReproClass A: a sharply demarcated, homogeneous low-signal intensity band on T2-weighted image, involving less than one-third of the total myometrial thickness (1; Endometrium, 2; junctional zone, 3; Outer myometrium). JZ-MRI: junctional zone- magnetic resonance imaging.

Class B: Subtle Changes

Class B represents a morphology similar to Class A but with certain precise changes. These include small focal changes such as microcysts (defined as cystic structures <5 mm), a mildly irregular contour, slight thickening of the JZ that remains below two-thirds of the myometrial thickness, or conversely hypotrophy, referring to a very thin or nearly absent JZ (Figure 2). These features are interpreted as early or borderline alterations, currently of unclear pathological significance. Introducing this category allows for a stricter definition of normality in Class A while separating out subtle deviations that may warrant closer observation. Class B thus functions as a buffer group for morphological variations of unclear clinical relevance, which may or may not influence reproductive outcome and warrant further study.

Class C: Focal Pathology

Class C is defined by the coexistence of normal and abnormal JZ segments. The abnormal areas are characterised by a complete loss of JZ differentiation and/or the presence of macrocysts (well defined cystic structures ≥5 mm). This category is thought to reflect localised dysfunction of the JZ and is generally associated with intermediate reproductive potential.

Initial clinical experience -across cases with both small and more extensive focal abnormalities- suggests that selected patients may benefit from targeted hysteroscopic resection. Smaller cystic or solid lesions can be removed using 5-fr instruments (Trophyscope XL, Figure 3), whereas larger focal pathology may require a more structured surgical approach with the 15-fr mini-resectoscope as previously described by our stepwise approach (Figure 4).[19] This technique promotes optimal postoperative healing and initial outcomes in terms of reproductive success appear promising, although formal validation is still needed.

Class D: Advanced or Global Disruption

Class D represents widespread architectural disruption of the JZ. It is defined by either a markedly hypertrophic JZ occupying more than two-thirds of the myometrial thickness or by a complete loss of JZ differentiation. In both presentations, the inner myometrium loses its normal layered organisation: this may occur through pronounced thickening or through homogenised low-signal intensity appearance in which the JZ can no longer be distinguished from the outer myometrium. Such uniform characteristics suggest that the tissue composition across the myometrial wall becomes

