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Intrauterine application of Budesonide-hyaluronic acid gel in patients with recurrent implantation failure and total loss of junctional zone differentiation on magnetic resonance imaging

Evy Gillet[1,2], Panayiotis Tanos[1,2], Helena Van Kerrebroeck[1], Stavros Karampelas[1,2], Marion Valkenburg[1], Istvan Argay[1], Alessa Sugihara[1], Stephan Gordts[1], Rudi Campo[1]

[1]Department of Obstetrics and Gynecology, Life Expert Centre, Leuven, Belgium
[2]Department of Obstetrics and Gynecology, Brugmann University Hospital, Brussels, Belgium

ABSTRACT

Background: Recurrent implantation failure (RIF) and repeated pregnancy loss remain major challenges in assisted reproductive technology, often without identifiable causes despite high-quality embryo transfers. Emerging evidence suggests that abnormalities in the junctional zone (JZ) of the uterus may impair implantation.

Objectives: To evaluate the efficacy of hysteroscopic (HSC) sub-endometrial exploration combined with intrauterine application of budesonide-enriched crosslinked hyaluronic acid (HA) gel on pregnancy outcomes in women with RIF and complete JZ loss on magnetic resonance imaging (MRI).

Methods: This single-centre observational pilot study included 20 women with RIF and MRI-confirmed loss of JZ differentiation. All patients had excellent cryopreserved blastocysts, either from an egg donation program or derived from their own autologous oocytes (<37 years). Under conscious sedation, patients underwent HSC sub-endometrial exploration with micro-incisions at the lateral walls and fundus, followed by intrauterine instillation of budesonide-enriched HyaRegen® gel. [BioRegen Biomedical (Changzhou) Co., Ltd].

Main Outcome Measures: Clinical pregnancy rate, live birth rate, and maternal/neonatal outcomes.

Results: Eighteen of 20 women (90%) conceived. In the donor group, all 9 pregnancies led to live births. In the autologous group, 8 of 9 pregnancies were successful; one was medically terminated at 20 weeks due to foetal malformation. All 17 neonates were healthy at birth and six-month follow-up.

Conclusions: Preliminary observations of this novel approach suggest that it may contribute to improving implantation and live birth rates in women with unexplained RIF and JZ abnormalities.

What is New? This study introduces a targeted intrauterine intervention for RIF patients with loss of JZ differentiation, combining HSC exploration and budesonide–HA gel therapy.

Keywords: Recurrent implantation failure, hysteroscopy, budesonide, hyaluronic acid, junctional zone, magnetic resonance imaging

Corresponding Author: Panayiotis Tanos, MD, Department of Obstetrics and Gynecology, Life Expert Centre, Leuven, Belgium; Department of Obstetrics and Gynecology, Brugmann University Hospital, Brussels, Belgium
E-mail: p.tanos@outlook.com **ORCID ID:** orcid.org/0000-0001-5742-0995
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Introduction

Recurrent implantation failure (RIF) and repeated pregnancy loss (RPL) remain major challenges in assisted reproductive technology (ART). Their prevalence varies depending on maternal age, embryo quality, uterine environment, and ART protocols.[1,2] Globally, miscarriage affects 15–20% of women under 35, rising to 40–50% in those over 40. Up to 75% of embryos fail to implant during ART, with RIF—defined as three or more failed ART transfers with good-quality embryos—affecting 10–15% of women.[1,3,4]

Despite high-quality embryo transfers, many RIF and RPL cases lack a clearly identifiable cause. While much attention is placed on embryo quality, the uterine environment deserves greater focus. Recent evidence highlights the importance of the junctional zone (JZ) or inner myometrium in reproductive success. The JZ regulates uterine peristalsis, implantation, and placentation. Disruptions, such as those seen in adenomyosis, have been linked to implantation failure and recurrent miscarriage.[5,6] Hysteroscopy offers the advantage of exploring the JZ beneath the endometrial surface, allowing for the identification of subtle abnormalities such as adenomyotic cysts or fibrotic lesions that may otherwise go undetected. This targeted assessment is particularly valuable in patients with unexplained implantation failure, where standard imaging may miss functionally relevant pathology.

