LE MONITORAGE DE STIMULATIONS OVARIENNES : DU PRÉSENT AU FUTUR

(3D AUTOMATISÉ, INTELLIGENCE ARTIFICIELLE, INTÉRÊT DU BILAN HORMONAL)

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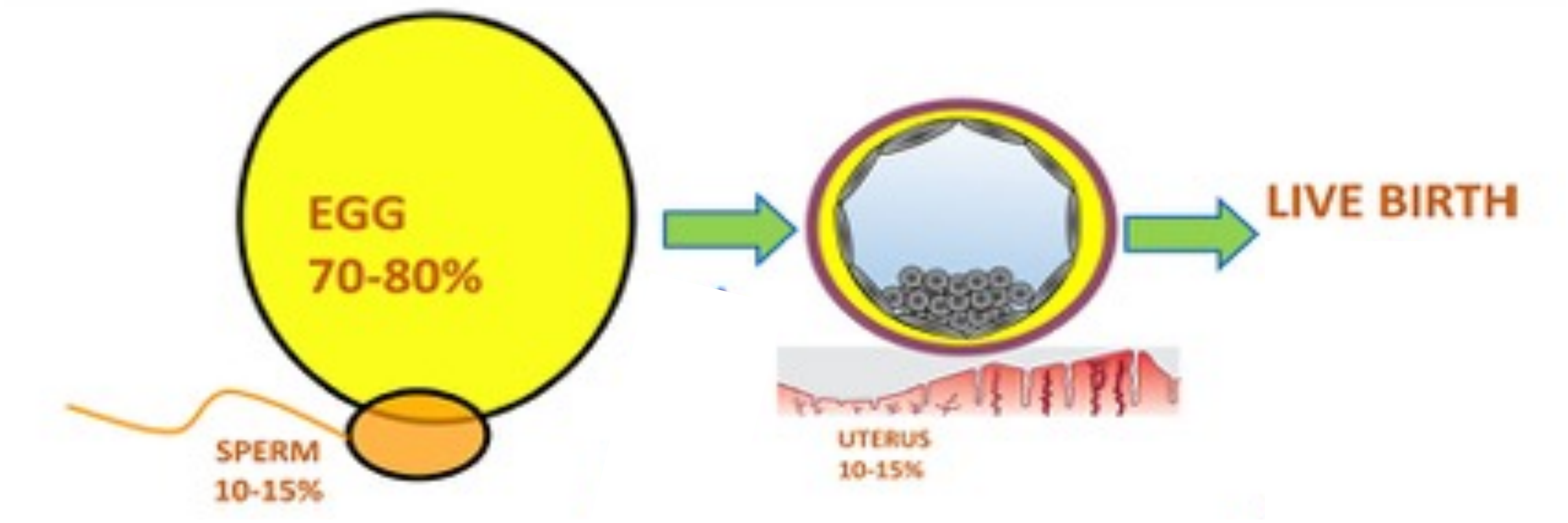
CHU LILLE

AMP Jeanne de Flandre

ufr3s faculté de médecine

Université de Lille

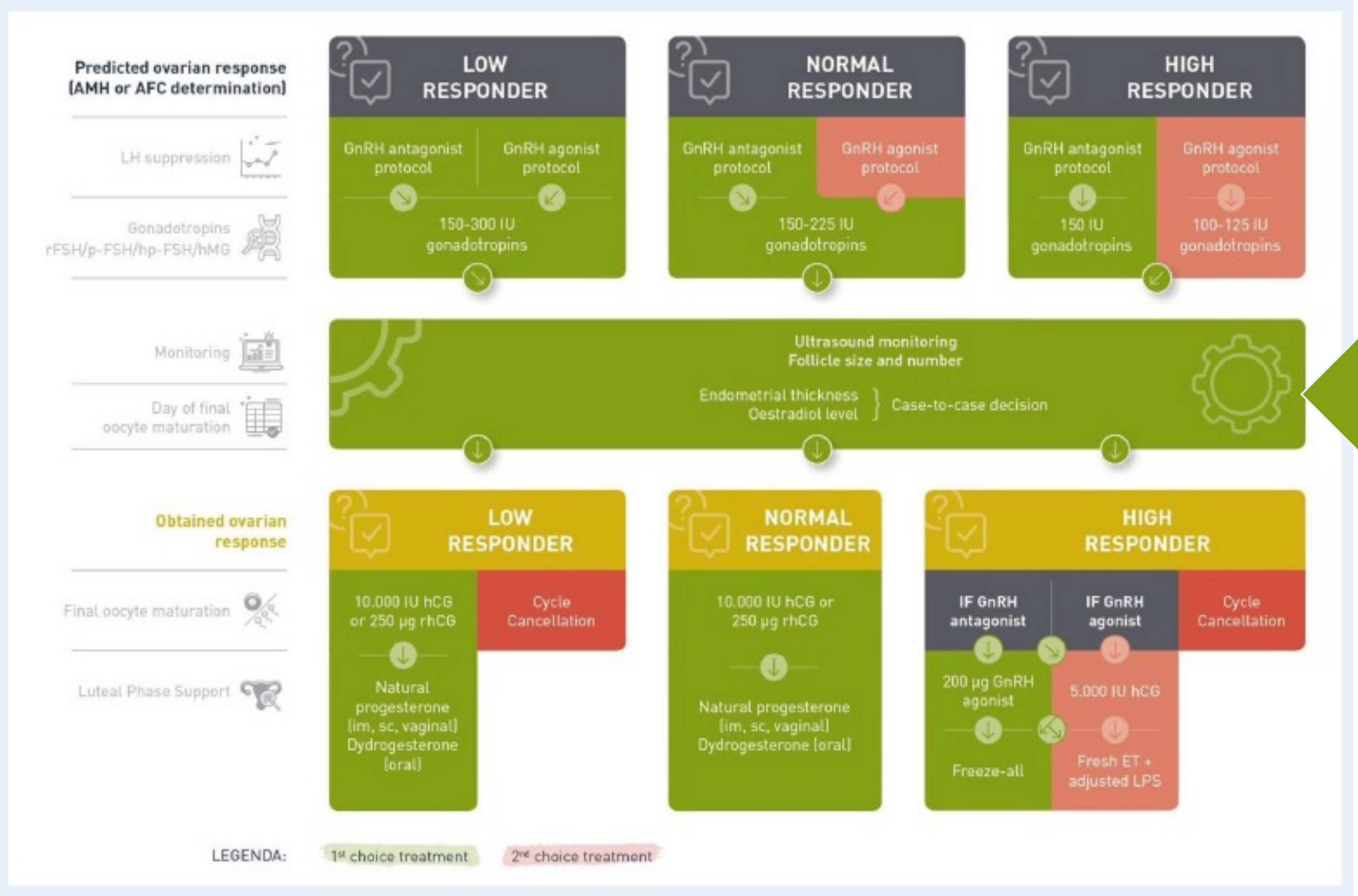
Importance relative des différents acteurs en Reproduction Humaine


EGG
70-80%
SPERM
10-15%
UTERUS
10-15%
LIVE BIRTH

Sakkas et al. Hum Reprod Update 2015

Human Reproduction Open, pp. 1–13, 2020
doi:10.1093/hropen/hoaa009

The ESHRE Guideline Group on Ovarian Stimulation *et al.*


Predicted ovarian response (AMH or AFC determination)
LH suppression
Gonadotropins rFSH/p-FSH/hp-FSH/hMG
Monitoring
Day of final oocyte maturation
Obtained ovarian response
Final oocyte maturation
Luteal Phase Support
LOW RESPONDER
GnRH antagonist protocol
GnRH agonist protocol
150-300 IU gonadotropins
NORMAL RESPONDER
GnRH antagonist protocol
GnRH agonist protocol
150-225 IU gonadotropins
HIGH RESPONDER
GnRH antagonist protocol
GnRH agonist protocol
150 IU gonadotropins
100-125 IU gonadotropins
Ultrasound monitoring
Follicle size and number
Endometrial thickness
Oestradiol level
Case-to-case decision
LOW RESPONDER
10.000 IU hCG or 250 µg rhCG
Cycle Cancellation
Natural progesterone (im, sc, vaginal) Dydrogesterone (oral)
NORMAL RESPONDER
10.000 IU hCG or 250 µg rhCG
Natural progesterone (im, sc, vaginal) Dydrogesterone (oral)
HIGH RESPONDER
IF GnRH antagonist
IF GnRH agonist
Cycle Cancellation
200 µg GnRH agonist
5.000 IU hCG
Freeze-all
Fresh ET + adjusted LPS
LEGENDA:
1st choice treatment
2nd choice treatment

La réunion de décision ou staff quotidien AMP

- Flux de patientes
- Nombre de POV, IIU, DEC/TEC réalisables/jour
- Intégrer des critères hormonaux et échographiques
- Critères de déclenchement

- Freeze-all ou « TEF » ?
- Informatisation en temps réel des tentatives
    - *Dilemme de la fiche de stim « papier »*
- Enseignement / formation
- Sérologies, RT-PCR Covid, Cs anesth & co…

Le minimum « syndical » d'un monitorage de l'ovulation

- Echographie endovaginale +++

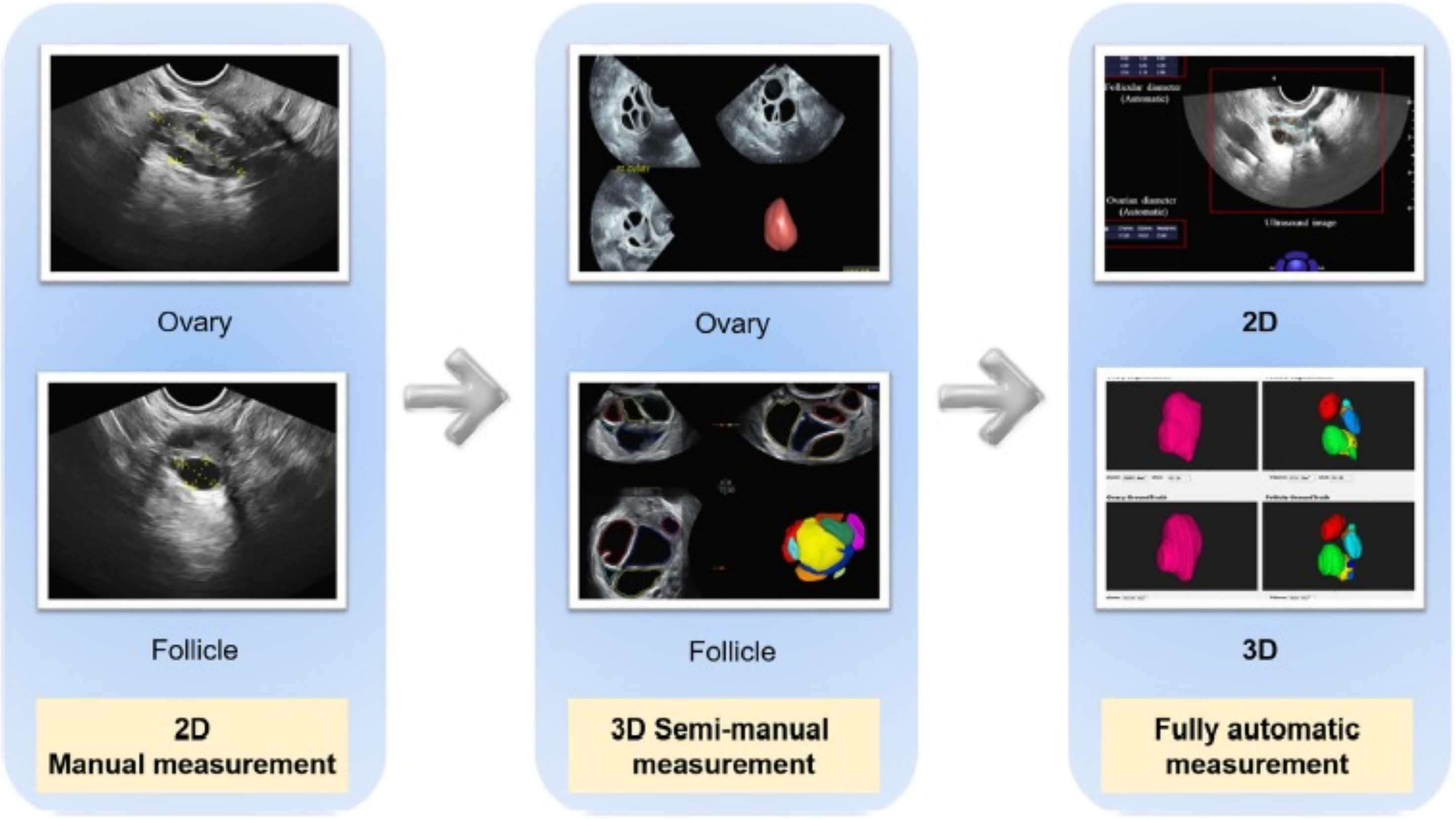
➢**La mesure du diamètre du (ou des) follicule(s) en croissance**

➢**La mesure de l'épaisseur endométriale**

(au minimum au moment du déclenchement)

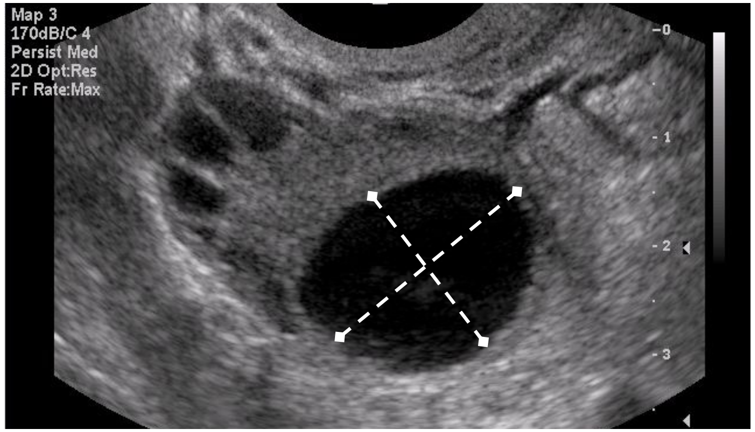
  - **Indiquer aspect de l'endomètre si besoin**