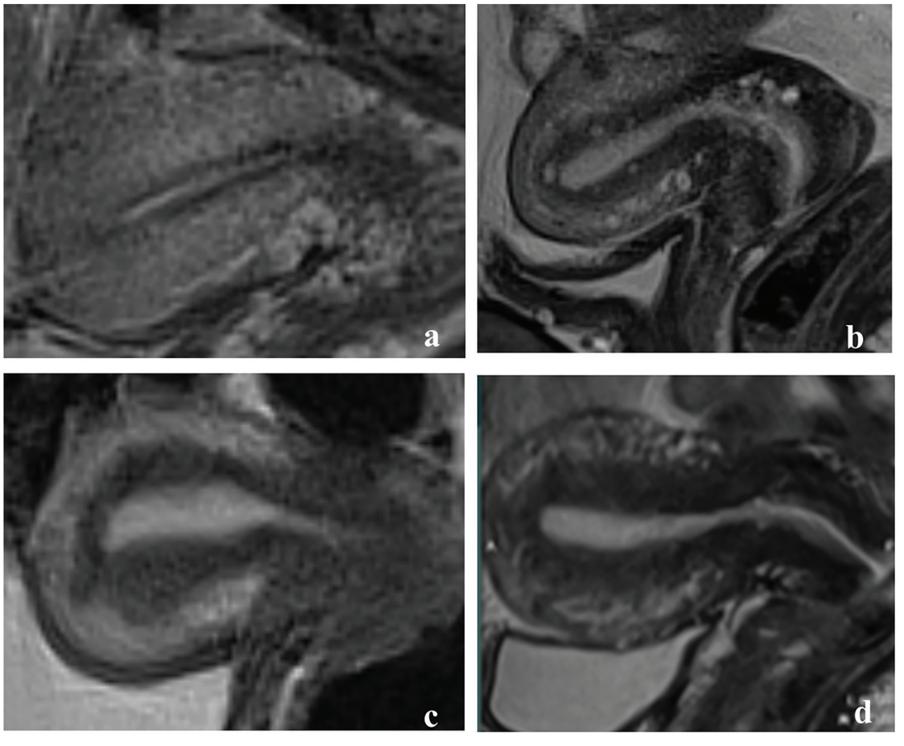

Figure 2. JZ-MRI ReproClass B subtle changes: hypotrophic JZ (a), Normal JZ with microcystic changes (b), Focal thickened JZ (c), Enlarged JZ occupying less than two-thirds of the total myometrial thickness (d). JZ-MRI: junctional zone- magnetic resonance imaging.

essentially identical -likely reflecting alterations in water and iron content together with loss of the typical zonal architecture. Clinically, Class D is associated with markedly reduced reproductive potential and appears to signify a severely compromised endo-myometrial environment. Importantly, these abnormalities may remain entirely undetected on standard ultrasound or hysteroscopy, highlighting the unique diagnostic value of MRI (Figure 5). Preliminary exploratory findings in this subgroup often reveal histological features consistent with adenomyosis, supporting the hypothesis of an inflammatory or non-functional JZ state. In such cases, hormonal suppression or targeted local anti-inflammatory strategies[20] may hold therapeutic potential, although these approaches require further systematic evaluation.

Discussion

In this article, we propose the JZ-MRI ReproClass, a four-tiered, morphology-based framework for describing JZ patterns on T2-weighted MRI. Developed from more than a decade of clinical experience in women with unexplained infertility, recurrent implantation failure, and recurrent pregnancy loss in the setting of normal embryo quality, the classification aims to provide a standardised way to describe JZ morphology in relation to reproductive performance (Figure 6). To our knowledge, this is the first classification system specifically designed to assess the JZ as a marker of uterine reproductive receptivity.

The JZ is a hormonally responsive and functionally dynamic interface whose MRI appearance can be influenced by factors such as hormonal milieu, chronic inflammation, altered uterine peristalsis, prior microtrauma, parity, and possibly microbiome-related changes. Recent MRI literature has expanded our understanding of the JZ, yet most published classifications focus primarily on adenomyosis or its diagnostic criteria.[7,18,21] While valuable for disease identification, these systems do not capture the broader spectrum of JZ morphology that may hold relevance for uterine receptivity. The JZ-MRI ReproClass therefore serves a different purpose: it provides a descriptive, MRI-specific framework for characterising JZ patterns across reproductive contexts, including cases without overt adenomyosis. It is not intended as a diagnostic tool for adenomyosis, but rather as a

