Department for Reproductive Medicine and Gynecologic Endocrinology
Ljubljanska 5
SI-2000 Maribor
Slovenija

ivf.mb@ukc-mb.si
www.ivf-mb.net

STARS IN ART

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Preovulatory follicle size and ultrasound monitoring in natural cycle

Veljko Vlaisavljević

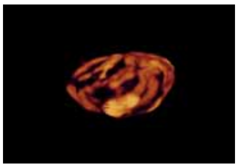
University Clinical Centre Maribor
Gynecology and Perinatology
Department for Reproductive Medicine and Gynecologic Endocrinology
ivf.mb@uni-mb.si
www.ivf-mb.net

Ultrasound and follicle monitoring & ART

Visualization of follicle	**Kratochwil**	1972
Echographic monitoring of follicle growth	**Hackelöer**	1977
Transabdominal follicle puncture	**Leitz**	1981
Ultrasonographically guided puncture with vaginal probe	**Dellenbach**	1984
Ultrasonographically guided puncture by transurethral approach	**Persons**	1985
Transvaginal puncture using vaginal probe	**Wikland**	1985

Evaluation of preovulatory follicle by ultrasound

- Follicle diameter
- Follicle growth pattern
- Follicular wall thickness
- Perifollicular vascularity
- Perifollicular blood flow

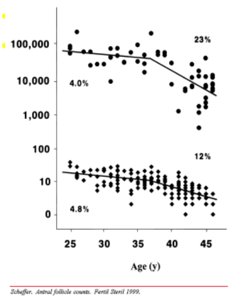


Follicular size & visualization by ultrasound

Stage	Follicular size (mm)
Primordial	0.03-0.04
Primary	0.05-0.06
Secondary	0.07-0.11
Preantral	0.12-0.20
Early antral	0.21-0.40
Antral	0.41-16.00
Preovulatory	16.1-20.00

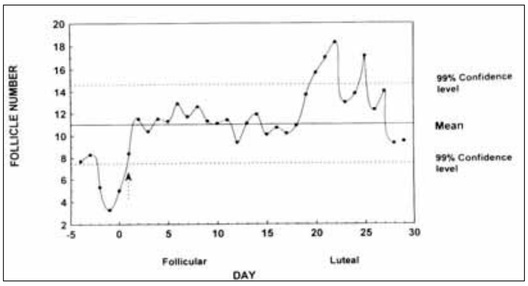
Gougeon A.Human Reprod 1986;1:81-7.

Ultrasound and ovarian reserve assessment



Scheffer GJ et al. Fertil Steril 1999;72:845-51.

Fluctuation in number of antral follicles in the ovulatory cycle visualized by 3D day-by-day ultrasound scan



Gore et al. Hum Reprod 1995;10,2313-9

Dominant preovulatory follicle

- Diameter at the time of LH surge
  18.1 – 22.6 mm
- Linear growth rate before LH peak:
  1.4 – 2.2 mm /day
- After the peak, growth increases very quickely

Pashe et a., Fertil Steril 1990:54:638-42.

Follicle diameter and time remaining to ovulation

(d=days,h=hours)

Mean diameter (mm)	Percentiles 10	25	50	75	90
14	1d+6h	1d+2h	2d+18h	5d+6h	7d+0h
15	1d	1d+12h	2d+18h	4d+18h	6d+6h
16	1d	1d+12h	2d+12h	4d	5d+12h
17	1d	1d+6h	2d+12h	3d+18h	5d
18	1d	1d+6h	2d	3d+6h	4d+12h
19	1d	1d+6h	2d	3d	4d
20	18h	1d	1d+18h	2d+18h	3d+18h
21	18h	1d	1d+12h	2d+12h	3d+6h
22	18h	1d	1d+12h	2d+6h	3d+6h
23	12h	18h	1d+6h	2d+6h	2d+18h
24	12h	18h	1d+6h	2d	2d+18h
25	12h	18h	1d+6h	2d	2d+18h

When is the correct moment to induce final oocyte maturation ?