Magnetic resonance imaging (MRI) has emerged as a superior modality for assessing the JZ, offering structural insights not captured by ultrasound (US) or even histology[7-9] Harmsen et al.[8], demonstrated that MRI, US, and histology evaluate distinct features, and routine histology cannot adequately reflect JZ function. Although the prognostic value of JZ imaging remains under investigation, its relevance in reproductive dysfunction is increasingly recognised.[10,11]

Therapeutic strategies to improve endo-myometrial receptivity are advancing. Hyaluronic acid (HA), a naturally occurring extracellular matrix component with regenerative, anti-adhesive, and anti-inflammatory properties, has demonstrated efficacy in promoting endometrial healing and reducing intrauterine adhesions.[12,13] Corticosteroids such as budesonide modulate the uterine immune environment by suppressing natural killer cell cytotoxicity and cytokine secretion, while promoting human chorionic gonadotropin production and trophoblast proliferation—key processes for successful implantation and early pregnancy maintenance.[14-19]

Study Objective

This pilot study evaluates a novel approach combining hysteroscopic (HSC) sub-endometrial exploration with intrauterine application of budesonide-enriched, crosslinked HA gel in women with RIF and total loss of JZ differentiation on MRI.

Methods

This single-centre observational pilot study was conducted at a specialised ambulatory care unit, the "Life Expert Centre". All participants provided written informed consent. The aim was to evaluate pregnancy and live birth outcomes following HSC sub-endometrial exploration combined with intrauterine application of a budesonide-loaded, crosslinked HA gel (BioRegen Biomedical, Changzhou Co., Ltd, China) in women diagnosed with RIF and total loss of JZ differentiation on MRI.

This study was conducted in accordance with the ethical standards outlined in the Helsinki Declaration and its later amendments and was approved by the Hospital Ethics Committee of CHU Brugmann (le Comité d'Ethique Hospitalier du CHU Brugmann), approval number CE 2024/111, date: 13.08.2024.

Inclusion and Exclusion Criteria

From September 2022, women seeking pregnancy were consecutively enrolled if they met the following criteria:

1. Diagnosis of RIF and/or RPL
2. Presence of excellent embryonic factor, with high-quality blastocyst formation
3. No major pathology seen on "one-stop" uterine assessment, including 2D/3D transvaginal US, ambulatory hysteroscopy, and contrast sonography
4. MRI confirmed total loss of JZ differentiation

Prior to inclusion, all patients had received a minimum of six months of hormonal therapy [gonadotropin-releasing hormone (GnRH) analogues or dienogest], followed by intramuscular platelet-rich plasma (PRP) therapy, and subsequently experienced at least two additional failed embryo transfers using high-quality blastocysts. Patients with chronic endometritis or abnormal HSC findings at the time of assessment were excluded. A minimum of two cryopreserved, excellent-quality embryos was required for inclusion.

Study Groups

Patients were divided into two groups based on oocyte source:

Group 1: 10 women with RIF despite transfer of high-quality embryos in an egg donation program.

Group 2: 10 women under the age of 37 with RIF, using embryos derived from their own healthy oocytes.

A summary of our study protocol is provided in Figure 1.

Imaging Criteria

All patients had no obvious abnormal HSC and/or ultrasonographic uterine findings prior to the occurrence of RIF. The US and HSC criteria used are shown in Figure 2. These include a triangular cavity with no morphological or intrauterine pathological changes. The one-stop procedure includes a transvaginal 2D and 3D US, followed by an ambulatory hysteroscopy and concluded by a contrast sonography.