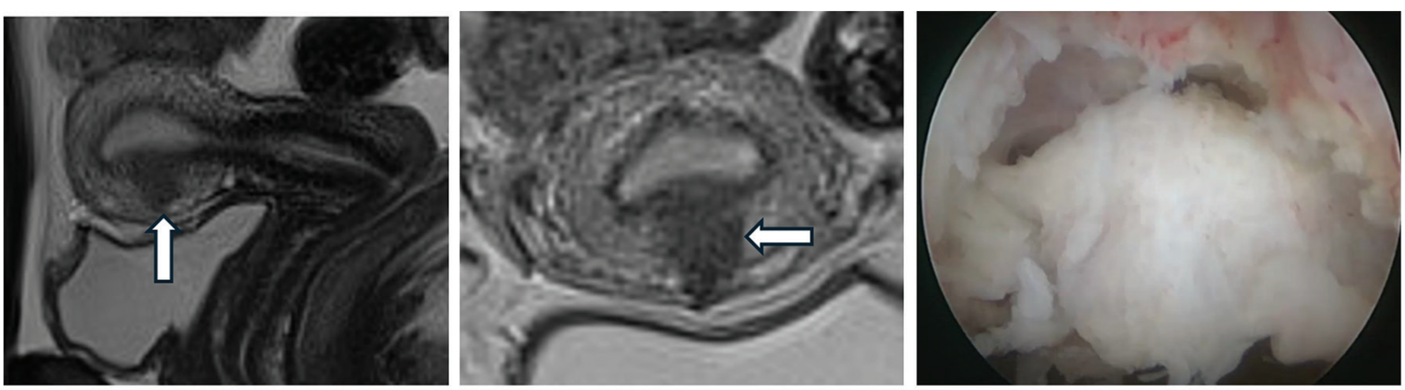

Figure 3. JZ-MRI ReproClass C small focal pathology corresponding with hysteroscopic view during excision. JZ-MRI: junctional zone-magnetic resonance imaging.

Figure 4. JZ-MRI ReproClass C large focal pathology with example of hysteroscopic cytoreductive surgery. JZ-MRI: junctional zone-magnetic resonance imaging.

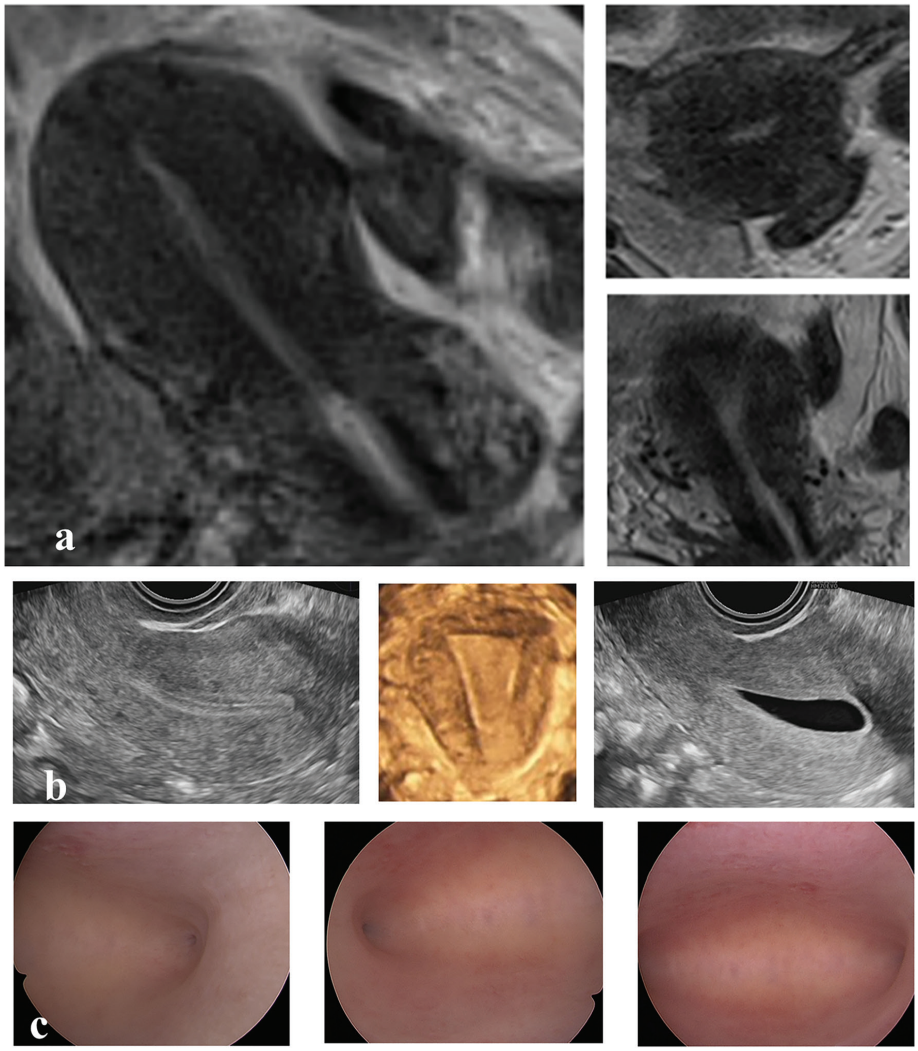

Figure 5. (a) Example of JZ ReproClass D with total loss of junctional zone differentiation. (b) Same patient with normal ultrasound and normal hysteroscopic findings (c).

phenotype-based approach to understanding intrinsic myometrial function.

