# Ultrasound Based Endometrial Receptivity Scoring Accurately Identifies IVF Cycles with Low Probability of Pregnancy

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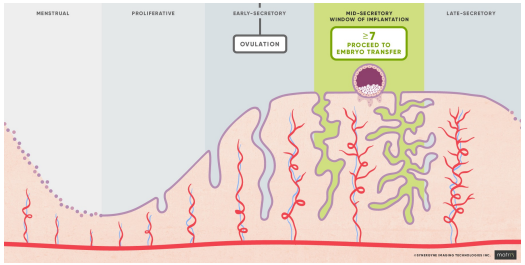
## Background

**Endometrium and Receptivity:**

The endometrium lines the uterine cavity and undergoes dramatic changes in response to reproductive hormones during the menstrual cycle. Cyclic development and differentiation of endometrial glandular tissues is crucial to implantation of embryos and ultimately, maintenance of a successful pregnancy. Echotextural details of optimal cycles have been elucidated (Baerwald A, 2004; Kadash M, 2003; Pierson R, 2005). Endometrial receptivity is defined as the physiologic condition of the uterine lining and its ability to recognize and implant an embryo or blastocyst. Endometrial receptivity assessment is currently not a standard practice in routine IVF procedures. Endometrial receptivity is a highly important aspect of successful IVF outcomes.




## usER Diagnostic Testing

A non-invasive *Ultrasound-based Endometrial Receptivity* test (usER) has been developed. The usER test (Matris™, Synergyne Imaging Technologies Inc.) assess the uterine lining in each IVF cycle being considered for embryo transfer (fresh or frozen embryo transfer) and during mock/preparatory cycles. **The goal of the usER test is to improve pregnancy rates and conserve embryo potential by avoiding embryo transfer into sub-optimally prepared endometria.**

**Workflow of usER Diagnostic:**

usER provides clinicians with a non-invasive real-time assessment of endometrial receptivity on a per-cycle basis:

- Transverse ultrasound images of uterine lining are acquired on day 3
- Images are uploaded to a secure server on the day of acquisition
- Multi-tiered algorithm is used to assign receptivity scores
- usER scores are returned to the clinic within 24 hours

**What usER scores mean:**

| Matris™ Score | Classification | Endometrium | Clinical RX (as per physician) |
|---|---|---|---|
| Greater than 7 | Optimal | • High state of receptivity<br>• Excellent glandular development<br>• Endometrial response to circulating hormones is appropriate<br>• Exhibits characteristics associated with high probability of pregnancy | Proceed to Embryo Transfer |
| 5.5 to 6.5 | Sub- Optimal | • Receptivity is weaker than expected in optimal cycle<br>• Glandular development is suboptimal<br>• Not well prepared for implantation<br>• Exhibits characteristics associated with lower than normal probability of pregnancy | Embryo Transfer Not Recommended* |
| 5.0 or lower | Deficient | • Poor state of endometrial receptivity<br>• Glandular development is not appropriate for stage of cycle<br>• Exhibits characteristics associated with low/ extremely low probability of pregnancy | Embryo Transfer Not Recommended |

High quality embryos transferred into high usER-scored endometrial environments (scores of 7.0 or greater) resulted in significantly higher pregnancy rates; approximately 22-25% of cycles are associated with low probability endometrial scores (Pierson R, 2012).

## Objectives

- To determine if the diagnostic usER test accurately identifies IVF cycles in which endometrial receptivity is poor and probability of pregnancy is low.
- To demonstrate that usER scores are not corelated with endometrial thickness.

## Study Design

- Retrospective analysis of all IVF cycles conducted at one ART centre that had usER scores, endometrial thickness measurements, and outcome data available (n=2274).
- Data were acquired from a chart review of deidentified patient files from 2014 – 2019.
- We conducted multifactor regression analyses to determine the relationships between endometrial thickness, usER score, and pregnancy outcome (positive $\beta$-hCG).