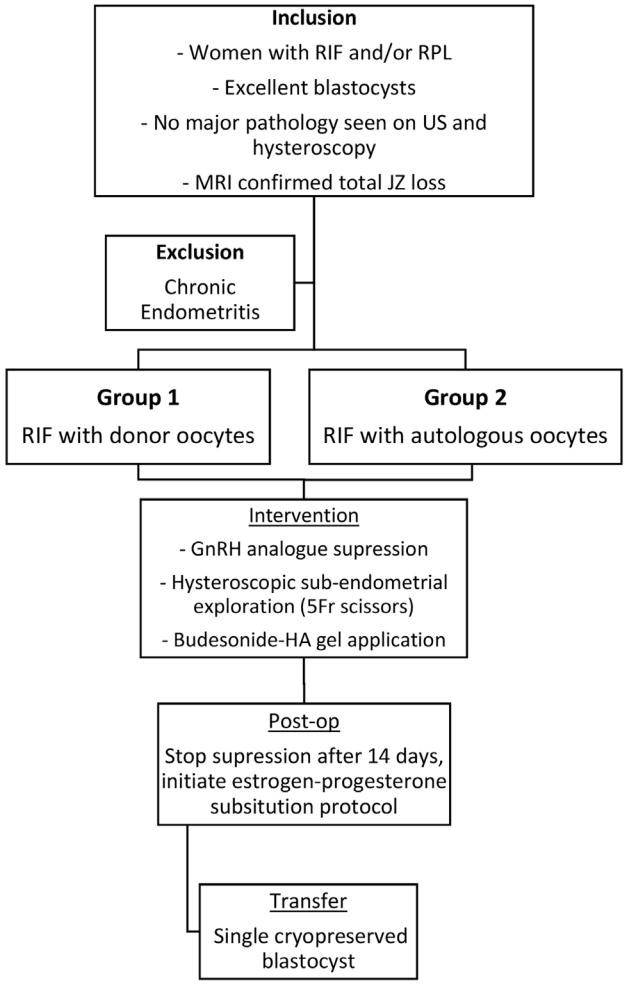

Figure 1. Study protocol.

RIF: Recurrent implantation failure, RPL: Repeated pregnancy loss, US: Ultrasound, MRI: Magnetic resonance imaging, JZ: Junctional zone, GnRH: Gonadotropin-releasing hormone, HA: Hyaluronic acid.

Magnetic Resonance Imaging of Junctional Zone

As shown on MRI, all patients showed a complete loss of JZ differentiation. In some instances, hormonal treatment or operative HSC did partially improve the JZ impairment, yet in all cases, the JZ remained disturbed. Figure 3 exemplifies the MRI of JZ in our study population.

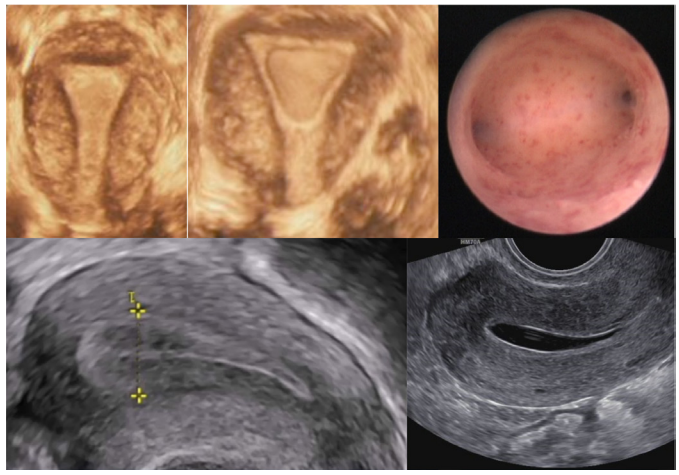

Figure 2. Normal ultrasound and hysteroscopy criteria.

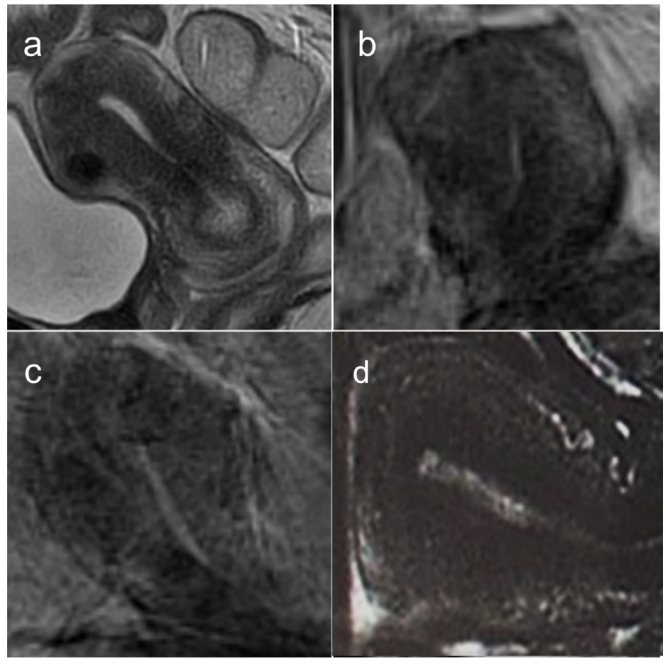

Figure 3. Magnetic resonance imaging reveals complete loss of junctional zone differentiation: junctional zone of a patient from study group 1 (a) and 2 (b); and junctional zone at intake of a patient (c) and after hormonal treatment (d).