(Paulson et al.1993)

When the dominant follicle allained 16-20 mm.

or

Estradiol levels were indicating satisfactory follicular development (>1.1 – 0.73 nmol/L).

Follicular diameter	Estradiol level
16 mm	1.1 nmol/L
18 mm	0.91 nmol/L
20 mm	0.73 nmol/L

When is the correct moment to induce final oocyte maturation ?

(Maribor IVF)

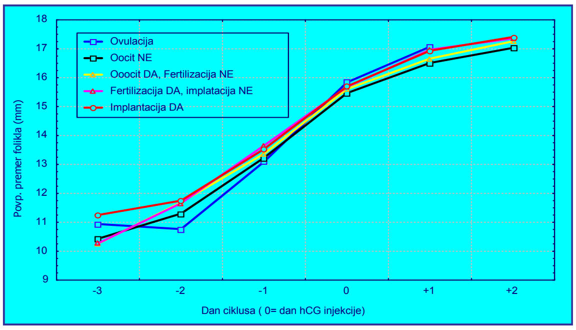
When the dominant follicle allained >15 mm.

and

Estradiol levels were indicating satisfactory follicular development

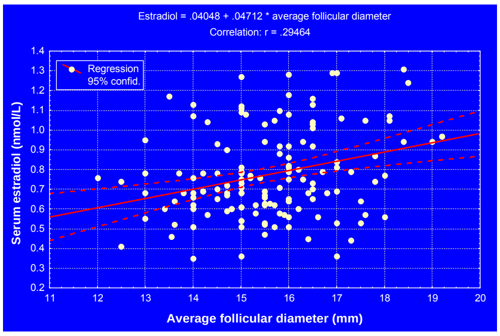
> 0.49 nmol/L

Mean follicle diameter and outcome in 305 natural IVF cycles



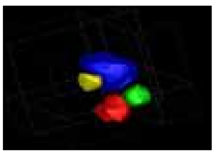
Correlation between serum estradiol and average follicular diameter in natural IVF/ICSI cycles

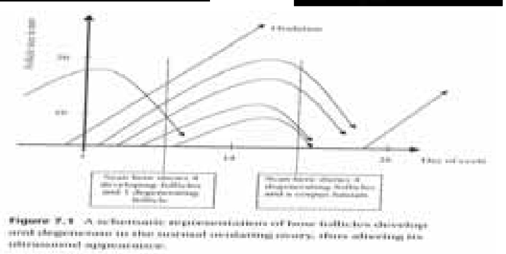
(Maribor IVF)



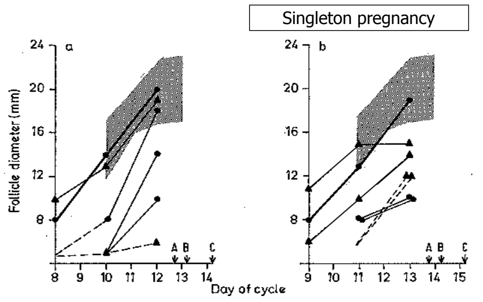
Serum estradiol and follicular diameter on the day od hCG administration in natural cycle

Estradiol (mean) nmol /L	Follicle diameter mm		Method	Author
1.17	19.6	(mean)	Fluoriomunometric	Cahill,1998
1.09	18.6	(max)	RIA Pantex	Lindheim 1997
1.05	19.3	(max)	RIA Pantex	Paulson 1994
0.78	19.5	(mean)	DPC RIA	Foulot 1989
0.59	18.9	(mean)	Pharmacia Delphia	Tomaževič 1999
0.76	15.6	(mean)	Abbott,AxSYM	Maribor 2000
	17.0	(max)		





