CHAPTER 16

WINDOW OF IMPLANTATION (WOI)

S. Suphan ERSAHIN

What is WOI?

The window of implantation (WOI) is accepted as that period when the endometrium is receptive for implantation of the embryo. This period is maintained by the action of estrogen and progesterone on the endometrial zone. WOI begins with apposition continues through attachment and invasion of the blastocyst to endometrium. The optimal time for WOI lies between postovulatory days +3 to +5, where luteal day +1 is the first day of exogenous progesterone treatment (1,2).

How can we detect WOI in women on natural cycles or undergoing ET?

Exact time of WOI is not clear and wide range of individual differences is possible. WOI is a specific time of the implantation process and begins 4–5 days after endogenous or exogenous progesterone exposure and ends up 9–10 days later (1,2). Conventionally, WOI is considered as occurring 8 to 10 days following ovulation and ends up within 2 or 3 days (3). WOI can also be defined between days 19 and 23 of the menstrual cycle (1,2).

Why is WOI important in ART cycles?

In order to increase clinical pregnancy rates in IVF/ICSI cycles many studies have focused predominantly on the understanding genetic and molecular basis of edometrium receptivity and optimization of embryo transfer time. The endometrium is accepted receptive for blastocyst during an individually defined period in which implantation zone allows attachment and invasion of embryo. Alteration in the individual receptivity status of many infertile women have been reported (4). Therefore, in order to improve implantation chance of each transferred embryo personalized diagnostic approach is required. This approach should be determined WOI time precisely and reliable manner. The endometrial receptivity array (ERA) is the only method of testing currently in use for this purpose (5). WOI time can be detected more accurately by using the ERA test.

	ERA test ¹⁻⁴	Ideal test?
Method	Microarray/transcriptomic	Proteomic
Samples	Endometrium biopsy	Blood
Timing biopsy	 Seven days after the LH surge in a natural cycle, At the end of 5 days of progesterone administration after estrogen priming. 	Whenever you want
Measured product	Genes	Genes, protein, and other markers
Why 238 genes	The number of 238 genes analyzed by ERA were chosen according to the results of 14 previous manuscripts searching for the transcriptomic analysis of endometrial receptivity.	Whole genome and receptivity marker analysis
Histology of endometrium	Independent of histology	Independent of histology
Classification of endometrium	Receptive, Pre-receptive, Post-receptive	Receptive or unreceptive
Reproducibility	40 months	During reproductive period

References

- 1. Martin J, Dominguez F, Avila S, Castrillo JL, Remoh J, Pellicer A, Simon C: Human endometrial receptivity: gene regulation. J ReprodImmunol 2002; 55:131–139.
- 2. Edwards RG: Physiological and molecular aspect of implantation. Hum Reprod 1995; 10:1–13.
- Wilcox AJ, Baird DD, Weinberg CR. Time of implantation of the conceptus and loss of pregnancy. N Engl J Med 1999; 340: 1796–1799
- 4. Koler M, Achache H, Tsafrir A et al. Disrupted gene pattern in patients with repeated in vitro fertilization (IVF) failure. Hum Reprod 2009; 24: 2541–2548
- 5. Diaz-Gimeno P, Horcajadas JA, Martínez-Conejero JA et al. A genomic diagnostic tool for human endometrial receptivity based on the transcriptomic signature. Fertil Steril 2011; 95: 50–60
- 6. Gellersen B, Brosens IA, Brosens JJ: Decidualization of the human endometrium: mechanisms, functions, and clinical perspectives. Semin Reprod Med 2007; 25:445–453.
- Loke YW, King A, Burrows TD: Decidua in human implantation. Hum Reprod 1995; 10(Suppl. 2):14–21.
- Hanna J, Goldman-Wohl D, Hamani Y, Avraham I, Greenfield C, Natanson-Yaron S, Prus D, Cohen-Daniel L, Arnon TI, Manaster I: Decidual NK cells regulate key developmental processes at the human fetal-maternal interface. Nat Med 2006;12:1065–1074.
- Wegmann TG, Lin H, Guilbert L, Mosmann TR: Bidirectional cytokine interactions in the maternal-fetal relationship: is successful pregnancy a TH2 phenomenon? Immunol Today 1993; 14:353–356.
- Dunn CL, Kelly RW & Critchley HO 2003 Decidualization of the human endometrial stromal cell: an enigmatic transformation. Reproductive Biomedicine Online 7 151–161.
- Paria BC, Reese J, Das SK & Dey SK 2002. Deciphering the cross-talk of implantation: advances and challenges. Sciences 296 2185–2188.

118

- Nikas G, Drakakis P, Loutradis D, Mara-Skoufari C, Koumantakis E, Michalas S, Psychoyos A: Uterine pinopodes as markers of the nidation window in cyclic women receiving exogenous oestradiol and progesterone. Hum Reprod 1995;10:1208–1213.
- 13. Galliano D, Pellicer A. MicroRNA and implantation. Fertil Steril 2014; 101: 1531-1544
- 14. Diaz-Gimeno P, Horcajadas JA, Martínez-Conejero JA et al. A genomic diagnostic tool for human endometrial receptivity based on the transcriptomic signature. Fertil Steril 2011; 95: 50–60
- Wilcox AJ, Baird DD, Weinberg CR. Time of implantation of the conceptus and loss of pregnancy. N Engl J Med 1999; 340: 1796–1799
- 16. Koler M, Achache H, Tsafrir A et al. Disrupted gene pattern in patients with repeated in vitro fertilization (IVF) failure. Hum Reprod 2009; 24: 2541–2548