Procedure

Under GnRH analogue suppression, HSC endo-myometrial exploration was performed in an ambulatory care setting under conscious sedation. All procedures were performed by a single, highly experienced surgeon (RC). The intervention was conducted using the TrophyScope® XL (Karl Storz, Tuttlingen, Germany), which has an outer diameter of 5.8 mm. Using 5 Fr scissors, micro-incisions were made in the lateral uterine walls and fundus to access the sub-endometrial myometrium. Subtle cystic or solid lesions, if identified, were excised. At the end of the procedure, 8 mL of gel—comprising 1.5 mg/3 mL budesonide pre-mixed with 5 mL of HyaRegen® crosslinked HA gel (final budesonide concentration: 0.19 mg/mL)—was instilled through the outer sheath of the Trophy® hysteroscope (Figure 4).

Fourteen days later, hormonal suppression was discontinued, and patients initiated estrogen–progesterone replacement to prepare for cryopreserved embryo transfer (FET).

Data Collection

Clinical records were reviewed for patient age, parity, history of ART failures and miscarriages, suspected causes of implantation failure, prior gynaecological surgeries, HSC and US findings, JZ-MRI evaluation (Figure 3), date of procedure, embryo transfer date, and pregnancy outcomes. Additional outcomes recorded included delivery mode, birth weight, perinatal complications, and neonatal health. All patients were contacted approximately six months postpartum to gather follow-up information on neonatal health and early development.