A key clinical observation underpinning the JZ-MRI ReproClass is the frequent discordance between ultrasound and MRI in assessing the JZ. Recent work by Harmsen et al.[7] similarly reported limited agreement between MRI- and ultrasound-based evaluations, highlighting that sonographic criteria cannot be directly translated to MRI. In our experience, women with recurrent implantation failure may show completely normal ultrasound and hysteroscopic findings, yet MRI reveals a total loss of JZ differentiation -an abnormality that would otherwise remain undetected (Figure 5). This discrepancy reflects fundamental differences between the modalities: ultrasound depicts macroscopic echotexture, whereas MRI captures tissue composition and microstructural organisation. The ability of MRI to reveal profound JZ disruption in patients with unexplained reproductive failure underscores the need for an MRI-specific descriptive framework and reinforces the clinical relevance of the JZ-MRI ReproClass.

Clinical Utility and Implications

The JZ-MRI ReproClass is intended as a functional imaging framework that captures a continuum of JZ morphology -from normal architecture to complete loss of differentiation (Figure 6). Its value is most evident in patients who present with unexplained implantation failure or pregnancy loss despite normal findings on ultrasound and hysteroscopy. In such situations, MRI can reveal intrinsic abnormalities of the inner myometrium that are not visible with other modalities.

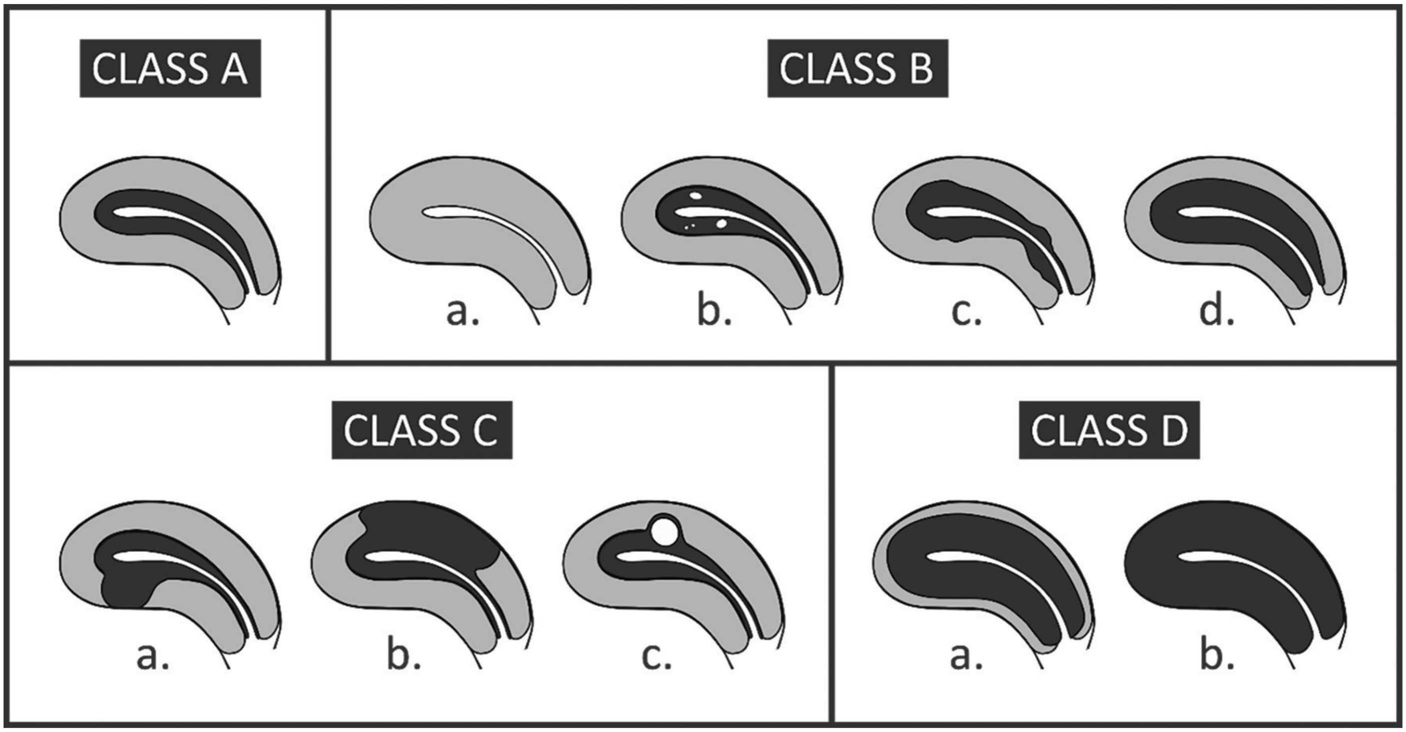

Figure 6. JZ-MRI ReproClass: a proposed classification system for JZ morphology based on reproductive performance. Class A: physiologically normal morphology, Class B: hypotrophic JZ (a), normal JZ with microcystic changes (b), focal thickened JZ (c), enlarged JZ occupying less than two-thirds of the total myometrial thickness (d); Class C: small focal pathology (a), large focal pathology (b), JZ macrocystic lesion (c); Class D: hypertrophic JZ occupying more than two-thirds of the myometrial thickness (a), total loss of JZ differentiation (b). JZ-MRI: junctional zone- magnetic resonance imaging.

By differentiating subtle, focal, and global patterns of JZ change, the classification can support more individualised clinical interpretation. It may assist with prognostic counselling, guide uterine preparation strategies, and help tailor embryo-transfer planning, particularly in assisted reproduction settings where embryo quality is known. The framework also facilitates clearer distinction between embryo-related and uterine-related contributors to implantation failure.