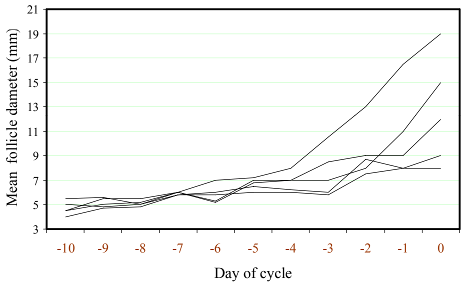
Growth of cohort of largest follicles in cycles stimulated with gonadotrophins



Nayudu et al. Hum Reprod 1991

Dynamics of follicle growth in 10 days before LH surge

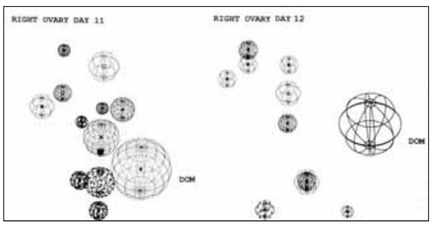
Vlaisavljević, Ultrazvuk 1991



Curves of follicular growth including two rapidly growing follicles and a cohort of slowly growing follicles. One follicle grew rapidly but a short time from day -2, the other from day -6 (most likely responsible for pregnancy).

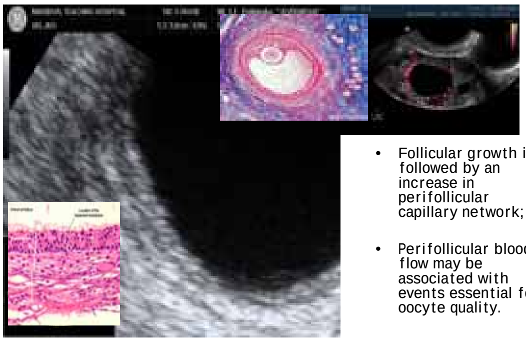
Influence of dominant follicle on development of adjacent cohort

Computer reconstruction of 3D model of the same ovary using day-by-day ultrasound scan



Gore et al. Hum Reprod 1997;12,22741-7

Perifollicular angiogenesis



- Follicular growth is followed by an increase in perifollicular capillary network;
- Perifollicular blood flow may be associated with events essential for oocyte quality.

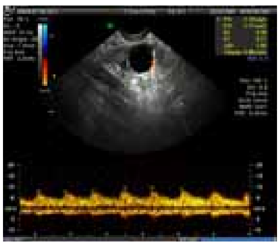
Vascularization studies in natural cycles

The value of different Doppler modalities in recognizing "pregnancy quality " follicles in unstimulated cycles by assessing perifollicular blood flow.

1. Conventional color Doppler (PI,RI,PSV)
2. Power Doppler
- Semiquantitative analysis
- 3D quantitative analysis

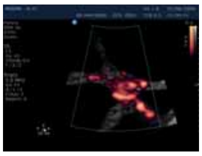
Doppler studies of perifollicular blood flow in unstimulated cycles

PSV, PI and RI in the perifollicular vessels change during the menstrual cycle.

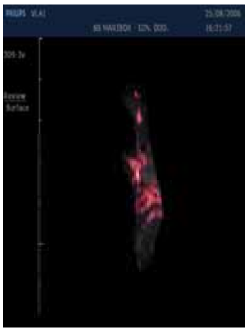


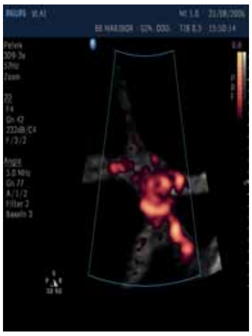
Collins et al. Hum Reprod 1991;
Kurjak et al. Fertil Steril 1991;
Campbell et al. Fertil Steril 1993;
Tan et al. Am J Obstet Gynecol 1996;
Lunenfeld et al. Hum Reprod 1996;
Zaidi et al. Ultrasound in Obstet Gynecol 1996;
Agrawal et al.Clinical Endocrinology 1999.