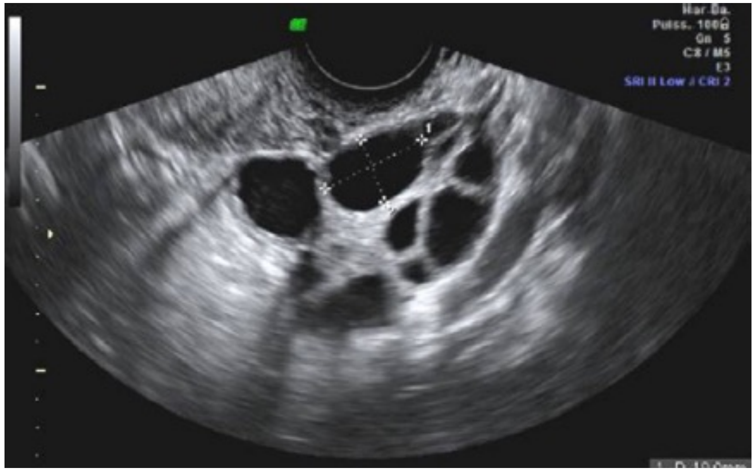
Les évolutions techniques…


Ovary
Follicle
2D
Manual measurement
Ovary
Follicle
3D Semi-manual
measurement
2D
3D
Fully automatic
measurement

Chen et al. J Ultrasound Med 2021

Estimation de la croissance folliculaire





Photos issues de Lamazou et Levaillant. Imagerie de la femme 2011

- Le diamètre moyen :
  - ✓ *moyenne des diamètres orthogonaux sur le plus grand plan du follicule.*
- Hors FIV : 1 ou 2 follicules dominants de structure sphérique
- Cas particulier de la FIV :
  - ✓ *pressions exercées par follicules en croissance adjacents ➔ perte de la structure sphérique des follicule➔ struct. complexes 3D.*
  - ✓ *Analyse soigneuse et individuelle de chaque follicule pour trouver le plus grand plan de chacun d'entre-eux.*

La maturité folliculaire

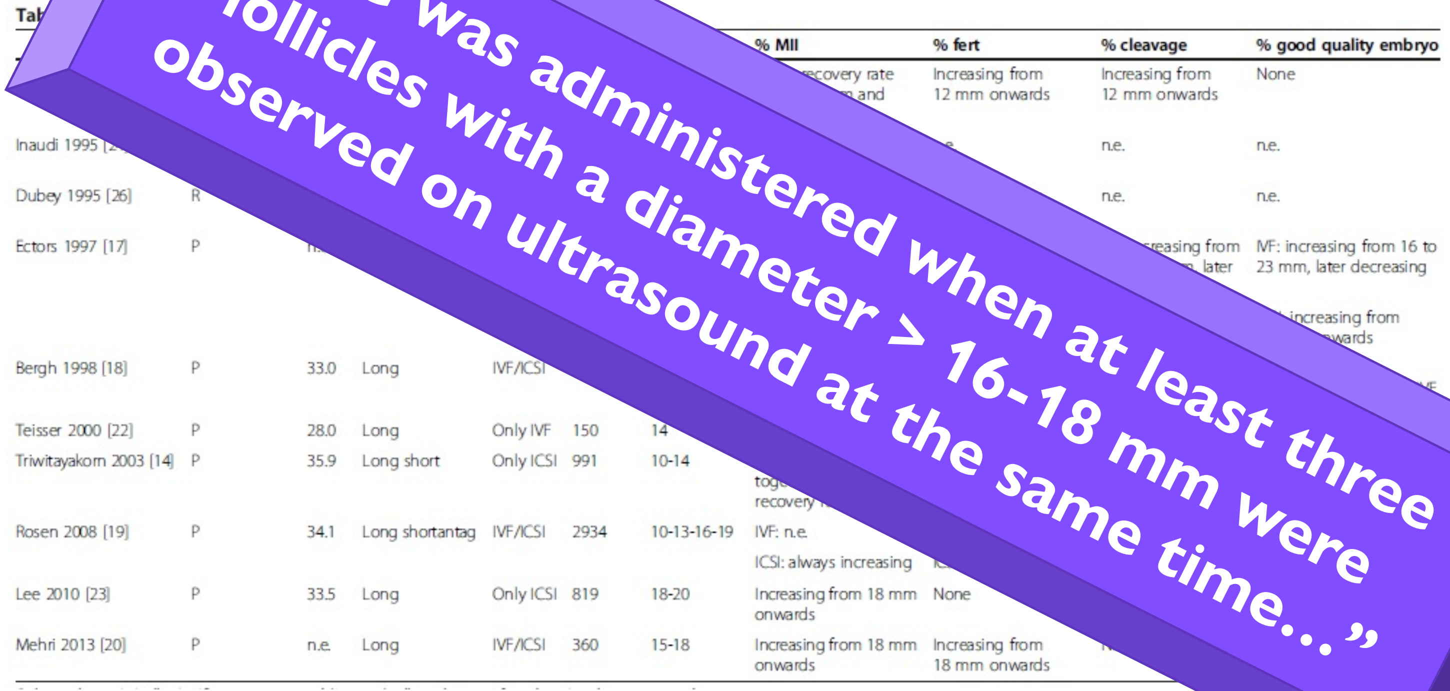
Revelli *et al. Reproductive Biology and Endocrinology* 2014, **12**:107
http://www.rbej.com/content/12/1/107

REPRODUCTIVE BIOLOGY AND ENDOCRINOLOGY

REVIEW **Open Access**

A critical review of bi-dimensional and three-dimensional ultrasound techniques to monitor follicle growth: do they help improving IVF outcome?

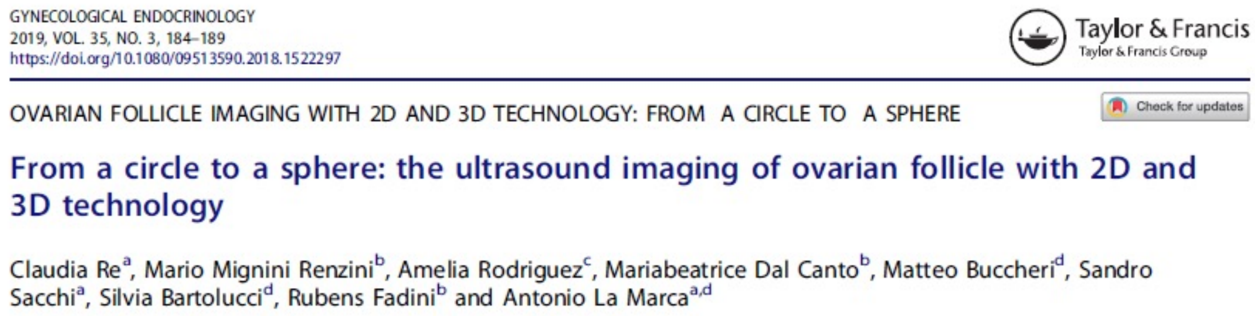
Alberto Revelli[1,2*], Giorgia Martiny[1], Luisa Delle Piane[2], Chiara Benedetto[1], Paolo Rinaudo[3] and Ilan Tur-Kaspa[4]



							% MII	% fert	% cleavage	% good quality embryo
								Increasing from 12 mm onwards	Increasing from 12 mm onwards	None
Inaudi 1995									n.e.	n.e.
Dubey 1995 [26]	R								n.e.	n.e.
Ectors 1997 [17]	P									IVF: increasing from 16 to 23 mm, later decreasing
Bergh 1998 [18]	P	33.0	Long	IVF/ICSI						
Teisser 2000 [22]	P	28.0	Long	Only IVF	150	14				
Triwitayakorn 2003 [14]	P	35.9	Long short	Only ICSI	991	10-14				
Rosen 2008 [19]	P	34.1	Long shortantag	IVF/ICSI	2934	10-13-16-19	IVF: n.e. ICSI: always increasing			
Lee 2010 [23]	P	33.5	Long	Only ICSI	819	18-20	Increasing from 18 mm onwards	None		
Mehri 2013 [20]	P	n.e.	Long	IVF/ICSI	360	15-18	Increasing from 18 mm onwards	Increasing from 18 mm onwards		

"hCG was administered when at least three follicles with a diameter > 16-18 mm were observed on ultrasound at the same time…"

Conclusions: The study of follicular size by 2D-US is of limited usefulness in helping in the identifica es containing the best oocytes and in choosing the best moment to trigger ovulation. Possibly the value of US in this area improved by large prospective studies in which automated 3D-US will be used.


GYNECOLOGICAL ENDOCRINOLOGY
2019, VOL. 35, NO. 3, 184–189
https://doi.org/10.1080/09513590.2018.1522297

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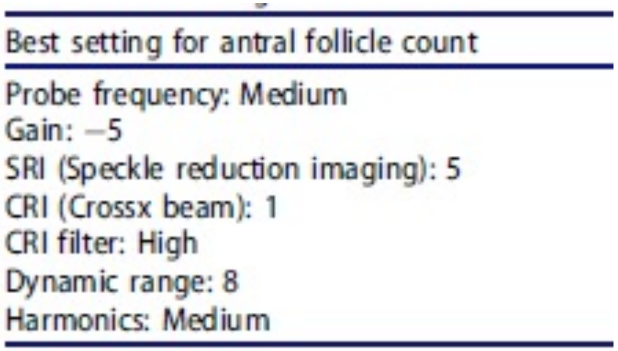
OVARIAN FOLLICLE IMAGING WITH 2D AND 3D TECHNOLOGY: FROM A CIRCLE TO A SPHERE

From a circle to a sphere: the ultrasound imaging of ovarian follicle with 2D and 3D technology

Claudia Re[a], Mario Mignini Renzini[b], Amelia Rodriguez[c], Mariabeatrice Dal Canto[b], Matteo Buccheri[d], Sandro Sacchi[a], Silvia Bartolucci[d], Rubens Fadini[b] and Antonio La Marca[a,d]


Best setting for antral follicle count

Probe frequency: Medium
Gain: –5
SRI (Speckle reduction imaging): 5
CRI (Crossx beam): 1
CRI filter: High
Dynamic range: 8
Harmonics: Medium

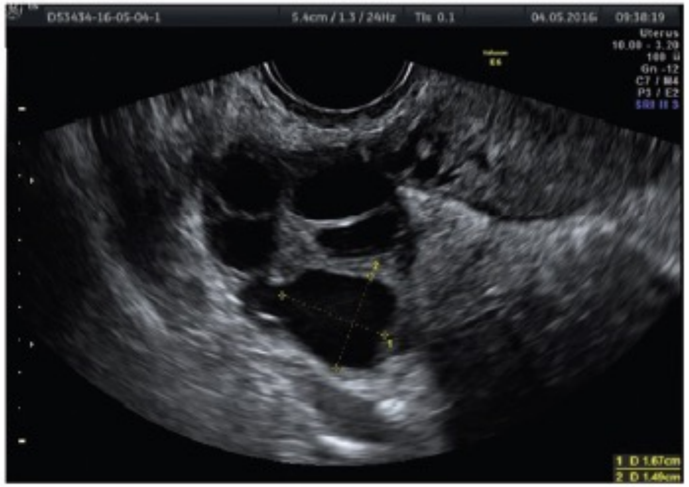

D53434-16-05-04-1
5.4cm / 1.3 / 24Hz
TIs 0.1
04.05.2016
09:38:19
1 D 1.67cm
2 D 1.49cm

Figure 2. Ovarian follicles have frequently an irregular shape and more than one diameter should be measured to calculate the mean dimension.