Although preliminary clinical experience suggests that focal abnormalities may respond to targeted hysteroscopic management and that diffuse disruption may warrant hormonal or anti-inflammatory approaches, such insights remain exploratory. Any therapeutic implications derived from the JZ-MRI ReproClass should therefore be regarded as hypothesis-generating. Above all, the classification provides a standardised descriptive language that enhances communication between radiologists and fertility specialists and lays the groundwork for more structured investigation of JZ-related reproductive dysfunction.

Strengths and Limitations

A key strength of the JZ-MRI ReproClass lies in its development within a comprehensive, multimodal diagnostic framework. All patients contributing to its conceptualisation were evaluated through a structured "one-stop uterine diagnosis" protocol incorporating transvaginal ultrasound, hysteroscopy, contrast sonography, and MRI. This integrative approach enabled direct cross-modal comparison and ensured that the classification emerged from clinically relevant correlations rather than isolated radiological interpretation.

The JZ-MRI ReproClass provides a clear and practical way to describe JZ morphology across the range of patterns encountered in reproductive medicine. By focusing on visual, phenotype-based features rather than strict quantitative measurements, the system avoids dependence on JZ thickness thresholds, which are known to vary with acquisition technique and show limited reproducibility. This morphology-driven approach aligns more closely with how clinicians interpret MRI in practice and offers a stable framework for characterising JZ appearance in a clinically meaningful way.

The JZ-MRI ReproClass has several important limitations. First, it is derived from consistent expert observation rather than from a prospectively collected or statistically modelled dataset. Although informal interobserver agreement has been high in our experience, the framework has not yet undergone formal validation across independent readers or centres. Standardisation of MRI acquisition protocols -particularly T2-weighted sequences, field strength, slice thickness, and assessment criteria- will be essential to ensure reproducibility and enable meaningful multicentre evaluation.