Problems in blood flow assessment in stimulated cycles



Difficulties in following the same follicle; identifying perifollicular vessels; tracing the embryo to the follicle.

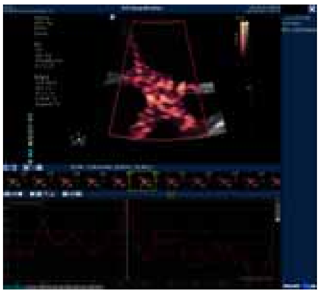




Quantitative pulsed Doppler indices of perifollicular blood flow and IVF outcome in stimulated cycled

PSV of individual follicles correlated with:

- oocyte recovery rate (*Nargund et al.,1996a,b*);
- fertilization rate (*Nargund et al.,1996a*);
- developmental potential of the oocyte (*Van Blerkom et al.,1997*);
- quality of preimplantation embryo (*Nargund et al.,1996a*).

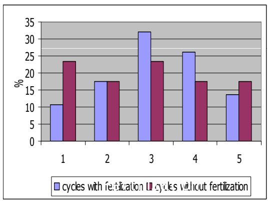


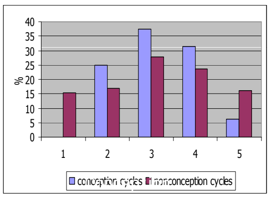
Power Doppler assessment of perifollicular vascularity in 141 unstimulated cycles

Semiquantitative analysis

1 Scarce dotted vascularity;
2 short linear segments of flow;
3 flow in less than 30% of follicular wall;
4 flow in 30-50% of follicular wall;
5 flow in more than 50% of follicular wall.

Distribution of perifollicular vascularity types in 141 natural IVF cycles with and without fertilization and conception

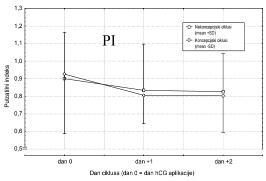


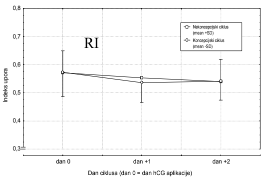


Gavric Lovrec V. et al. WMW 2003

Dinamic PI and RI in conceptied and nonconcepted 210 natural IVF cycle

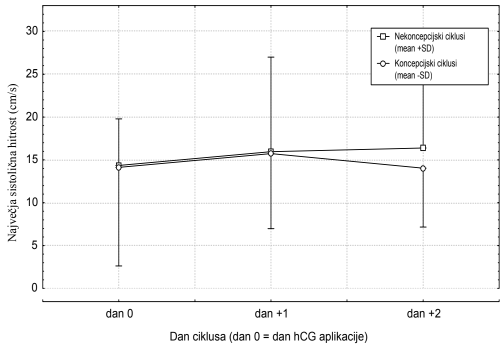
Measurements performed on day 0 (hCG administration) and day +1 and day +2



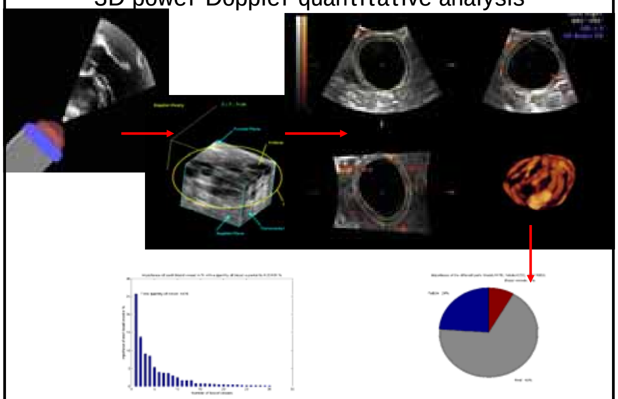


Gavric Lovrec,V.: WKW 2003

Dinamic PSV in nonstimulated cycles



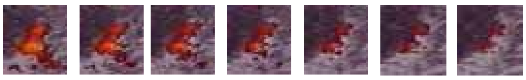
3D power Doppler quantitative analysis



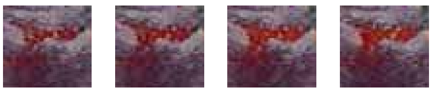
Contribution of individual blood vessels

