Echographic assessment of endometrial receptivity after embryo transfer

Romana Dmitrovic
Croatia

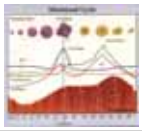
Uterine receptivity

- 80-85% of embryos transferred fail to implant
- Robert G. Edwards - implantation rates under 30 percent are the most disappointing statistic of human IVF
- "Therefore a better comprehension of implantation, and the relative importance of the factors involved, is warranted"
  Diedrich 2007

Louise Brown in 1978

Uterine receptivity

- Synchrony between embryo and endometrium = pregnancy
- Asynchrony
  - failure to achieve pregnancy
  - fetal malformations
  - changes in fetal growth and metabolism



Barnes, Theriogenology 2000

Transvaginal ultrasonography

- Endometrial biopsy – "gold standard"
  - Endometrial advancement = hiperechogenicity prior to ovulation
  - Endometrial advancement >3 days = no pregnancy

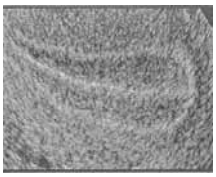
    Lass, Hum Reprod 1998
- TVU
  - Non-invasive, practical
  - Information on uterine receptivity
    - Endometrial echogenicity
    - Uterine vascular network
    - Uterine contractility

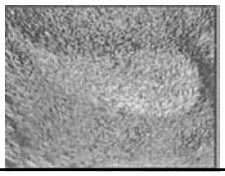
Echogenicity

- Endometrial hyperechogenicity prior to ovulation is a poor prognostic factor for pregnancy

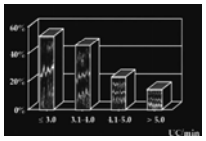
  Sher 1991, Fanchin 2000, Lindhart 2006
- Women with a triple-line pattern on the day of oocyte retrieval conceived in 80.0% of cases

  Järvelä 2005





Uterine contractility

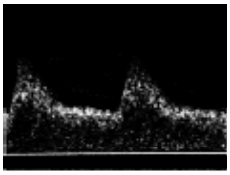


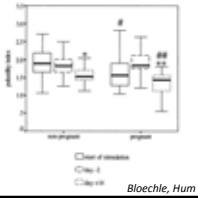
- 209 women, 220 cycles
- High frequency uterine contractions on the day of ET negatively affect IVF–ET outcome
- If frequency of contractions fall, CPR rises

Fanchin, Hum Reprod 1998

Uterine perfusion

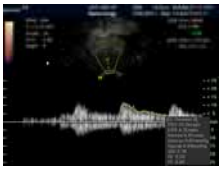
- 16 pregnant, 54 non–pregnant patients
- Beginning of stimulation, day of HCG, day 28
- Statistical differences:
  - Beginning of stimulation, high resistance in non-pregnant
  - Day 28, low resistance in pregnant
- Increased uterine impedance leads to lower pregnancy rates in IVF-ET





Bloechle, Hum Reprod 1997

Uterine perfusion

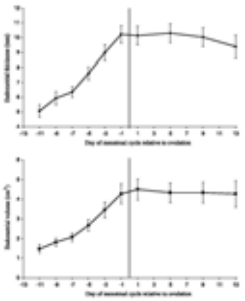


	Pregnant (n-27)	Non pregnant (n-27)	
	Day 27	Day 27	
	Mean ± SD	Mean ± SD	p
Uterine artery RI	0,79 ± 0,13	0,71 ± 0,16	0,082
Uterine artery PI	1,85 ± 0,73	1,60 ± 0,86	0,314
Spiral artery RI	0,59 ± 0,19	0,54 ± 0,18	0,133
Spiral artery PI	1,01 ± 0,67	1,12 ± 0,47	0,086

•27 pregnant, 27 non-pregnant
•No difference in uterine or spiral artery

Dmitrovic, PhD thesis, Ljubljana 2008

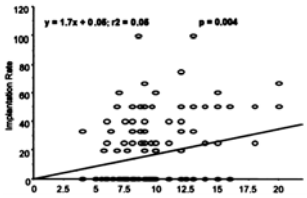
Endometrial thickness and volume in normal menstrual cycle



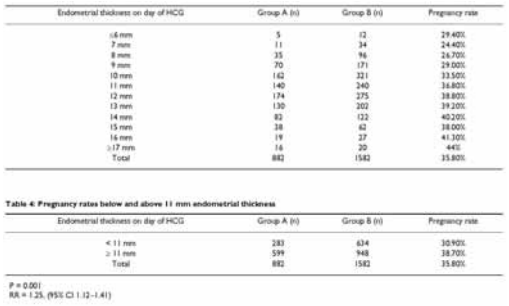
Raine-Fenning, BJOG 2004

Endometrial thickness as predictor of subsequent pregnancy?