The classification also focuses specifically on intrinsic JZ abnormalities. In our cohort of women entering an egg donation program, intrinsic JZ-related changes were far more common than extrinsic myometrial disease, such as outer myometrial adenomyosis or deep infiltrating endometriosis. As a result, extrinsic pathology was not incorporated into the current framework. The relevance of extrinsic disease to reproductive outcomes may differ in other clinical populations,[22,23] and represents an important direction for future investigation.

Finally, any therapeutic approaches associated with specific JZ-MRI ReproClass categories remain experience-based and exploratory. Their apparent utility in clinical practice should be regarded as hypothesis-generating rather than evidence-based, and confirmation through controlled prospective studies will be required.

Future Directions

Future work should prioritise the prospective validation of the JZ-MRI ReproClass. A multicentre study using standardised 2T MRI protocols and harmonised T2-weighted sequence parameters will be essential to evaluate interobserver reproducibility and the stability of the proposed categories. Blinded dual-reader assessment with κ-statistics would provide a robust measure of agreement, while secondary analyses could explore associations with implantation and live-birth outcomes. Establishing these methodological foundations is critical for broader clinical adoption.

Further research is also needed to clarify the hormonal, inflammatory, and biomechanical mechanisms that may underlie JZ dysfunction. A better understanding of why certain MRI phenotypes are associated with impaired receptivity could help identify patients who might benefit from targeted interventions. In parallel, therapeutic strategies -whether surgical, hormonal, or anti-inflammatory- should be examined within controlled prospective designs, as current impressions remain exploratory.

Incorporating the JZ-MRI ReproClass into assisted reproduction registries and future clinical trials may facilitate longitudinal data collection and allow progressive refinement of diagnostic thresholds. Ultimately, standardised imaging protocols, reproducible assessment criteria, and well-designed prospective studies will be essential to establish this classification as a reliable and clinically meaningful tool in reproductive medicine.

Conclusion

In conclusion, the JZ-MRI ReproClass provides a structured, phenotype-based framework for interpreting JZ morphology on MRI and offers a new way to conceptualise JZ-related uterine function in reproductive medicine. Grounded in extensive clinical experience, it captures the full spectrum of JZ appearances- from normal organisation to complete architectural loss- and highlights patterns that may hold functional relevance for implantation and pregnancy. By introducing a standardised descriptive language, the classification strengthens communication between radiologists and fertility specialists and supports more individualised diagnostic thinking, particularly in patients with unexplained implantation failure or miscarriage despite normal conventional imaging. Although therapeutic implications remain exploratory, the JZ-MRI ReproClass establishes a foundation on which future physiological studies, interobserver validation, and targeted interventions can be built. Developing a reproducible, MRI-specific approach to JZ assessment is an essential step toward a more coherent understanding of inner myometrial function. Ultimately, this framework aims to advance both clinical practice and research by providing a consistent point of reference for investigating the role of the JZ in reproductive performance.

Acknowledgements: The authors would like to thank Dr. Tanos Panayiotis for his valuable assistance and support in the preparation of this work. We thank Bart Saerens and Willem Maetens for helping us draft the visual classification.

Contributors: Surgical and Medical Practices: R.C., H.V.K., E.G., Concept: R.C., Design: R.C., E.G., Data Collection or Processing: R.C., E.G., Analysis or Interpretation: R.C., S.G., H.V.K., E.G., Literature Search: R.C., S.G., H.V.K., E.G., Writing: R.C., S.G., H.V.K., E.G.

Funding: The authors declare that no funding was received for conducting this study.

Competing interests: One of the authors, Stephan Gordts, is a member of the editorial board of the Facts, Views and Vision in ObGyn. However, he was not involved in any stage of the editorial decision-making process for this manuscript. The manuscript was evaluated independently by editors from other institutions. The other authors declare no conflicts of interest.

Ethical approval: Not applicable.

Informed consent: Not applicable.

Data sharing: All data are available upon request from the corresponding author.

Transparency: The authors affirm that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

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