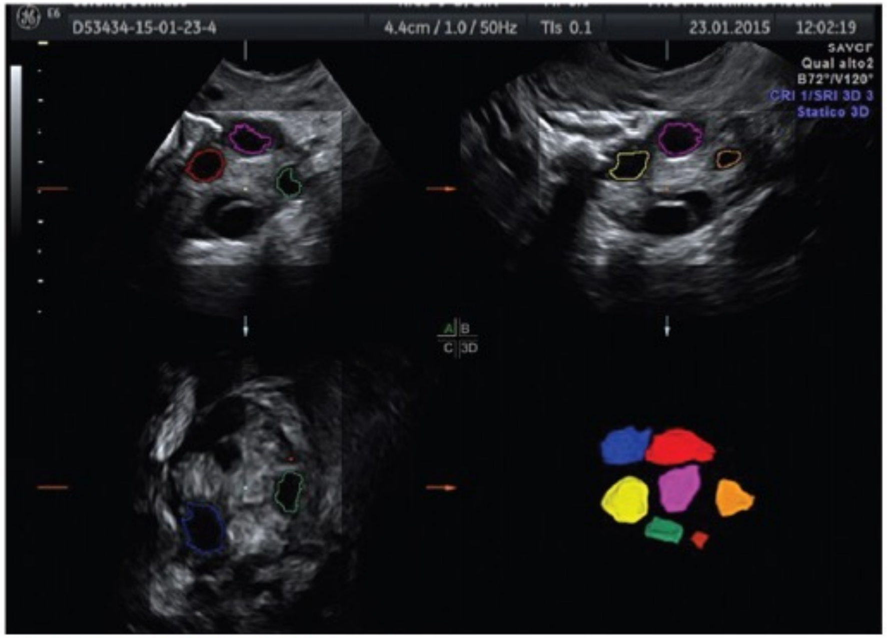
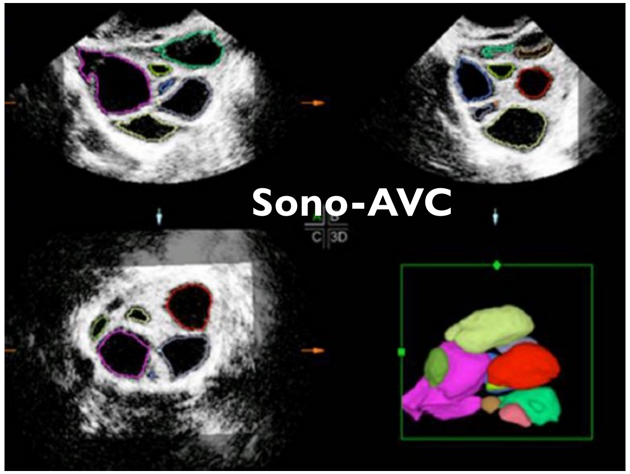
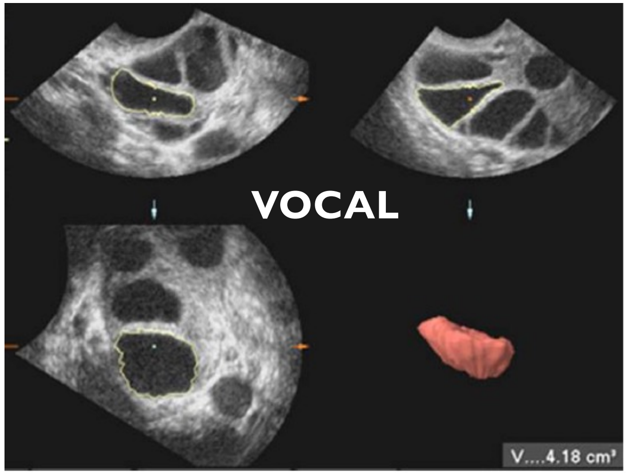

D53434-15-01-23-4
4.4cm / 1.0 / 50Hz
TIs 0.1
23.01.2015
12:02:19
SAVCr
Qual alto2
B72°/V120°
CRI 1/SRI 3D 3
Statico 3D
A B
C 3D

Figure 3. The follicular measurement using sonoAVC, mulitplanar view.

Monitorage automatisé 3D: quel apport?





- Acquisition rapide par balayage du « volume » ovarien

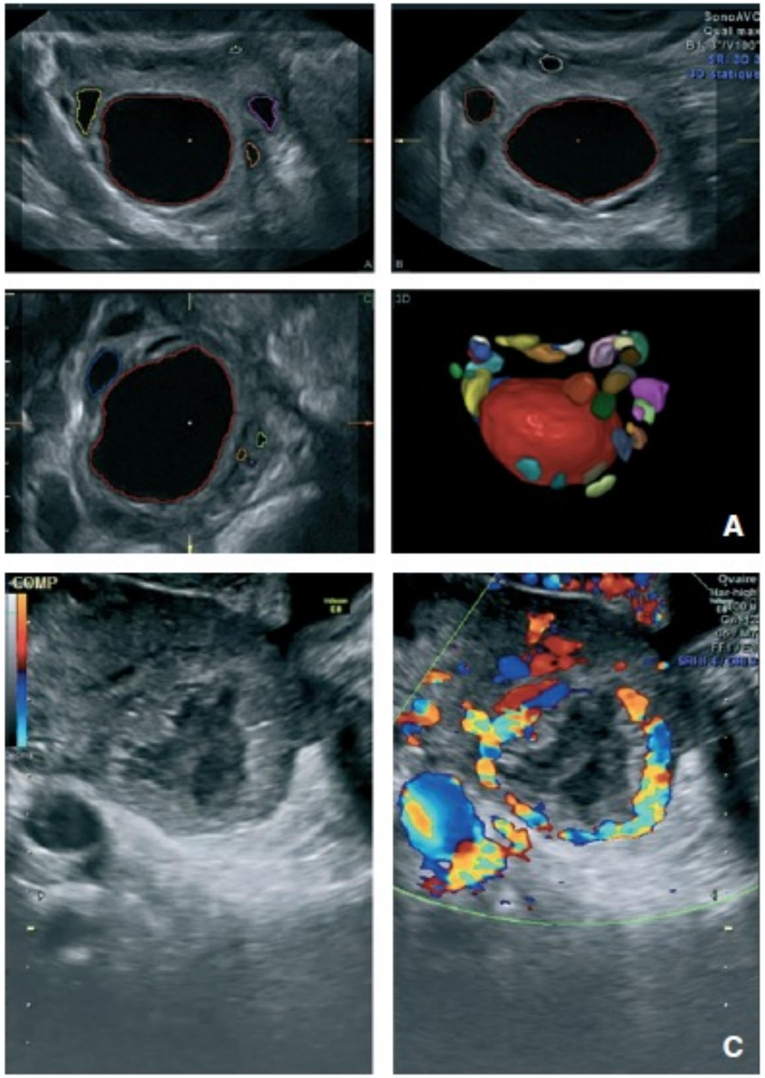
- En théorie :
  - ✓ *Evaluation du diamètre moyen de tous les follicules*
  - ✓ *Evaluation des volumes de chacun des follicules*
  - ➔ **Plus de précision et de reproductibilité pour apprécier la maturité folliculaire?**

- En pratique :
  - ✓ *le mode Sono-AVC est applicable sans retouche chez 60%-70% des patientes…*
  - ✓ *dans au moins 30-40% des cas : travail de l'image 3D après l'examen… parfois long et fastidieux…*

- Les problèmes techniques persistants : ovaires volumineux, ovaires « lointains »…

Photos issues de Lamazou et Lavaillant. Imagerie de la femme 2011

Monitorage hors-FIV



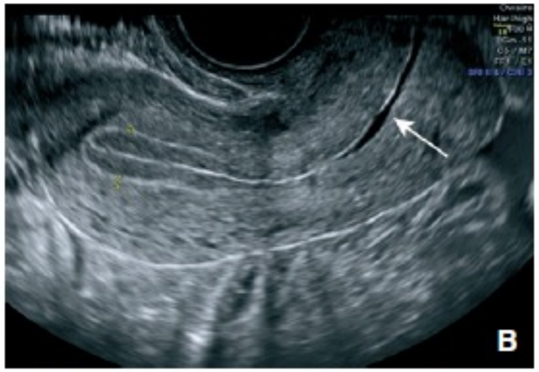


Figure 43. Monitorage périovulatoire en induction monofolliculaire.
A. Échographie 3D en mode *Sonography-based automatic volume calculation* (SonoAVC$^{\text{TM}}$) : ovaires micropolykystiques sous clomifène j13 : follicule pré-ovulatoire unique de 23 mm (en rouge) associé à de nombreux microfollicules inférieurs à 10 mm.
B. Endomètre préovulatoire en « cible » (11 mm) et glaire cervicale bien visible (flèche).
C. Doppler : corps jaune postovulatoire triangulaire avec couronne vasculaire typique.

Toute référence à cet article doit porter la mention : Ardaens Y, Robin G. Imagerie de l'hypofertilité de la femme. EMC - Radiologie et imagerie médicale - génito-urinaire - gynéco-obstétricale - mammaire 2018;13(4):1-23 [Article 34-620-E-10].

Monitorage de la croissance folliculaire en FIV

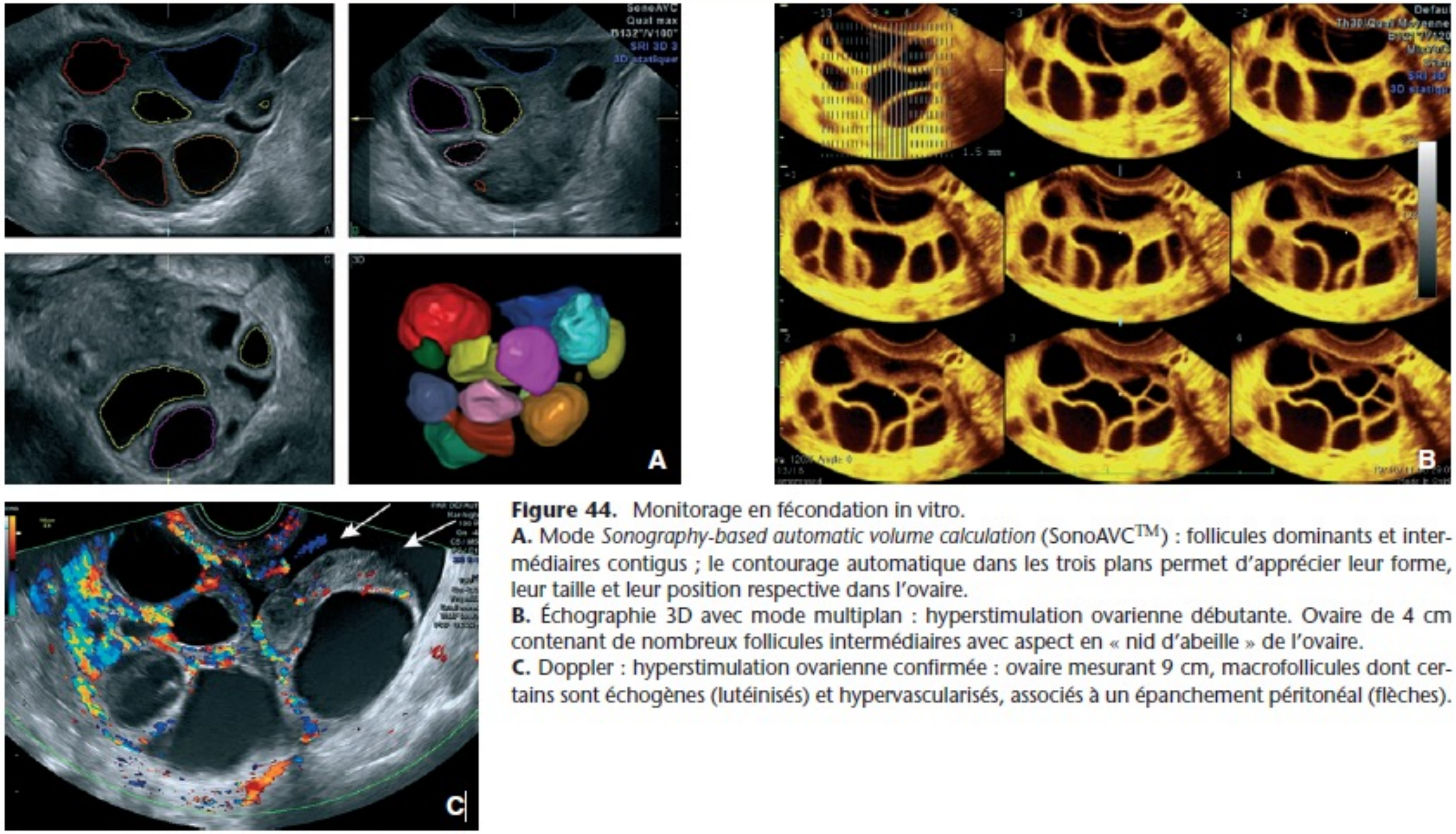
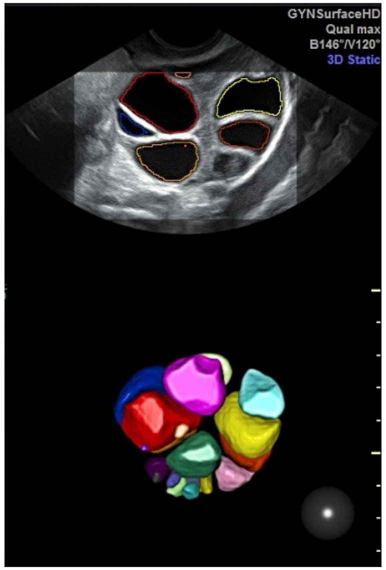


Figure 44. Monitorage en fécondation in vitro.
A. Mode *Sonography-based automatic volume calculation* (SonoAVC^{TM}) : follicules dominants et intermédiaires contigus ; le contourage automatique dans les trois plans permet d'apprécier leur forme, leur taille et leur position respective dans l'ovaire.
B. Échographie 3D avec mode multiplan : hyperstimulation ovarienne débutante. Ovaire de 4 cm contenant de nombreux follicules intermédiaires avec aspect en « nid d'abeille » de l'ovaire.
C. Doppler : hyperstimulation ovarienne confirmée : ovaire mesurant 9 cm, macrofollicules dont certains sont échogènes (lutéinisés) et hypervascularisés, associés à un épanchement péritonéal (flèches).



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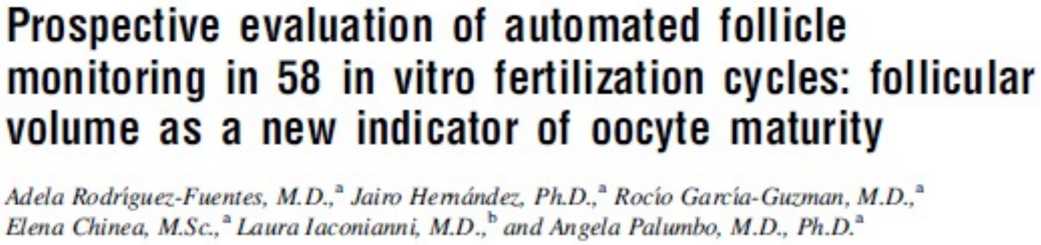
Et si on parlait de « volume folliculaire »?