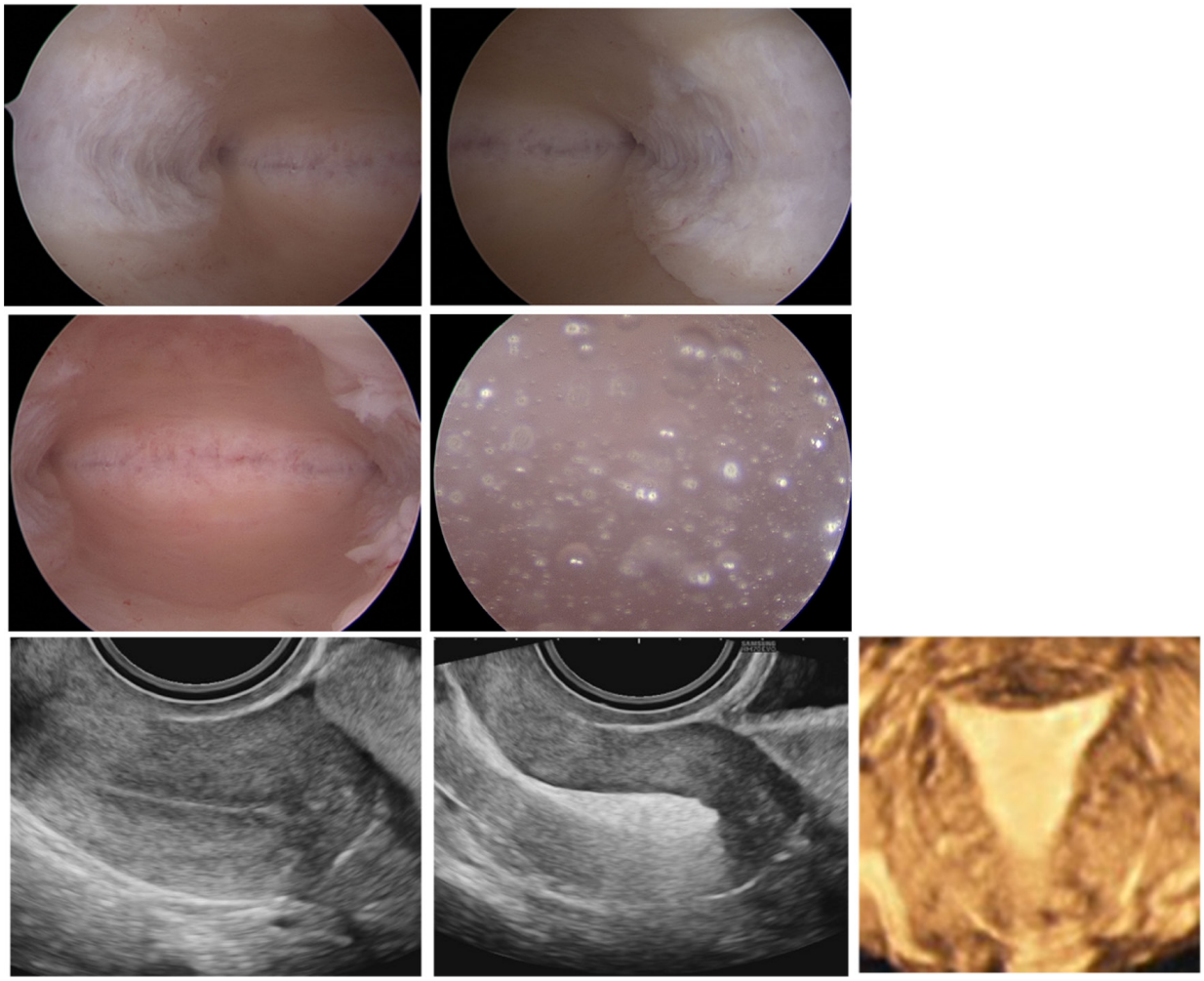

Figure 4. Technique of sub-endometrial exploration and application of budesonide-loaded crosslinked hyaluronic acid gel applied intrauterine.

Results

Demographics and Preoperative Characteristics

Twenty women were included. Study group 1 included 10 women who received ART involving donated oocytes, while study group 2 included 10 women who received embryo or blastocyst transfer involving their own healthy embryos. Patients' demographic data can be found in Table 1.

The mean age was 44.5 and 34.4 years in study groups 1 and 2, respectively. Two patients in group 1 and three patients in group 2 had secondary infertility. Previous gynaecological treatments included (adeno)myomectomy (all laparoscopic apart from 1 per laparotomy), HSC correction of dysmorphic uteri, HSC endo-myometrial exploration, and laparoscopic removal of adhesions.

Pregnancy Outcomes and Live Birth Rate

In both study groups, 9 of 10 women became pregnant after the procedure. In study group 1, which received donated oocytes, all 9 women delivered healthy babies. In study group 2, where the embryological fertility factor could be ensured with one's own oocytes, 8 of 9 pregnancies resulted in live births of healthy babies. One patient needed her pregnancy interrupted at week 20 due to foetal malformation.

Table 1 shows gestational age at delivery, mode of delivery, birth weight, and potential complications at delivery of the 9 and 8 delivered babies in study groups 1 and 2, respectively. All 17 babies were healthy at birth and showed healthy evolution in the first follow-up. The range of gestational age at birth was between 26 weeks and 42 weeks in study group 1 and between 34 weeks and 40 weeks in study group 2. In study group 1, 2 babies were delivered vaginally, and 7 were delivered by C-section. Five babies of women in study group 2 were delivered by C-section, and 3 by vaginal delivery. Birth weight ranged between 1050 g and 4500 g in study group 1 and between 2270 g and 4030 g in study group 2. Six out of 9 deliveries of group 1 were uneventful. However, 3 out of 9 patients (33%) had postpartum complications: one patient required a hysterectomy due to placenta accreta, one patient had placenta praevia, and one woman had postpartum haemorrhage (needing 3 units of blood). Seven out of 8 births in study group 2 were without complications, while one patient had preterm premature rupture of membranes and tested positive for Group B strep bacteria, yet without further complications. Follow-up on neonatal health at approximately six months postpartum revealed no reported complications or concerns.

Table 1. Patients' demographic and outcome data.

	Group 1 Donated oocytes n=10	**Group 2 Healthy own oocytes n=10**
Mean age (years)	**44.5 ± 3.7**	34.4 ± 2.5
Parity	P0: 8 P1: 2	P0: 7 P1: 2 P1: 1
Live birth	9	8
Gestational age (weeks)	36.78 ± 4.69	37.5 ± 1.88
Delivery method	C-section: 7 Vaginal: 2	C-section: 5 Vaginal: 3
Birth weight (g)	2807 ± 989	3298 ± 606.76
Complications	Hysterectomy: 1 Placenta praevia: 1 PPH: 1	PPROM, GBS+: 1

± values indicate standard deviation.
PPROM: Preterm premature rupture of membranes, GBS+: Group B strep bacteria, PPH: Post partum haemorrhage.

Discussion

Main Findings

This observational pilot study demonstrates promising outcomes in a cohort of women with RIF and/or RPL, all of whom presented with MRI-confirmed total loss of JZ differentiation and had experienced multiple failed ART cycles despite the transfer of high-quality blastocysts. Following HSC sub-endometrial exploration and intrauterine application of a budesonide-loaded crosslinked HA gel, clinical pregnancy and live birth rates reached 90% in both donor and autologous oocyte groups. This approach appears to improve implantation success and reduce miscarriage rates, without any reported treatment-related complications, suggesting a potential therapeutic benefit of targeting the sub-endometrial environment in this challenging population.