- A topic of 30-years debate
- Several factors influence the early pregnancy rate
  - embryo quality
  - patient's age
  - endometrial thickness and pattern



Remohi, Hum Reprod 1997, Raga, Hum Reprod 1999; Schild, Hum Reprod 1999; Yaman, F&S 2000; Bassil, UOG 2001



Endometrial thickness on day of HCG	Group A (n)	Group B (n)	Pregnancy rate
≤6 mm	5	12	29.40%
7 mm	11	34	24.40%
8 mm	35	96	26.70%
9 mm	70	171	29.00%
10 mm	162	321	33.50%
11 mm	140	240	36.80%
12 mm	174	275	38.80%
13 mm	130	202	39.20%
14 mm	82	122	40.20%
15 mm	38	62	38.00%
16 mm	19	27	41.30%
≥17 mm	16	20	44%
Total	882	1582	35.80%

Table 4: Pregnancy rates below and above 11 mm endometrial thickness

Endometrial thickness on day of HCG	Group A (n)	Group B (n)	Pregnancy rate
< 11 mm	283	634	30.90%
≥ 11 mm	599	948	38.70%
Total	882	1582	35.80%

P = 0.001
RR = 1.25, (95% CI 1.12–1.41)

- 2500 cycles, day of HCG
- Endometrial thickness cannot predict pregnancy
- Pregnancies on thin endometrium
- Pregnancy is more likely on thicker endometrium

Al-Ghamdi, Reprod Biol Endocrinol 2008

Early luteal phase

	Pregnant (N=27)		Non-pregnant (N=27)
	Day of cycle	Endometrial thickness	Endometrial thickness
Endometrial thickness (mm)	Day of HCG	**10,69**	**11,0**
Endometrial thickness (mm)	22	**12,96**	**12,56**
Endometrial volume (ml)	22	**5,85**	**4,8**
PI	22	**1,66**	**1,58**
Estradiol (nmol/l)	22	**1,64**	**1,09**
Progesterone (nmol/l)	22	**79,3**	**60,8**
Beta HCG (IU/L)	22	**6,15**	**2,04***

Dmitrovic, J Assist Reprod Gen 2008

Endometrial thickness in luteal phase of conception cycles

	Pregnant			Non-pregnant	
	Day of cycle	N	Endometrial thickness	N	Endometrial thickness
Rabinowitz 1986	28	10	**15***	37	13
Vlaisavljevic 2001	26	29	**13.8**	93	10,9
Dmitrovic 2008	28	27	**17,5***	27	10

*Significant

Endometrial thickness in normal vs. abnormal pregnancy

	Day of cycle	Normal pregnancy	Abnormal pregnancy	Ectopic
Spandorfer 1996	28	13,4*	9,3	5,9
Banerjee 2001	30	10,9*	8,9	6,5
Dmitrovic 2008	28	17,5*	12,6	

* - Significant

Endometrial volume as predictor of subsequent pregnancy

- No difference in endometrial volume between conception and non-conception cycles

Table 3: Summary of data published about the role of 3D-ultrasound for predicting outcome in IVF program

Author	N	Primary outcome	3D Method	Day 3D US	Sub endometrial area	Pregnancy rate (PR)	Findings
Raga (65)	72	Pregnancy rate	Multislice	Embryo transfer		29.2%	No pregnancy if endometrial volume < 1 ml If endometrial volume ≥ 2 ml, no difference in PR
Schild (64)	47	Pregnancy rate	Multislice	Oocyte retrieval		31.9%	No difference in endometrial volume between conception and non-conception cycles
Yaman (66)	65	Pregnancy rate	Multislice	HCG		32.3%	No difference in endometrial volume between conception and non-conception cycles No pregnancy if endometrial volume < 2.5 ml
Zollner (67)	125	Pregnancy rate	Multislice	Embryo transfer		27.2%	PR 35% if endometrial volume ≥ 2.5 ml PR 9% if endometrial volume < 2.5 ml

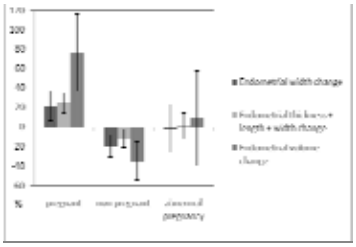
Alcazar, Reprod Biol Endocrinol 2006

Endometrial volume in luteal phase of conception cycles

	Pregnant		Non-pregnant	
	Day of cycle	Volume (ml)	Day of cycle	Volume (ml)
Martins 2007	24	6,49*	24	3,16
Zohav 2007	33	8*		
Dmitrovic 2008	28	10*	28	3,4

* - Significant

- 27 pregnant, 27 non-pregnant; ~22 vs. ~27 day of cycle
- Endometrial thickness, height, width, volume
- Prominent endometrial volume growth in pregnant, decrease in non-pregnant, both in abnormal



Dmitrovic, PhD thesis, Ljubljana 2008

Conclusions

- No definite clinically applicable ultrasonic receptivity marker in luteal phase of the cycle has been discovered yet
- Areas to investigate:
  - Endometrial thickness and volume longitudinal changes throughout the cycle and their relation to biochemical/hormonal changes
  - Endometrial thickness and volume in ectopic pregnancy