Prospective evaluation of automated follicle monitoring in 58 in vitro fertilization cycles: follicular volume as a new indicator of oocyte maturity

Adela Rodríguez-Fuentes, M.D.,[a] Jairo Hernández, Ph.D.,[a] Rocío García-Guzman, M.D.,[a] Elena Chinea, M.Sc.,[a] Laura Iaconianni, M.D.,[b] and Angela Palumbo, M.D., Ph.D.[a]

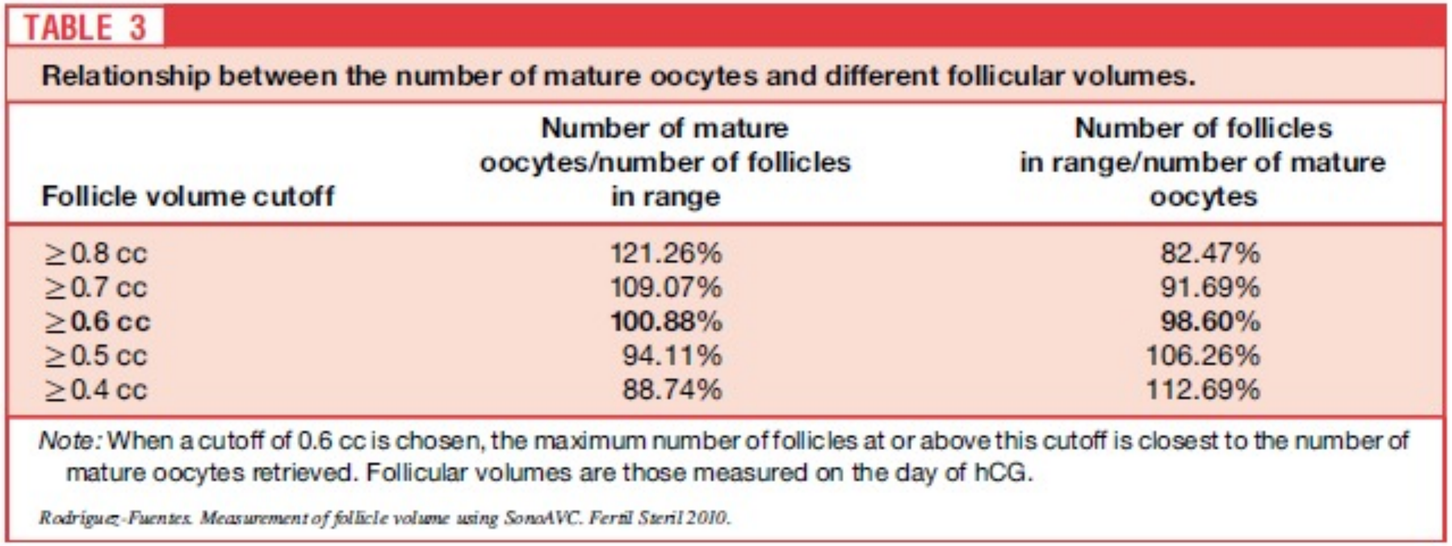


TABLE 3

Relationship between the number of mature oocytes and different follicular volumes.

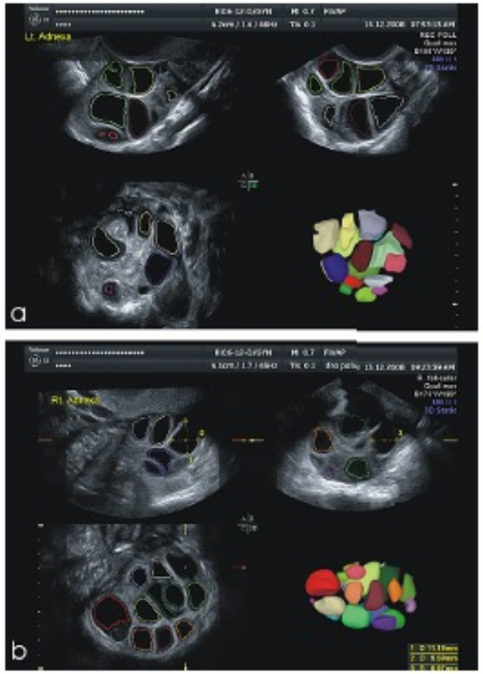
Follicle volume cutoff	Number of mature oocytes/number of follicles in range	Number of follicles in range/number of mature oocytes
≥0.8 cc	121.26%	82.47%
≥0.7 cc	109.07%	91.69%
≥0.6 cc	**100.88%**	**98.60%**
≥0.5 cc	94.11%	106.26%
≥0.4 cc	88.74%	112.69%

Note: When a cutoff of 0.6 cc is chosen, the maximum number of follicles at or above this cutoff is closest to the number of mature oocytes retrieved. Follicular volumes are those measured on the day of hCG.

Rodriguez-Fuentes. Measurement of follicle volume using SonoAVC. Fertil Steril 2010.

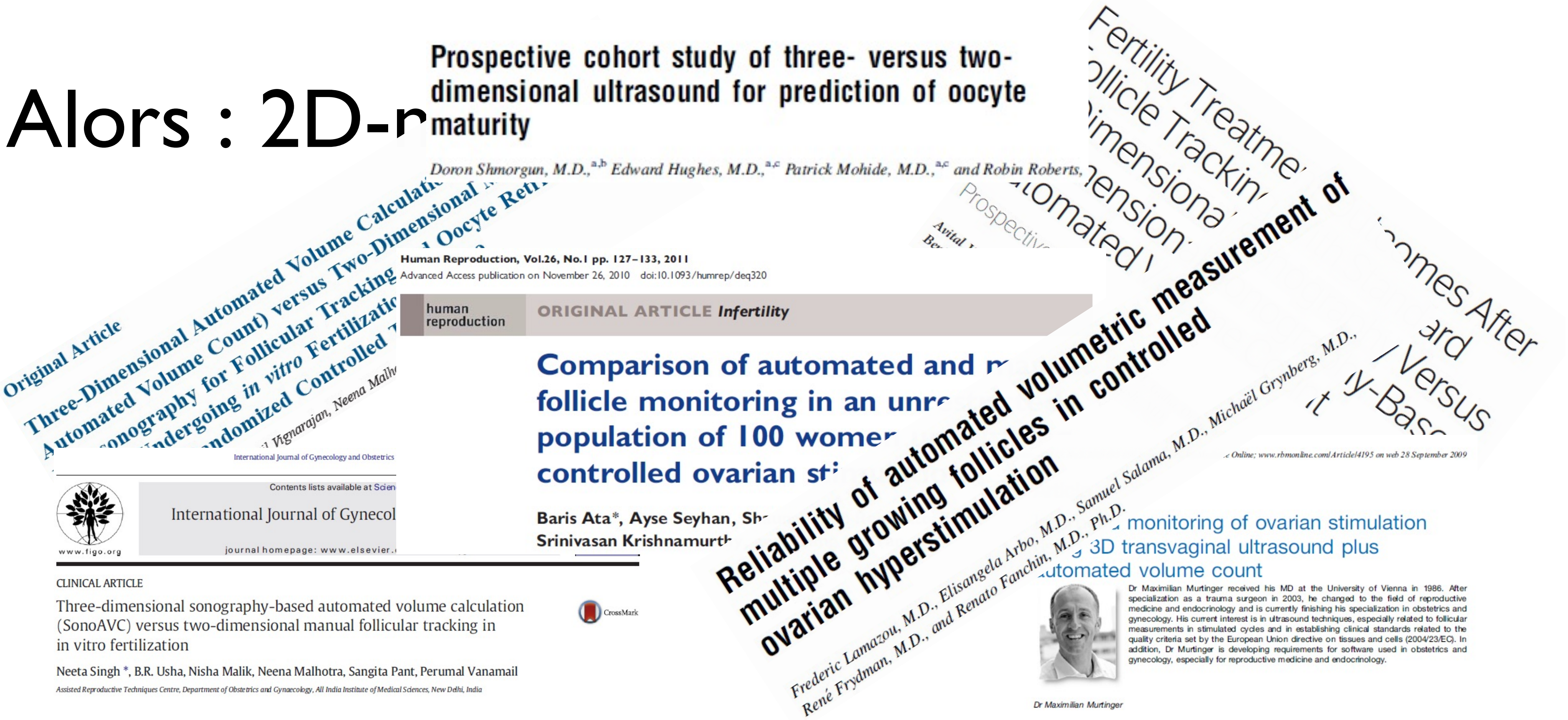
FIGURE 1

(**a**) Example of a patient with good quality of image. All follicles were picked up automatically and no postprocessing work was necessary. (**b**) Example of a patient with poor quality of image: note that one follicle needed manual measurement.



Rodriguez-Fuentes. Measurement of follicle volume using SonoAVC. Fertil Steril 2010.

Alors : 2D-r



Prospective cohort study of three- versus two-dimensional ultrasound for prediction of oocyte maturity

Doron Shmorgun, M.D.,[a,b] Edward Hughes, M.D.,[a,c] Patrick Mohide, M.D.,[a,c] and Robin Roberts,

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Original Article

Three-Dimensional Automated Volume Calculatio
Automated Volume Count) versus Two-Dimensional
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Vignarajan, Neena Malh

Human Reproduction, Vol.26, No.1 pp. 127–133, 2011
Advanced Access publication on November 26, 2010 doi:10.1093/humrep/deq320

human reproduction **ORIGINAL ARTICLE** ***Infertility***

Comparison of automated and m
follicle monitoring in an unre
population of 100 women
controlled ovarian sti

Baris Ata*, Ayse Seyhan, Sh
Srinivasan Krishnamurth

Reliability of automated volumetric measurement of multiple growing follicles in controlled ovarian hyperstimulation

Frederic Lamazou, M.D., Elisangela Arbo, M.D., Samuel Salama, M.D., Michaël Grynberg, M.D., René Frydman, M.D., and Renato Fanchin, M.D., Ph.D.

e Online; www.rbmonline.com/Article/4195 on web 28 September 2009

monitoring of ovarian stimulation
3D transvaginal ultrasound plus
utomated volume count

Dr Maximilian Murtinger received his MD at the University of Vienna in 1986. After specialization as a trauma surgeon in 2003, he changed to the field of reproductive medicine and endocrinology and is currently finishing his specialization in obstetrics and gynecology. His current interest is in ultrasound techniques, especially related to follicular measurements in stimulated cycles and in establishing clinical standards related to the quality criteria set by the European Union directive on tissues and cells (2004/23/EC). In addition, Dr Murtinger is developing requirements for software used in obstetrics and gynecology, especially for reproductive medicine and endocrinology.

Dr Maximilian Murtinger

International Journal of Gynecology and Obstetrics

Contents lists available at Scien

International Journal of Gynecol

www.figo.org journal homepage: www.elsevier.

CLINICAL ARTICLE

Three-dimensional sonography-based automated volume calculation (SonoAVC) versus two-dimensional manual follicular tracking in in vitro fertilization

Neeta Singh *, B.R. Usha, Nisha Malik, Neena Malhotra, Sangita Pant, Perumal Vanamail

Assisted Reproductive Techniques Centre, Department of Obstetrics and Gynaecology, All India Institute of Medical Sciences, New Delhi, India

CrossMark

➔ Automated Sono-AVC ultrasound can be used interchangeably with manual 2D USG for follicle tracking during COS giving comparable ART outcomes with the added advantage of saving time.

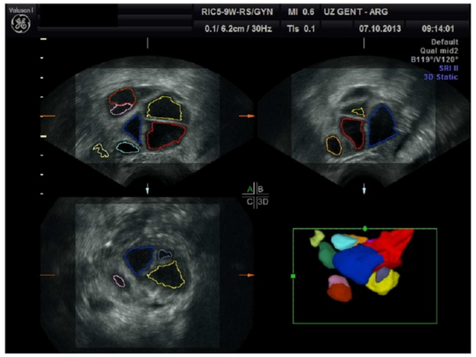
frontiers in
SURGERY

REVIEW ARTICLE
published: 28 May 2014
doi: 10.3389/fsurg.2014.00018

The value of automated follicle volume measurements in IVF/ICSI

*Frank Vandekerckhove**†*, Victoria Bracke*† *and Petra De Sutter*

Centre for Reproductive Medicine, University Hospital Ghent, Ghent, Belgium



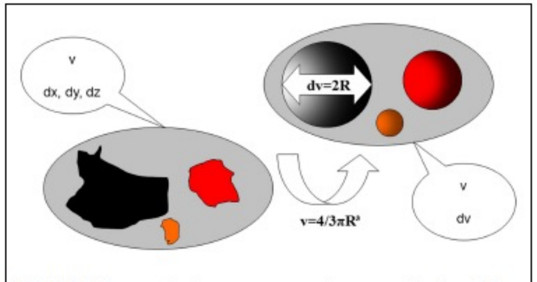
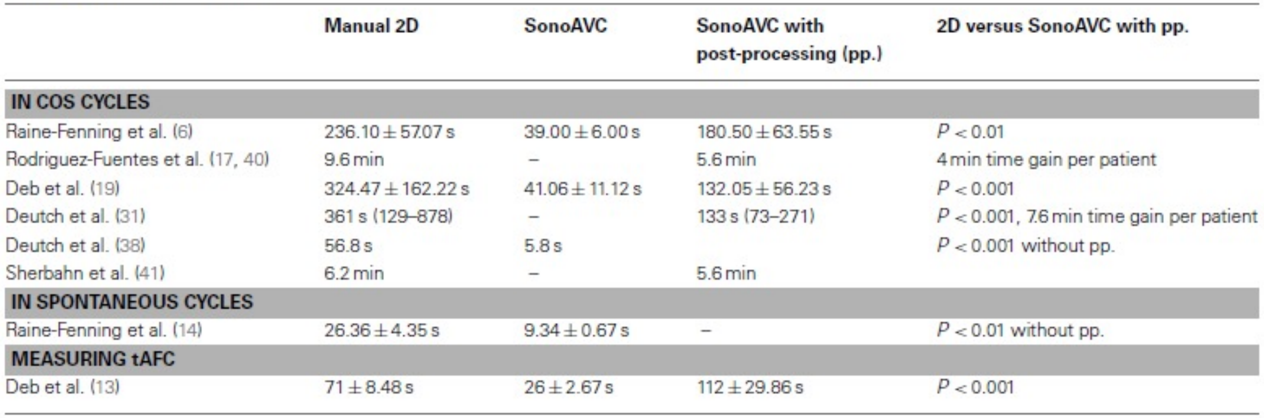


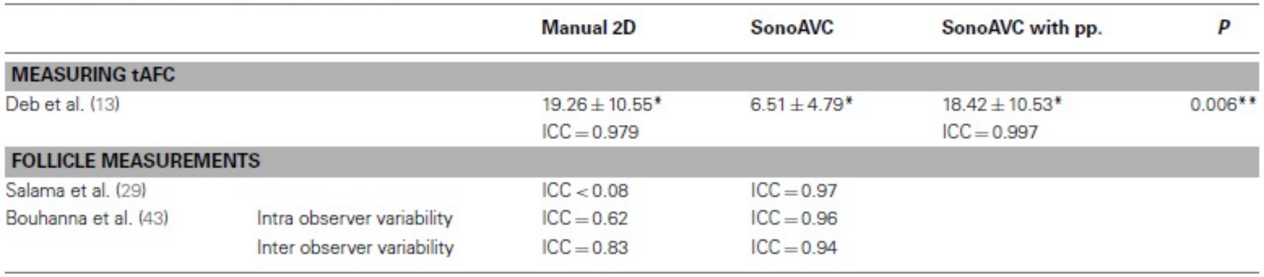
FIGURE 2 | The use of volume measurements compared to classical two-dimensional diameters of follicles. *v*, follicular volume; *dx*, *dy*, *dz*, follicular diameters in three planes; *R*, follicular radius (diameter/2); *dv*, reconstructed follicular diameter.