These outcomes align with existing evidence supporting the use of HA in reproductive medicine, particularly its role in enhancing endo-myometrial receptivity and reducing intrauterine adhesions.[19-22] HA provides a scaffold that supports cell proliferation and migration, essential for endo-myometrial regeneration.[23,24] By maintaining a physical barrier in the uterine cavity, HA prevents adhesions and preserves the normal architecture necessary for embryo implantation.[24] However, conventional HA has limitations due to its fluid nature and rapid degradation, which may reduce its efficacy.[25] This study utilised crosslinked HA gel, which has enhanced viscosity and prolonged *in vivo* persistence, allowing for a more sustained effect in reducing postoperative adhesions and improving pregnancy rates following ART.[25-27] The addition of budesonide—a corticosteroid with potent local anti-inflammatory and immunosuppressive effects—likely contributes to the improved uterine microenvironment, promoting trophoblast invasion and successful implantation.[28,29]

Abnormalities in the JZ, such as thickening or loss of differentiation, have been closely associated with impaired implantation, recurrent miscarriage, and other reproductive disorders.[30,31] Research by Brosens et al.[31] emphasises the importance of the JZ in the implantation process and suggests that evaluating the JZ as a distinct entity is crucial for understanding and addressing reproductive failures. Imaging techniques such as high-resolution US and MRI allow for the detailed assessment of the JZ, enabling the identification of structural and functional abnormalities that could contribute to reproductive challenges.[31]

We hypothesise that loss of JZ differentiation on MRI reflects an inflammatory uterine state contributing to unexplained RIF. Targeted HSC delivery of regenerative and anti-inflammatory agents to the endo-myometrial interface may therefore enhance uterine receptivity. This could be of equal importance in other inflammatory diseases such as chronic endometritis and endometriosis.[32]

Remarkably, in study group one, 1/3 patients had post-partum complications, including bleeding and dysfunctional placentation. These events are more likely related to known risk factors such as advanced maternal age and possibly an ageing uterus.

Strengths and Limitations

A notable strength of this study is the homogeneity of the patient population: all participants had experienced multiple failed embryo transfers with confirmed high-quality blastocysts and no major uterine pathology on US or hysteroscopy, yet demonstrated total JZ disruption on MRI. This allowed for a focused investigation of a relatively underexplored anatomical target—namely, the sub-endometrial myometrium—as a potential contributor to implantation failure. Another strength is the integration of a biologically plausible, multimodal strategy: HSC exploration of the sub-endometrial interface, combined with regenerative (HA) and anti-inflammatory (budesonide) therapy. This is supported by recent insights into endometrial and myometrial receptivity and the role of local immune modulation in implantation success.

On the other hand, limitations are present. The sample size is small, and the observational nature of the study precludes causal inference. Without a control group, the independent contributions of sub-endometrial exploration, HA, or budesonide cannot be determined. Additionally, while MRI provides valuable insight into JZ integrity, its interpretation is subjective and not yet standardised across clinical practice. The impact of prior treatments—including hormonal suppression and PRP—on outcomes cannot be excluded. Lastly, while the live birth rate is promising, the generalizability of results to broader ART populations, including those with normal JZ imaging or different endometrial pathologies, remains unknown.

Clinical and Policy Implications

These findings offer preliminary support for a new diagnostic and therapeutic pathway in patients with unexplained RIF or RPL. The presence of JZ abnormalities, as assessed by MRI, may represent an overlooked contributor to implantation failure, especially when standard diagnostic workup appears normal. This calls for more routine consideration of the JZ as a functional and structural entity in reproductive assessments. Therapeutically, the combination of HSC sub-endometrial exploration with targeted intrauterine drug delivery may address local inflammation and architectural disruption that impede implantation. If validated in larger cohorts, this approach could be integrated into ART protocols for selected patients who demonstrate persistent reproductive failure despite optimal embryo quality and hormonal preparation. From a clinical policy perspective, the data underscore the importance of individualised diagnostics in ART. The findings also highlight the need to expand imaging protocols beyond basic ultrasonography to include MRI in certain high-risk or treatment-resistant cases.

Unanswered Questions and Future Research

Several key questions remain. The relative contribution of each intervention component—sub-endometrial exploration, HA, and budesonide—requires clarification. Controlled, randomised studies are needed to determine whether this combination offers superior outcomes compared to standard care or monotherapy approaches.