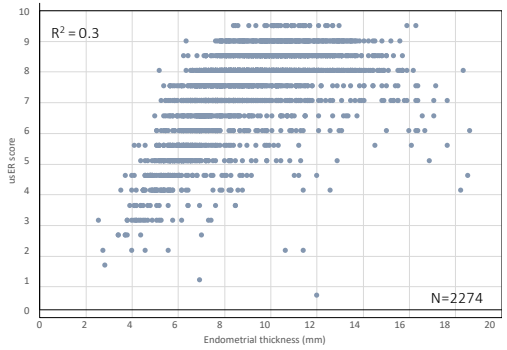
## Results

**1) Patients with low usER-scoring endometria were statistically equivalent to those with high scoring endometria.**

| Patient Demographics | usER score 7 or above (n, %, or mean) | User score below 7 (n, %, or mean) | p-value |
|---|---|---|---|
| Number of frozen cycles (n) | 1383 | 389 | -- |
| Number of fresh cycles (n) | 314 | 190 | -- |
| Number of cycles total (n) | 1697 | 579 | -- |
| Percent total cycles fresh vs frozen embryo | | | .00401 (chi-square) |
| Number of cycles received embryo transfer (n) | 1611 | 179 | <0.0001 (chi-square) |
| Average patient age (years) | 36.663 | 36.578 | .9875 (MannWhitney) |
| Patient age range (years) | 24-50 | 24-52 | -- |
| Primary Infertility Diagnosis: | | | .704 (chi-square) |
| Male Factor Infertility (%) | 349 | 110 | |
| Female Factor Infertility (%) | 763 | 276 | |
| Male and Female Factor Infertility (%) | 189 | 61 | |
| Unknown / Idiopathic Infertility (%) | 395 | 132 | |

A significantly higher percentage of cycles with low usER scores did not receive embryo transfer. This is attributed to the clinical guidance to defer embryo transfer when the scores are below 7.

**2) usER scores are not correlated with endometrial thickness.**



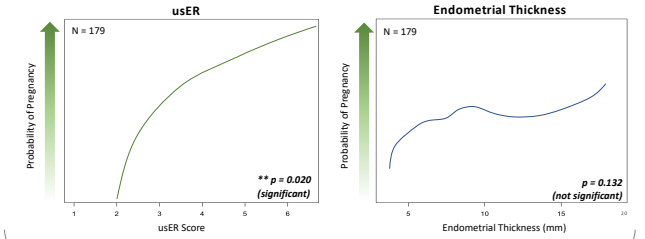

The distribution of endometrial thickness (horizontal axis) and usER score (vertical axis) is illustrated. Each spot represents one patient cycle. Regression analysis resulted in $R^2$ = 0.3 (negligible correlation) between endometrial thickness and usER score. Endometrial thickness and usER score report fundamentally different information.

**3) usER test accurately identified endometria with low probability of supporting pregnancy.**

- Cycles considered (n = 2274)
- 579 cycles deferral recommended due to low usER scores
- 179 proceeded to SET against recommendation.

- Regression analysis of the 179 low usER score cycles that received ET against recommendation

- Low usER score reliably predicted the outcome of 'not pregnant' (p=0.020).
- ET was not a significant predictor of pregnancy outcome (p=0.132).




Each step lower in usER score is tightly linked to lower probability of pregnancy (left). In the same group of patients, endometrial thickness did not correlate to pregnancy result (right).

**4) Other key factors were not statistically significant predictors of pregnancy outcome.**

| Variable | Estimate | Standard Error | t-value | p-value |
|---|---|---|---|---|
| usER Score | 0.074117 | 0.036397 | 2.036 | 0.0432** |
| Endometrial Thickness | 0.023409 | 0.016316 | 1.435 | 0.1531 |
| Cycle Type | -0.020755 | 0.112311 | -0.185 | 0.8535 |
| Embyros Transferred | 0.065626 | 0.106357 | 0.617 | 0.5380 |
| ASA use | -0.042631 | 0.095234 | -0.448 | 0.6550 |
| Protocol Category | 0.038189 | 0.032908 | 1.161 | 0.2474 |
| Patient age | -0.015241 | 0.008256 | -1.846 | 0.0666 |

usER score was a statistically significant predictor of pregnancy outcome. Patient age, cycle type (fresh / frozen-thaw), number of embryos transferred, ASA use, endometrial thickness, and protocol type were not significant predictors of pregnancy outcome.

## Conclusions & Impact of Findings

- Patient demographics show that low usER-scoring cycles affect patients equally (low usER score is not correlated to age / fertility diagnosis / number of embryos / ect.)
- usER score and endometrial thickness measurements are fundamentally different and report different clinical information.
- Low usER scores reliably predict the outcome 'not pregnant' while other factors do not.

usER testing provides a 'current cycle' method for assessing endometrial receptivity. Ultimately, deferral of low probability cycles prevents embryo wastage (314 embryos were conserved by usER in the present analysis) and provides opportunity to improve pregnancy outcomes.

## References & Additional Resources

SYNERGYNE IMAGING TECHNOLOGIES, INC.

TRIO ADVANCING REPRODUCTIVE CARE

UNIVERSITY OF SASKATCHEWAN