Table 2 | Evaluation of work flow.



	Manual 2D	SonoAVC	SonoAVC with post-processing (pp.)	2D versus SonoAVC with pp.
IN COS CYCLES				
Raine-Fenning et al. (6)	236.10 ± 57.07 s	39.00 ± 6.00 s	180.50 ± 63.55 s	$P < 0.01$
Rodriguez-Fuentes et al. (17, 40)	9.6 min	–	5.6 min	4 min time gain per patient
Deb et al. (19)	324.47 ± 162.22 s	41.06 ± 11.12 s	132.05 ± 56.23 s	$P < 0.001$
Deutch et al. (31)	361 s (129–878)	–	133 s (73–271)	$P < 0.001$, 7.6 min time gain per patient
Deutch et al. (38)	56.8 s	5.8 s		$P < 0.001$ without pp.
Sherbahn et al. (41)	6.2 min	–	5.6 min	
IN SPONTANEOUS CYCLES				
Raine-Fenning et al. (14)	26.36 ± 4.35 s	9.34 ± 0.67 s	–	$P < 0.01$ without pp.
MEASURING tAFC				
Deb et al. (13)	71 ± 8.48 s	26 ± 2.67 s	112 ± 29.86 s	$P < 0.001$

Table 3 | Investigation of operator independence.

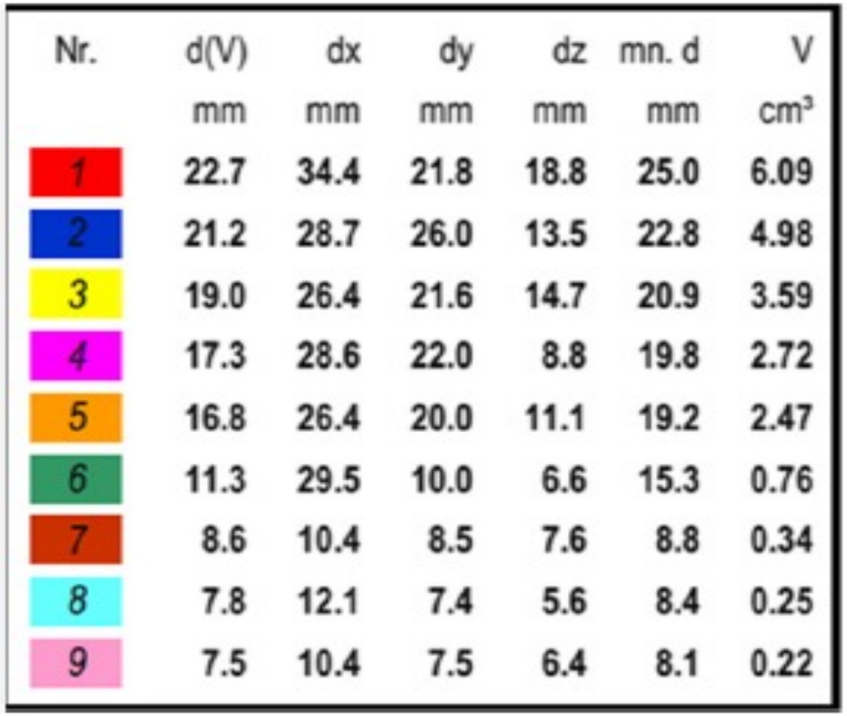


		Manual 2D	SonoAVC	SonoAVC with pp.	*P*
MEASURING tAFC					
Deb et al. (13)		19.26 ± 10.55* ICC = 0.979	6.51 ± 4.79*	18.42 ± 10.53* ICC = 0.997	0.006**
FOLLICLE MEASUREMENTS					
Salama et al. (29)		ICC < 0.08	ICC = 0.97		
Bouhanna et al. (43)	Intra observer variability	ICC = 0.62	ICC = 0.96		
	Inter observer variability	ICC = 0.83	ICC = 0.94		

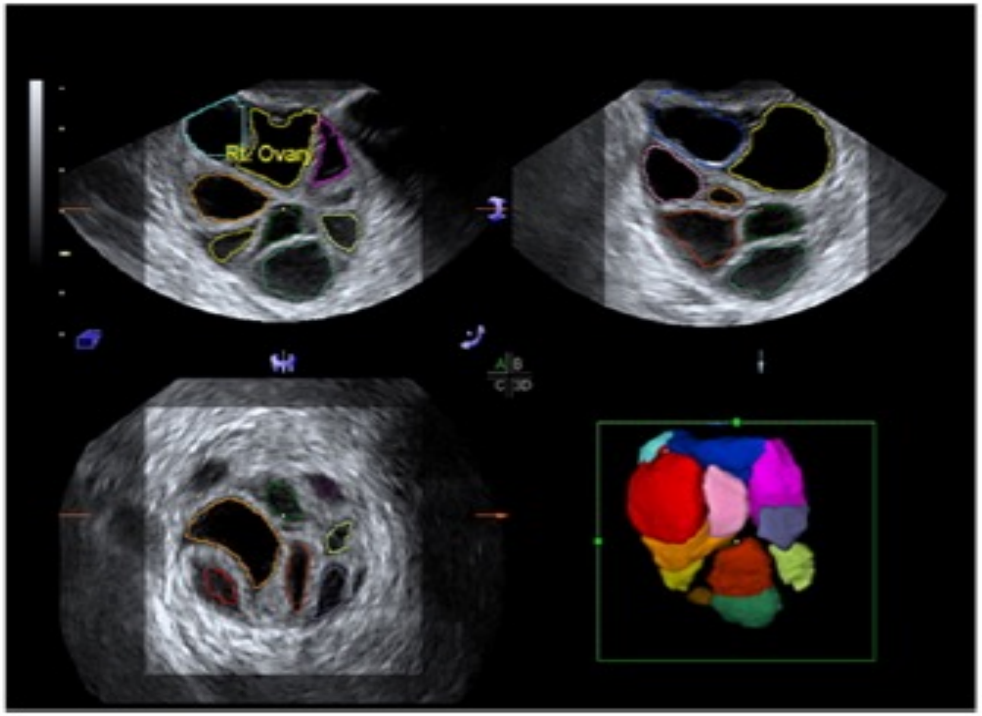
*ICC, intra class correlation coefficient; *Mean ± SD; **Comparison of manual 2D and SonoAVC with pp.*

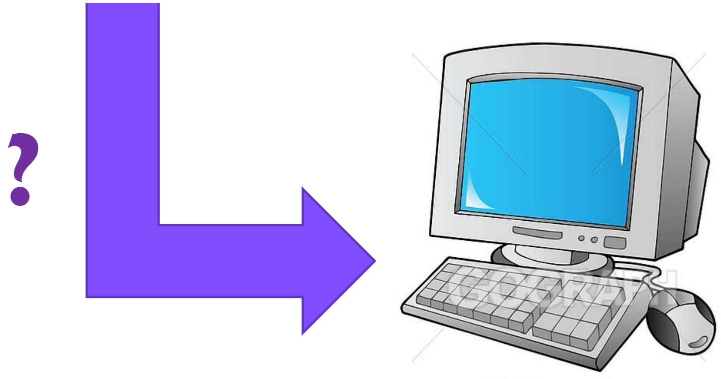
Conclusion: ***This overview of previously published literature shows how Sono-AVC offers advantages for clinical practice, without losing any accuracy or reliability. Doctors should be motivated to the general use of follicular volumes instead of follicular diameters.***

N. Singh et al. / International Journal of Gynecology and Obstetrics 131 (2015) 166–169



Nr.	d(V) mm	dx mm	dy mm	dz mm	mn. d mm	V cm^3
1	22.7	34.4	21.8	18.8	25.0	6.09
2	21.2	28.7	26.0	13.5	22.8	4.98
3	19.0	26.4	21.6	14.7	20.9	3.59
4	17.3	28.6	22.0	8.8	19.8	2.72
5	16.8	26.4	20.0	11.1	19.2	2.47
6	11.3	29.5	10.0	6.6	15.3	0.76
7	8.6	10.4	8.5	7.6	8.8	0.34
8	7.8	12.1	7.4	5.6	8.4	0.25
9	7.5	10.4	7.5	6.4	8.1	0.22



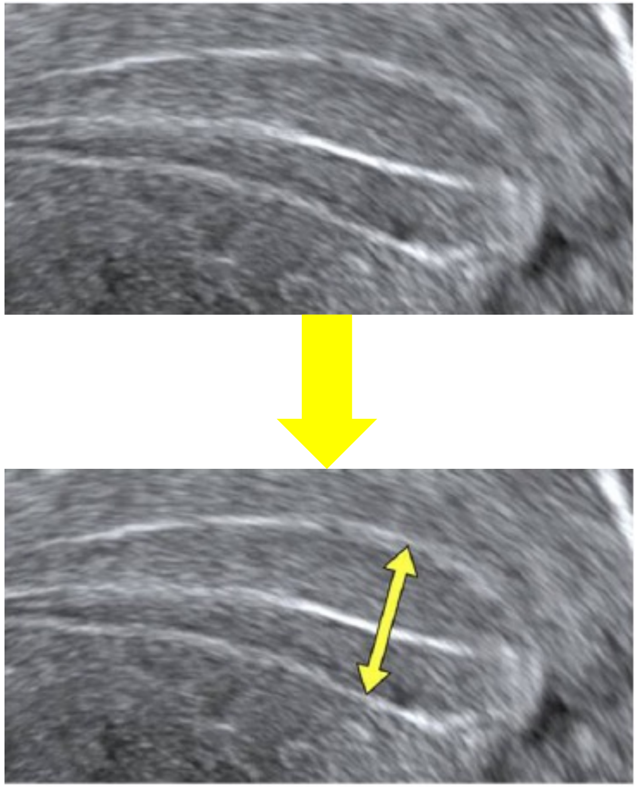


→ Logiciel AMP du centre → ABM

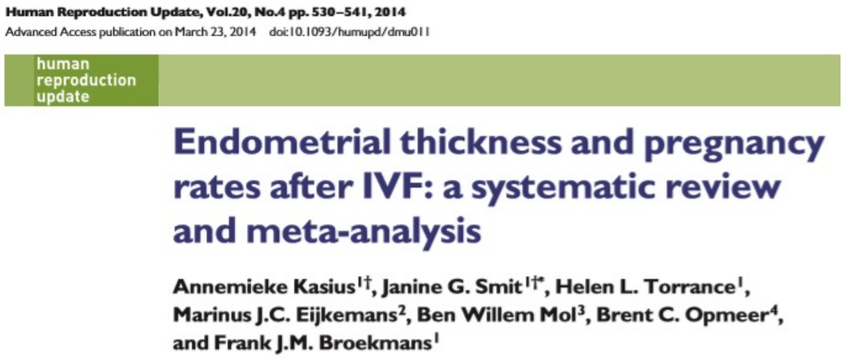
(JFIV© ou MEDIFIRST©)

Le monitorage de la croissance endométriale : la mesure de l’épaisseur endomètriale

- Elle doit se faire au niveau du fond utérin (zone « en grain de café »).
- Noter l’aspect : « 3F », échogénicité…
- La mesure se fait de la jonction endomètre—myomètre antérieur jusqu’à cette même jonction postérieure **perpendiculairement** à l’axe de la cavité utérine.