Volume ratios: blood vessels, the follicle and the surrounding tissue

Blood vessels count



Blood vessel bifurcation: one detected region overlaps two or more regions in the subsequent frames.



Blood vessels join: two or several detected region are overlapped by one region in the subsequent images.

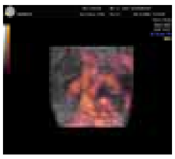
Vascular network surrounding dominant follicles in pregnant and not pregnant IVF/ICSI natural cycles on day of oocyte pick up

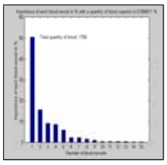
Vlaisavljevic et al, Ultrasound Obstet Gynecol 2003;22:520-6.

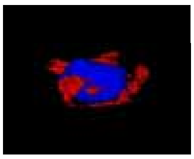
	Vascular network in 5mm capsule (%)	Pulsatility index	Resistence index	Peak systolic velocity (cm/s)	Vessel 1	Vessel 2	Vessel 3
Pregnant	**19.2 ± 16.8***	0.84±0.2	0.55 ±0.1	8.4 ±3.2	**20.6 ±10.1**	14.8 ± 7.1	10.0 ± 3.8
Not pregnant	**10.5 ±7.1**	0.82±0.2	0.51 ±0.1	12.8±7.4	**39.7 ± 19.1**	14.0 ± 5.6	9.4 ± 3.5

*boderline statistical significance (F=2.457, p=0.074)

Measurement of perifollicular blood flow of the dominant preovulatory follicle using three-dimensional power Doppler

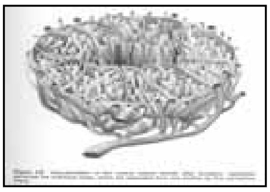






Conclusion: It can be hypotesized that the follicles containing oocytes able to produce a pregnancy have a distinctive and more uniform perifollicular vascular network.

Capillary network in CL



1. Oxigen, nutrients and hormone precursors to steroidigenic cells
2. Release of progesterone
3. Damage after OPU

Mature corpus luteum (CL): highest blood flow in any tissue in human body

Distribution of blood volume in 6 largest blood vessels in the perifollicular network pre- and 35 hours after hCG administration in 21 dominant follicles

Vlaisavljevic et al., in press

	Vascular network in 5mm capsule (%)	Vessel 1	Vessel 2	Vessel 3	Vessel 4	Vessel 5	Vessel 6
Pre hCG	**3.5 ± 3.6**	**50.5±28.1**	14.0 ±7.6	8.0 ± 4.8	5.1 ± 3.1	3.2 ± 2.5	2.2 ± 2.1
Post hCG	**7.8 ±10.1**	**29.1 14.1**	17.2 ±8.5	10.5 ±5.1	6.4 ± 2.1	5.0 ± 1.8	3.5 ± 1.7

Conclusions I

- Follicle diameter and growth dynamics are important factors for the prediction of LH surge (and/or hCG administration) in natural cycle
- The critical follicle diameter for LH surge also depends on the lengh of menstrual cycle
- Estradiol level has important role in accurate timing of hCG administration in natural cycle

Conclusions II

- Quantitative pulsed Doppler indices are not useful in recognising pregnancy quality follicles in natural cycle;
- Power Doppler assessment of perifollicular blood flow has a limited value in prediciting follicle quality;
- Follicles, associated with conception, have a high percentage of volume showing power Doppler flow signal, their vascularization is more uniform.