Understanding the underlying biological mechanisms is essential for optimising this treatment strategy and identifying patient subgroups most likely to benefit. Future studies should investigate how budesonide modulates immune cell populations and cytokine profiles within the endo-myometrial environment, and how HA contributes to tissue remodelling and repair at the level of the JZ. Elucidating these pathways may help refine patient selection and uncover new therapeutic targets for improving endometrial receptivity and implantation success. Additionally, the prognostic value of MRI-detected JZ abnormalities remains to be fully established. Larger studies should examine correlations between different degrees of JZ disruption and reproductive outcomes, as well as potential reversibility following treatment.

Conclusion

To conclude, this pilot study suggests that HSC sub-endometrial exploration with application of budesonide-loaded crosslinked HA gel may be associated with improved pregnancy and live birth outcomes in women with RIF and JZ abnormalities. While the findings are encouraging, the study's observational nature and small sample size limit definitive conclusions. Controlled trials in larger populations are needed to validate these results and to investigate the therapeutic potential and mechanisms of this combined approach in reproductive medicine.

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Informed consent: Informed consent was obtained from all individual participants included in this study.

Data sharing: All data is available to be shared upon request to 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.

References

1. Cimadomo D, de Los Santos MJ, Griesinger G, Lainas G, Le Clef N, McLernon DJ, et al. ESHRE good practice recommendations on recurrent implantation failure. Hum Reprod Open. 2023;2023:23.
2. CDC, US Centers for Disease Control and Prevention. ART Success Rates. Available at: https://www.cdc.gov/art/artdata/index.html (Accessed August 2024).
3. HHS, US Department of Health and Human Services. Fact sheet: In vitro fertilization (IVF) use across the United States. Available at: https://www.hhs.gov/about/news/2024/03/13/fact-sheet-in-vitro-fertilization-ivf-use-across-united-states.html (Accessed August 2024).
4. Strumpf E, Lang A, Austin N, Derksen SA, Bolton JM, Brownell MD, et al. Prevalence and clinical, social, and health care predictors of miscarriage. BMC Pregnancy Childbirth. 2021;21:185.
5. Leyendecker G, Bilgicyildirim A, Inacker M, Stalf T, Huppert P, Mall G, et al. Adenomyosis and endometriosis. Re-visiting their association and further insights into the mechanisms of auto-traumatisation. An MRI study. Arch Gynecol Obstet. 2015;291:917-32.
6. Tanos V, Laidlaw J, Tanos P, Papadopoulou A. New insights into the neural network of the nongravid uterus. Adv Clin Exp Med. 2022;31:1153-62.
7. Hricak H, Alpers C, Crooks LE, Sheldon PE. Magnetic resonance imaging of the female pelvis: initial experience. AJR Am J Roentgenol. 1983;141:1119-28.
8. Harmsen MJ, Trommelen LM, de Leeuw RA, Tellum T, Juffermans LJM, Griffioen AW, et al. Uterine junctional zone and adenomyosis: comparison of MRI, transvaginal ultrasound and histology. Ultrasound Obstet Gynecol. 2023;62:42-60.
9. Lee JK, Gersell DJ, Balfe DM, Worthington JL, Picus D, Gapp G. The uterus: in vitro MR-anatomic correlation of normal and abnormal specimens. Radiology. 1985;157:175-9.
10. Gordts S, Brosens JJ, Fusi L, Benagiano G, Brosens I. Uterine adenomyosis: a need for uniform terminology and consensus classification. Reprod Biomed Online. 2008;17:244-8.
11. Tanos V, Tanos P, Georgiou J. Monitoring contractility of junctional zone endometrium across menstrual cycle using the ElectroUteroGraph (EUG): a clinical evaluation. Appl Sci. 2024;14:546.
12. Aya KL, Stern R. Hyaluronan in wound healing: rediscovering a major player. Wound Repair Regen. 2014;22:579-93.
13. Hu X, Wu H, Yong X, Wang Y, Yang S, Fan D, et al. Cyclical endo-myometrial repair and regeneration: molecular mechanisms,

diseases, and therapeutic interventions. MedComm (2020). 2023;4:425.