Photos issues de Lamazou et Lavaillant. Imagerie de la femme 2011



Human Reproduction Update, Vol.20, No.4 pp. 530–541, 2014
Advanced Access publication on March 23, 2014 doi:10.1093/humupd/dmu011

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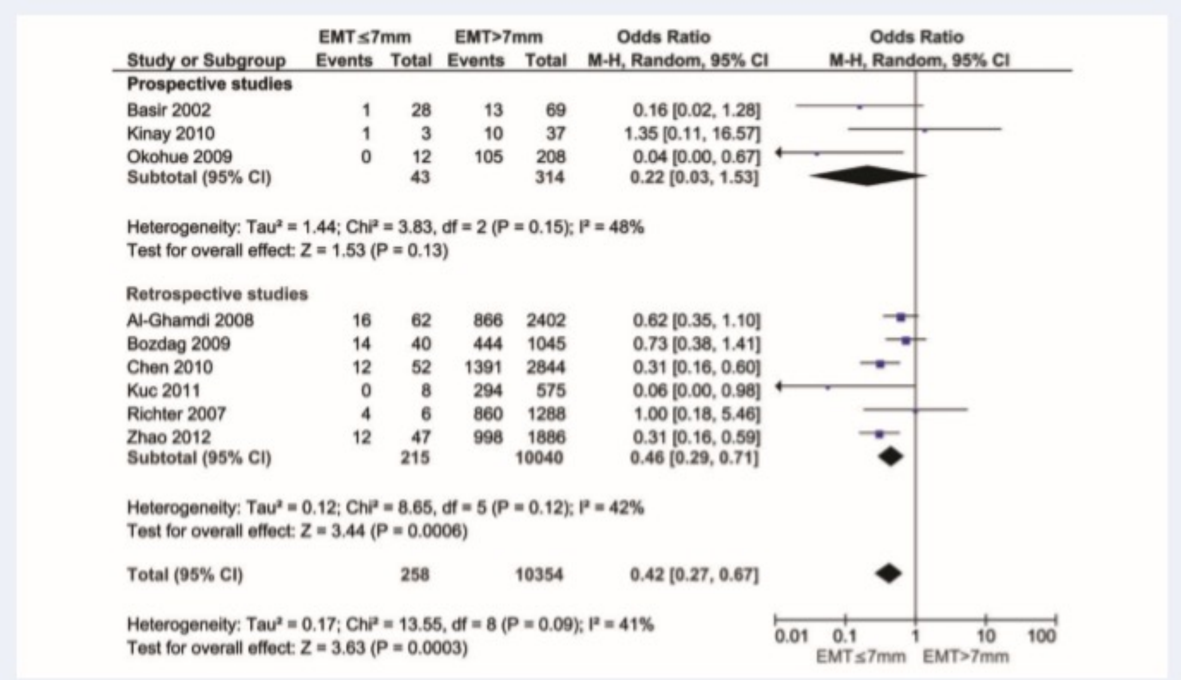
Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis

Annemieke Kasius[1†], Janine G. Smit[1†*], Helen L. Torrance[1], Marinus J.C. Eijkemans[2], Ben Willem Mol[3], Brent C. Opmeer[4], and Frank J.M. Broekmans[1]



	EMT≤7mm		EMT>7mm		Odds Ratio
Study or Subgroup	Events	Total	Events	Total	M-H, Random, 95% CI
Prospective studies					
Basir 2002	1	28	13	69	0.16 [0.02, 1.28]
Kinay 2010	1	3	10	37	1.35 [0.11, 16.57]
Okohue 2009	0	12	105	208	0.04 [0.00, 0.67]
Subtotal (95% CI)		**43**		**314**	**0.22 [0.03, 1.53]**
Heterogeneity: Tau² = 1.44; Chi² = 3.83, df = 2 (P = 0.15); I² = 48%					
Test for overall effect: Z = 1.53 (P = 0.13)					
Retrospective studies					
Al-Ghamdi 2008	16	62	866	2402	0.62 [0.35, 1.10]
Bozdag 2009	14	40	444	1045	0.73 [0.38, 1.41]
Chen 2010	12	52	1391	2844	0.31 [0.16, 0.60]
Kuc 2011	0	8	294	575	0.06 [0.00, 0.98]
Richter 2007	4	6	860	1288	1.00 [0.18, 5.46]
Zhao 2012	12	47	998	1886	0.31 [0.16, 0.59]
Subtotal (95% CI)		**215**		**10040**	**0.46 [0.29, 0.71]**
Heterogeneity: Tau² = 0.12; Chi² = 8.65, df = 5 (P = 0.12); I² = 42%					
Test for overall effect: Z = 3.44 (P = 0.0006)					
Total (95% CI)		**258**		**10354**	**0.42 [0.27, 0.67]**
Heterogeneity: Tau² = 0.17; Chi² = 13.55, df = 8 (P = 0.09); I² = 41%					
Test for overall effect: Z = 3.63 (P = 0.0003)					

Figure 6 Forest plot of clinical pregnancy for women with EMT ≤ 7 mm and women with EMT > 7 mm. The probability of clinical pregnancy is significantly lower for women with EMT ≤ 7 mm. The I^2 statistic was 41%, indicating that study heterogeneity was low.

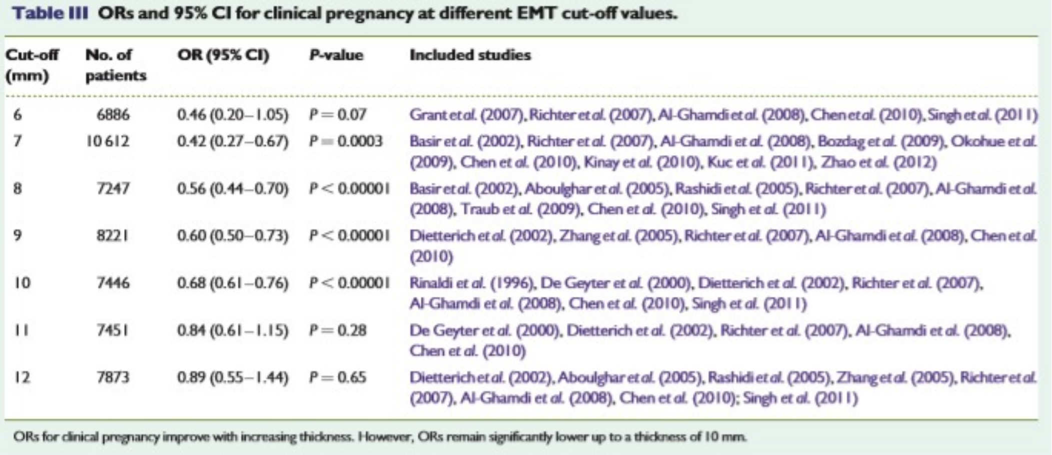


Table III ORs and 95% CI for clinical pregnancy at different EMT cut-off values.

Cut-off (mm)	No. of patients	OR (95% CI)	*P*-value	Included studies
6	6886	0.46 (0.20–1.05)	$P = 0.07$	Grant *et al.* (2007), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Chen *et al.* (2010), Singh *et al.* (2011)
7	10 612	0.42 (0.27–0.67)	$P = 0.0003$	Basir *et al.* (2002), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Bozdag *et al.* (2009), Okohue *et al.* (2009), Chen *et al.* (2010), Kinay *et al.* (2010), Kuc *et al.* (2011), Zhao *et al.* (2012)
8	7247	0.56 (0.44–0.70)	$P < 0.00001$	Basir *et al.* (2002), Aboulghar *et al.* (2005), Rashidi *et al.* (2005), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Traub *et al.* (2009), Chen *et al.* (2010), Singh *et al.* (2011)
9	8221	0.60 (0.50–0.73)	$P < 0.00001$	Dietterich *et al.* (2002), Zhang *et al.* (2005), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Chen *et al.* (2010)
10	7446	0.68 (0.61–0.76)	$P < 0.00001$	Rinaldi *et al.* (1996), De Geyter *et al.* (2000), Dietterich *et al.* (2002), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Chen *et al.* (2010), Singh *et al.* (2011)
11	7451	0.84 (0.61–1.15)	$P = 0.28$	De Geyter *et al.* (2000), Dietterich *et al.* (2002), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Chen *et al.* (2010)
12	7873	0.89 (0.55–1.44)	$P = 0.65$	Dietterich *et al.* (2002), Aboulghar *et al.* (2005), Rashidi *et al.* (2005), Zhang *et al.* (2005), Richter *et al.* (2007), Al-Ghamdi *et al.* (2008), Chen *et al.* (2010); Singh *et al.* (2011)

ORs for clinical pregnancy improve with increasing thickness. However, ORs remain significantly lower up to a thickness of 10 mm.

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Endometrial thickness and pregnancy rates after IVF: a systematic review and meta-analysis

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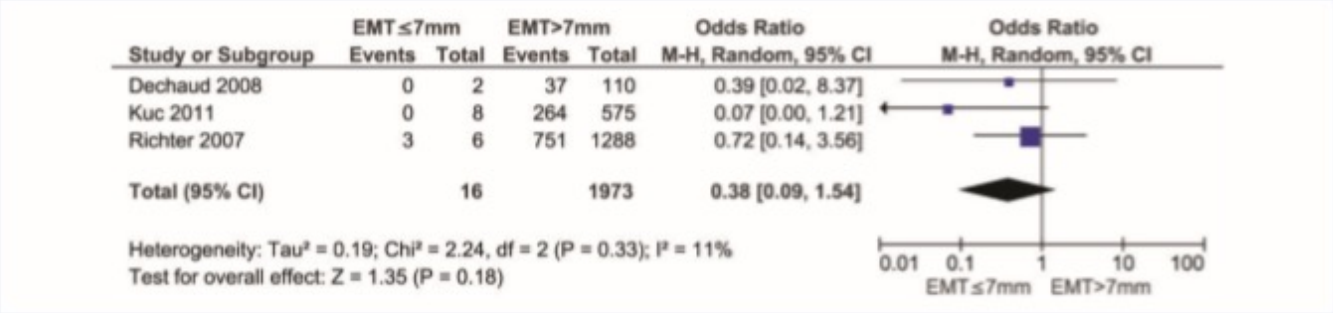


Study or Subgroup	EMT≤7mm Events	EMT≤7mm Total	EMT>7mm Events	EMT>7mm Total	Odds Ratio M-H, Random, 95% CI
Dechaud 2008	0	2	37	110	0.39 [0.02, 8.37]
Kuc 2011	0	8	264	575	0.07 [0.00, 1.21]
Richter 2007	3	6	751	1288	0.72 [0.14, 3.56]
Total (95% CI)		**16**		**1973**	**0.38 [0.09, 1.54]**

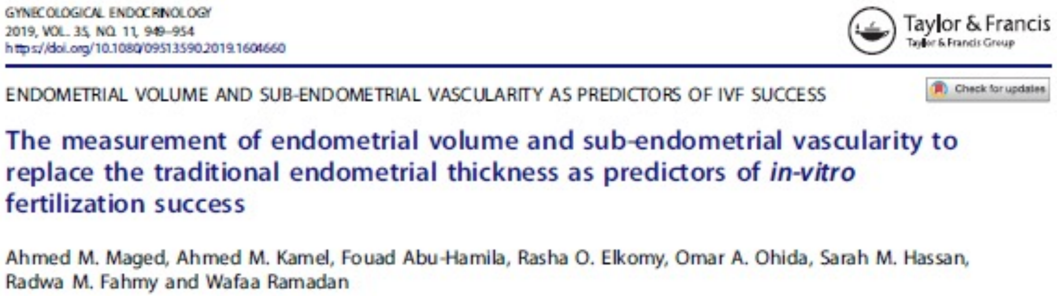
Heterogeneity: Tau² = 0.19; Chi² = 2.24, df = 2 (P = 0.33); I² = 11%
Test for overall effect: Z = 1.35 (P = 0.18)

Figure 5 Forest plot of ongoing pregnancy and live birth for women with EMT $\leq$ 7 mm and EMT $>$ 7 mm. Chances of live birth and ongoing pregnancy are lower for women with EMT $\leq$ 7 mm, but the results are not significant. The I^2 statistic of 11% indicates that study heterogeneity was low. CI, confidence interval.

- Tenir compte de l'épaisseur… mais pas que…
    - Quelques grossesses ont été rapportées sur des épaisseurs endométriales très faibles (4mm)
    - Importance de l'aspect (échogénicité)… et d'autres paramètres encore « mystérieux » (vascularisation…)?

- Quant au volume endométrial : pas plus prédictif du succès de la FIV que l'épaisseur endométriale?

Alcazar et al. Reprod Biol Endocrinol 2006



GYNECOLOGICAL ENDOCRINOLOGY
2019, VOL. 35, NO. 11, 949–954
https://doi.org/10.1080/09513590.2019.1604660

Taylor & Francis
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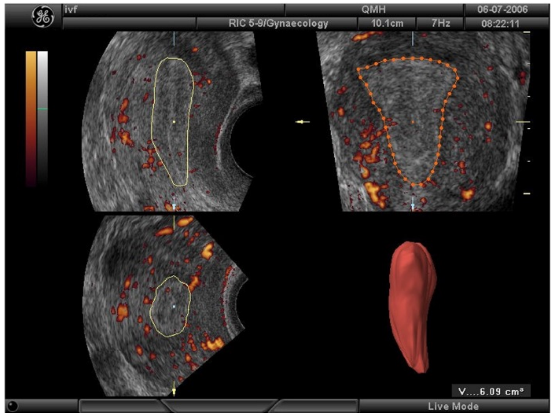
ENDOMETRIAL VOLUME AND SUB-ENDOMETRIAL VASCULARITY AS PREDICTORS OF IVF SUCCESS

Check for updates

The measurement of endometrial volume and sub-endometrial vascularity to replace the traditional endometrial thickness as predictors of *in-vitro* fertilization success

Ahmed M. Maged, Ahmed M. Kamel, Fouad Abu-Hamila, Rasha O. Elkomy, Omar A. Ohida, Sarah M. Hassan, Radwa M. Fahmy and Wafaa Ramadan

J Ultrasound Med 2021; 9999:1–9



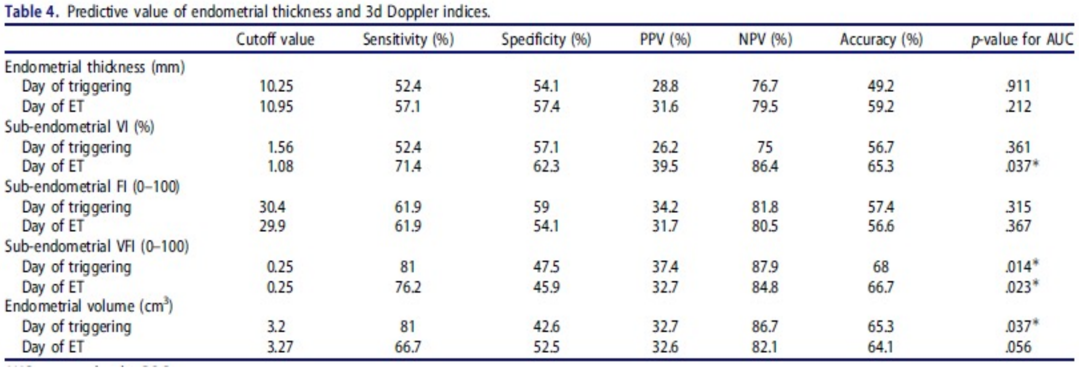
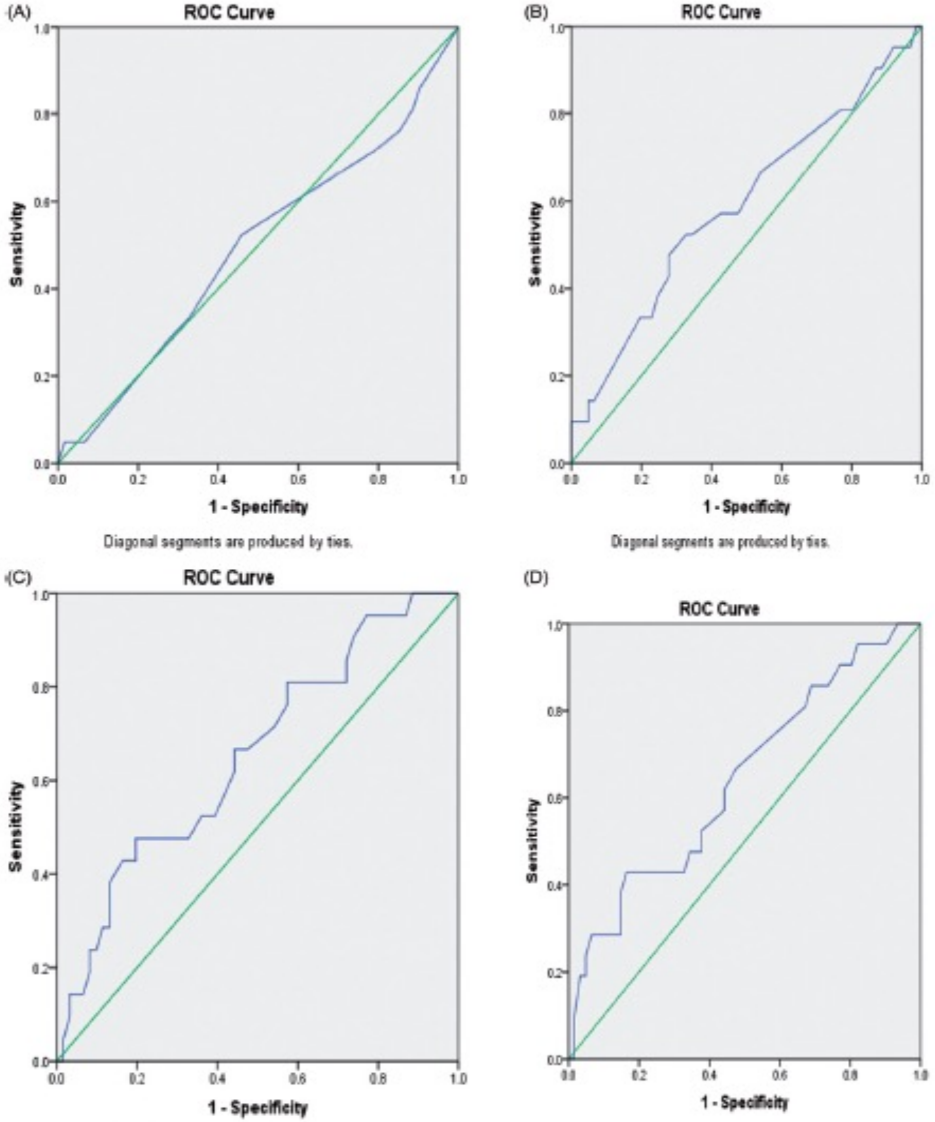


Table 4. Predictive value of endometrial thickness and 3d Doppler indices.

	Cutoff value	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)	*p*-value for AUC
Endometrial thickness (mm)							
Day of triggering	10.25	52.4	54.1	28.8	76.7	49.2	.911
Day of ET	10.95	57.1	57.4	31.6	79.5	59.2	.212
Sub-endometrial VI (%)							
Day of triggering	1.56	52.4	57.1	26.2	75	56.7	.361
Day of ET	1.08	71.4	62.3	39.5	86.4	65.3	.037*
Sub-endometrial FI (0–100)							
Day of triggering	30.4	61.9	59	34.2	81.8	57.4	.315
Day of ET	29.9	61.9	54.1	31.7	80.5	56.6	.367
Sub-endometrial VFI (0–100)							
Day of triggering	0.25	81	47.5	37.4	87.9	68	.014*
Day of ET	0.25	76.2	45.9	32.7	84.8	66.7	.023*
Endometrial volume (cm^3)							
Day of triggering	3.2	81	42.6	32.7	86.7	65.3	.037*
Day of ET	3.27	66.7	52.5	32.6	82.1	64.1	.056



A : thickness at hCG-D ;
C : volume at hCG-D ;

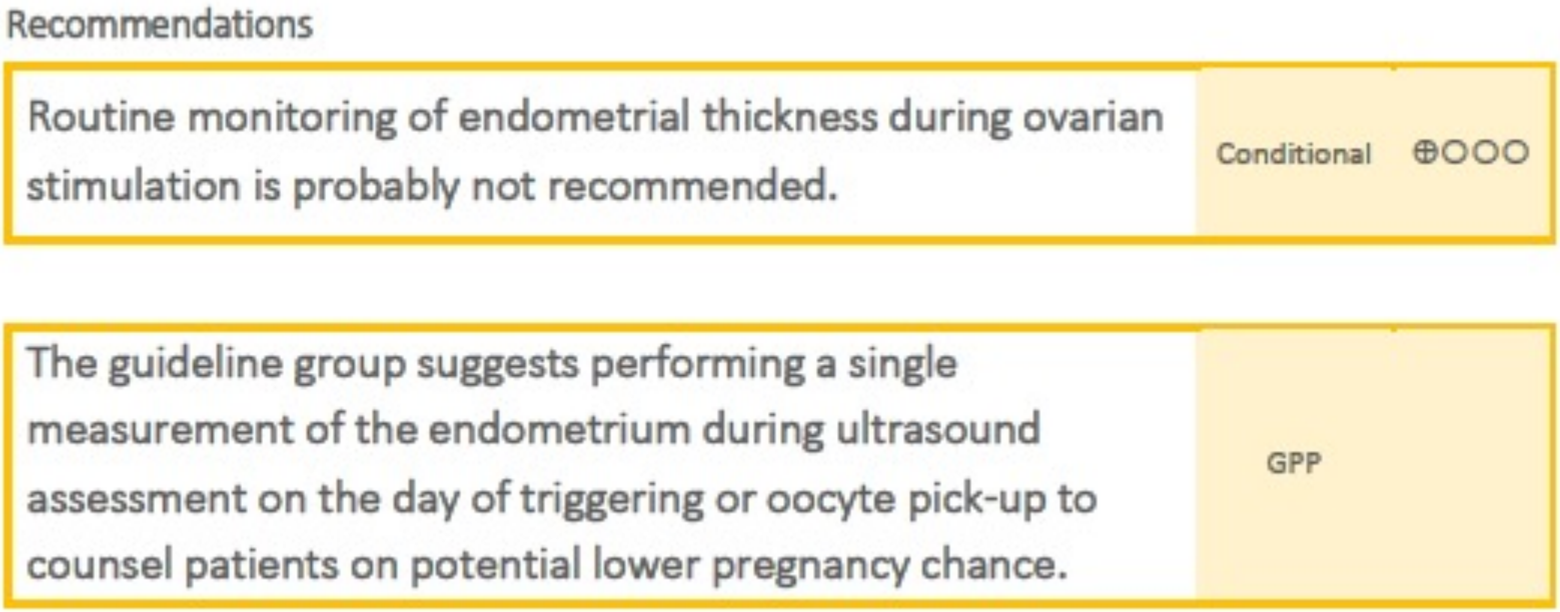
B: thickness at FET
D : volume at FET

Human Reproduction Open, pp. 1–13, 2020
doi:10.1093/hropen/hoaa009

human reproduction open
ESHRE PAGES

ESHRE guideline: ovarian stimulation for IVF/ICSI†

The ESHRE Guideline Group on Ovarian Stimulation, Ernesto Bosch[1], Simone Broer[2], Georg Griesinger[3], Michael Grynberg[4], Peter Humaidan[5], Estratios Kolibianakis[6], Michal Kunicki[7], Antonio La Marca[8], George Lainas[9], Nathalie Le Clef[10], Nathalie Massin[11], Sebastiaan Mastenbroek[12], Nikolaos Polyzos[13], Sesh Kamal Sunkara[14], Tanya Timeva[15], Mira Töyli[16], Janos Urbancsek[17], Nathalie Vermeulen[10], and Frank Broekmans[2,*]

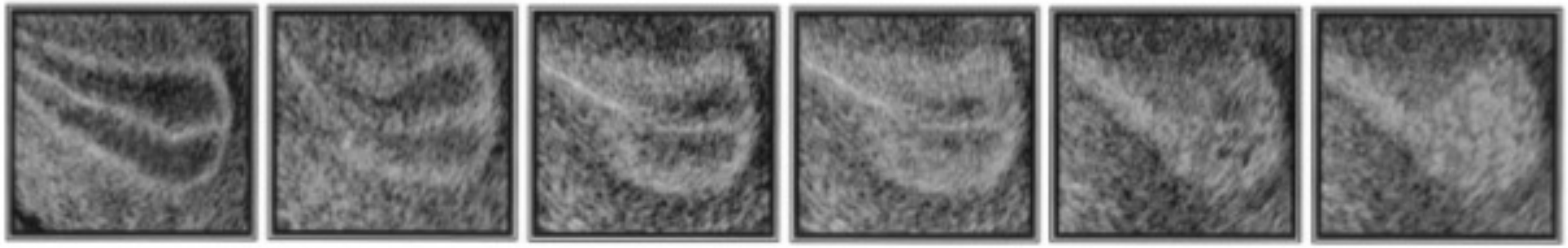


Recommendations

Routine monitoring of endometrial thickness during ovarian stimulation is probably not recommended.	Conditional	⊕○○○

The guideline group suggests performing a single measurement of the endometrium during ultrasound assessment on the day of triggering or oocyte pick-up to counsel patients on potential lower pregnancy chance.	GPP	

L'endomètre au cours de la transition folliculo-lutéale

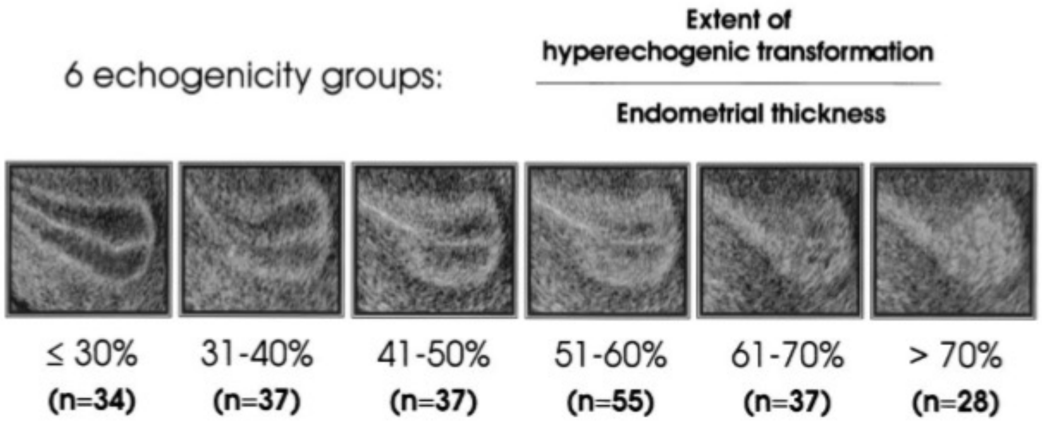


- De plus en plus échogène

- Attention aux utérus intermédiaires !!!

FIGURE 2

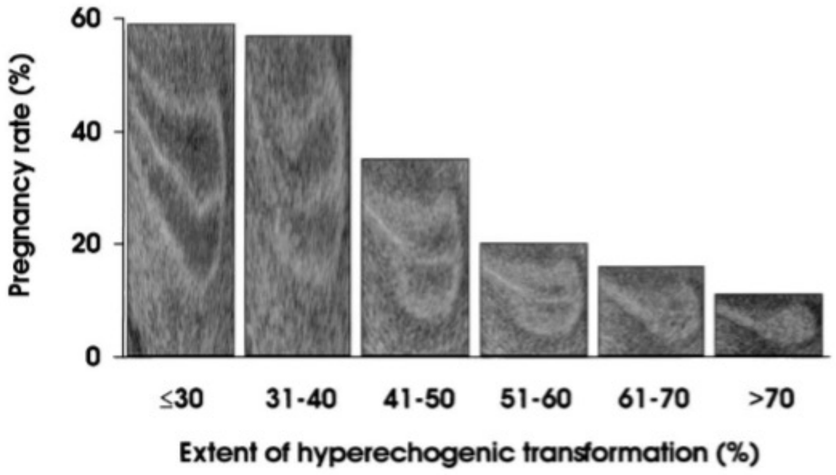
The cycles were sorted into six groups according to the extent of the upward hyperechogenic transformation of the endometrium.