14. Fan J, Zhong Y, Chen C. Combined treatment of prednisone and aspirin, starting before ovulation induction, may improve reproductive outcomes in ANA-positive patients. Am J Reprod Immunol. 2016;76:391-5.
15. Fawzy M, El-Refaeey AA. Does combined prednisolone and low molecular weight heparin have a role in unexplained implantation failure? Arch Gynecol Obstet. 2014;289:677-80.
16. Forges T, Monnier-Barbarino P, Guillet-May F, Faure GC, Béné MC. Corticosteroids in patients with antiovarian antibodies undergoing in vitro fertilization: a prospective pilot study. Eur J Clin Pharmacol. 2006;62:699-705.
17. Li X, Wu L, Zhou Y, Fan X, Huang J, Wu J, et al. New crosslinked hyaluronan gel for the prevention of intrauterine adhesions after dilation and curettage in patients with delayed miscarriage: a prospective, multicenter, randomized, controlled trial. J Minim Invasive Gynecol. 2019;26:94-9.
18. Siristatidis C, Dafopoulos K, El-Khayat W, Salamalekis G, Anifandis G, Vrantza T, et al. Administration of prednisolone and low molecular weight heparin in patients with repeated implantation failures: a cohort study. Gynecol Endocrinol. 2018;34:136-9.
19. Lu Y, Yan J, Liu J, Tan J, Hong Y, Wei D, et al. Prednisone for patients with recurrent implantation failure: study protocol for a double-blind, multicenter, randomized, placebo-controlled trial. Trials. 2020;21:719.
20. Dou Y, Yu T, Li Z, Wang J, Jiang Y, Liu Y. Short- and long-term outcomes of postoperative intrauterine application of hyaluronic acid gel: a meta-analysis of randomized controlled trials. J Minim Invasive Gynecol. 2022;29:934-42.
21. Fei Z, Xin X, Fei H, Yuechong C. Meta-analysis of the use of hyaluronic acid gel to prevent intrauterine adhesions after miscarriage. Eur J Obstet Gynecol Reprod Biol. 2020;244:1-4.
22. Sroussi J, Bourret A, Pourcelot AG, Thubert T, Lesavre M, Legendre G, et al. Does hyaluronic acid gel reduce intrauterine adhesions after dilation and curettage in women with miscarriage? A multicentric randomized controlled trial (HYFACO Study). Am J Obstet Gynecol. 2022;227:597.
23. Vitale SG, Riemma G, Carugno J, Perez-Medina T, Alonso Pacheco L, Haimovich S, et al. Postsurgical barrier strategies to avoid the recurrence of intrauterine adhesion formation after hysteroscopic adhesiolysis: a network meta-analysis of randomized controlled trials. Am J Obstet Gynecol. 2022;226:487-98.
24. Harrity C, Shkrobot L, Walsh D, Marron K. ART implantation failure and miscarriage in patients with elevated intracellular cytokine ratios: response to immune support therapy. Fertil Res Pract. 2018;4:7.
25. Wu T, Fang T, Dong Y, Mao J, Wang J, Zhao M, et al. Comparison of secondary prevention following hysteroscopic adhesiolysis in the improvement of reproductive outcomes: a retrospective cohort study. J Clin Med. 2023;13:73.
26. Hooker AB, de Leeuw RA, Twisk JWR, Brölmann HAM, Huirne JAF. Reproductive performance of women with and without intrauterine adhesions following recurrent dilatation and curettage for miscarriage: long-term follow-up of a randomized controlled trial. Hum Reprod. 2021;36:70-81.
27. Mao X, Tao Y, Cai R, Zhang J, Gao H, Chen Q, et al. Cross-linked hyaluronan gel to improve pregnancy rate of women patients with moderate to severe intrauterine adhesion treated with IVF: a randomized controlled trial. Arch Gynecol Obstet. 2020;301:199-205.
28. Orvieto R. Controlled ovarian hyperstimulation--an inflammatory state. J Soc Gynecol Investig. 2004;11:424-6.
29. Bashiri A, Halper KI, Orvieto R. Recurrent implantation failure-update overview on etiology, diagnosis, treatment and future directions. Reprod Biol Endocrinol. 2018;16:121.
30. Barbanti C, Centini G, Lazzeri L, Habib N, Labanca L, Zupi E, et al. Adenomyosis and infertility: the role of the junctional zone. Gynecol Endocrinol. 2021;37:577-83.
31. Brosens I, Derwig I, Brosens J, Fusi L, Benagiano G, Pijnenborg R. The enigmatic uterine junctional zone: the missing link between reproductive disorders and major obstetrical disorders? Hum Reprod. 2010;25:569-74.
32. Kalaitzopoulos DR, Catena U, Schwartz AK, Schoretsanitis G, Leeners B, Drakopoulos P, et al. Chronic endometritis and endometriosis: two sides of the same coin? Reprod Sci. 2025;32:474-87. Erratum in: Reprod Sci. 2025;32:919.