6 echogenicity groups:
Extent of hyperechogenic transformation
Endometrial thickness
≤ 30%
(n=34)
31-40%
(n=37)
41-50%
(n=37)
51-60%
(n=55)
61-70%
(n=37)
> 70%
(n=28)

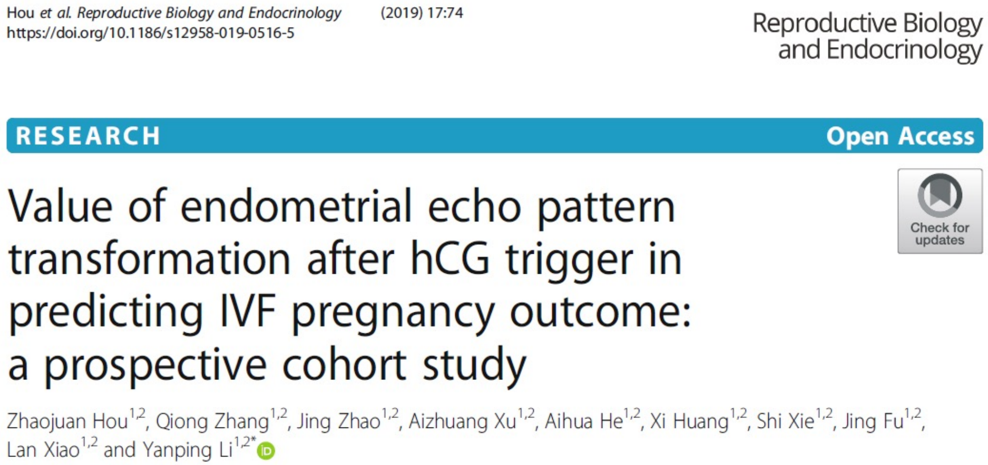
Fanchin. Endometrial echogenicity and receptivity. Fertil Steril 1999.

FIGURE 3

Clinical pregnancy rates according to the extent of hyperechogenic endometrial transformation assessed on the day of hCG administration ($P < .001$).



Fanchin. Endometrial echogenicity and receptivity. Fertil Steril 1999.


Hou *et al. Reproductive Biology and Endocrinology* (2019) 17:74
https://doi.org/10.1186/s12958-019-0516-5

Reproductive Biology
and Endocrinology

RESEARCH **Open Access**

Value of endometrial echo pattern transformation after hCG trigger in predicting IVF pregnancy outcome: a prospective cohort study

Zhaojuan Hou[1,2], Qiong Zhang[1,2], Jing Zhao[1,2], Aizhuang Xu[1,2], Aihua He[1,2], Xi Huang[1,2], Shi Xie[1,2], Jing Fu[1,2], Lan Xiao[1,2] and Yanping Li[1,2*]

- **A total of 146 infertile women undergoing their first IVF cycle.**
- **A series of endometrial echo pattern monitoring was carried out in these patients after hCG trigger: hCG day, OPU + 1, OPU + 2, OPU + 3**

Conclusions: The endometrial echogenicity value on OPU + 2 was recommended to evaluate endometrial receptivity. It seemed appropriate for clinicians to provide a 'freeze all' IVF cycle and transfer in a subsequent frozen-thawed embryos cycle when echogenicity value <60% on OPU + 2.

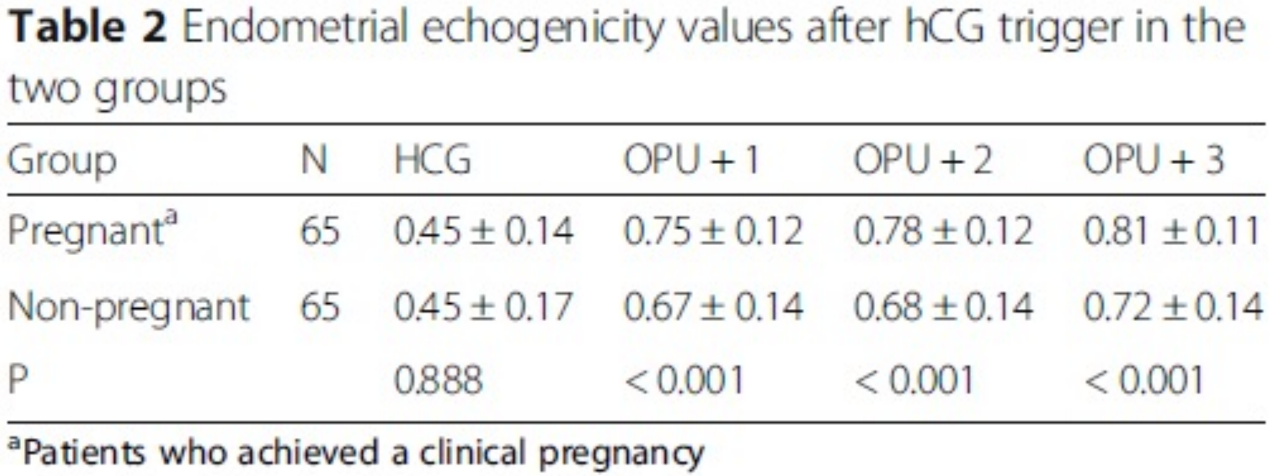


Table 2 Endometrial echogenicity values after hCG trigger in the two groups

Group	N	HCG	OPU + 1	OPU + 2	OPU + 3
Pregnant[a]	65	0.45 ± 0.14	0.75 ± 0.12	0.78 ± 0.12	0.81 ± 0.11
Non-pregnant	65	0.45 ± 0.17	0.67 ± 0.14	0.68 ± 0.14	0.72 ± 0.14
P		0.888	< 0.001	< 0.001	< 0.001

[a] Patients who achieved a clinical pregnancy

ET LES DOSAGES HORMONAUX?

Human Reproduction Open, pp. 1–13, 2020
doi:10.1093/hropen/hoaa009

human reproduction open

ESHRE PAGES

ESHRE guideline: ovarian stimulation for IVF/ICSI†

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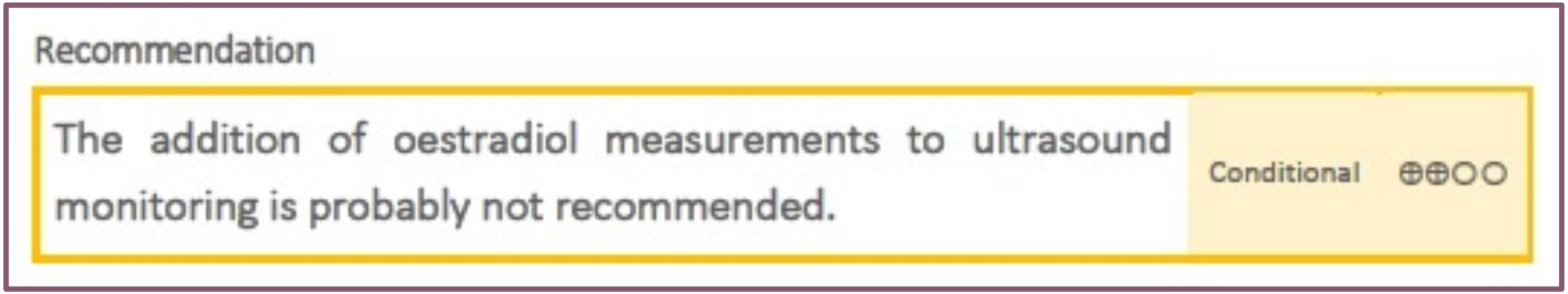
Recommandation basée sur Kwan et al. Cochrane 2014:
- 6 RCT → 781 femmes

Le dosage d'œstradiol ne semble pas améliorer les performances de l'écho pour prédire :

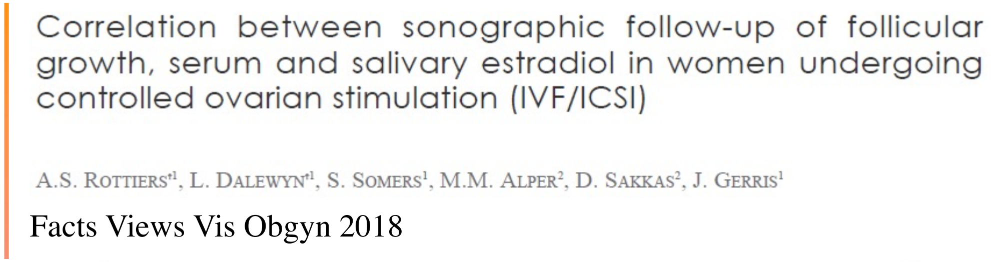
- Le risque OHSS
- Le nombre d'ovocytes prélevés
- Les chances de grossesse clinique

Mais peut-être en pratique utile pour « ajuster » sa stimulation en cas d'échec… mais pas vraiment d'études!!



Recommendation

The addition of oestradiol measurements to ultrasound monitoring is probably not recommended.	Conditional	⊕⊕○○

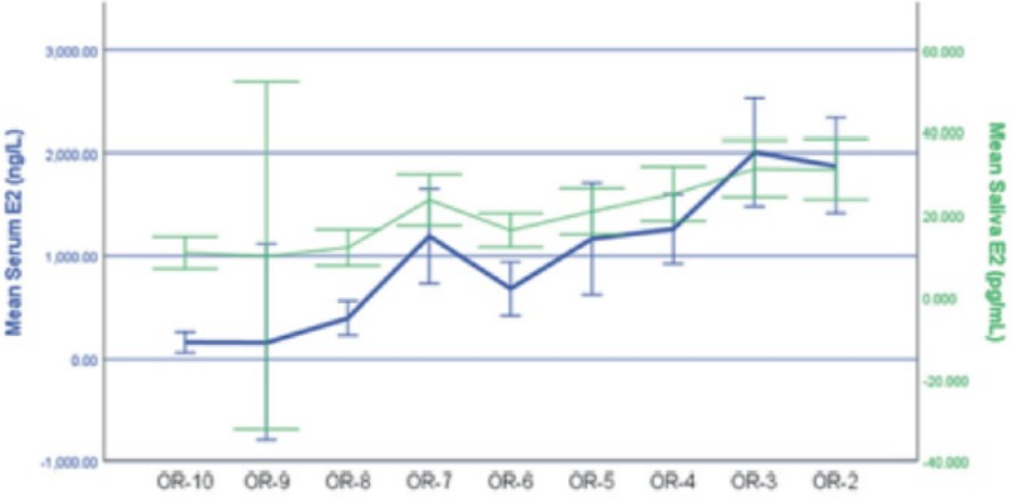


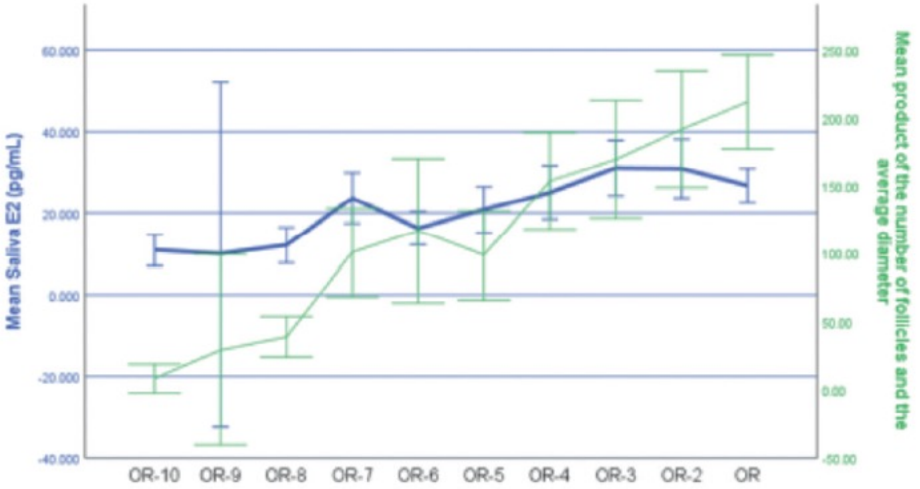
Correlation between sonographic follow-up of follicular growth, serum and salivary estradiol in women undergoing controlled ovarian stimulation (IVF/ICSI)

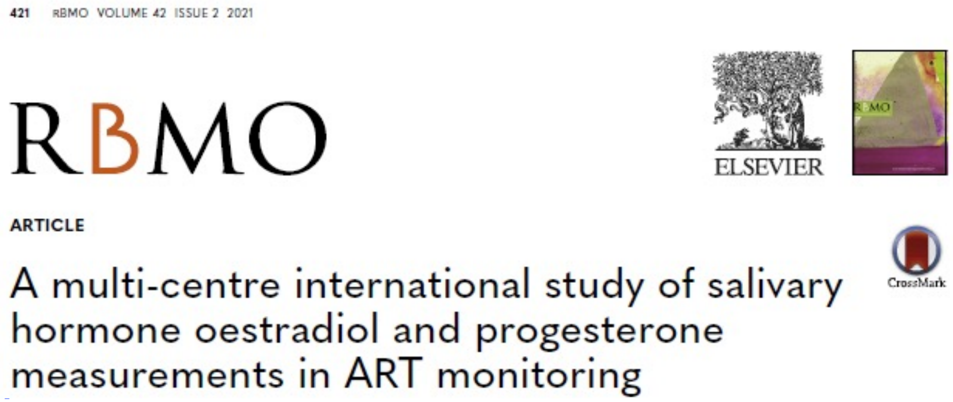
A.S. Rottiers*[1], L. Dalewyn*[1], S. Somers[1], M.M. Alper[2], D. Sakkas[2], J. Gerris[1]

Facts Views Vis Obgyn 2018

- ➢ **Strong correlation between serum and salivary E2 concentrations.**
- ➢ **In addition, both are strongly correlated with the product of the number of follicles and their average diameter, measured by TVUS.**







421 RBMO VOLUME 42 ISSUE 2 2021

RBMO

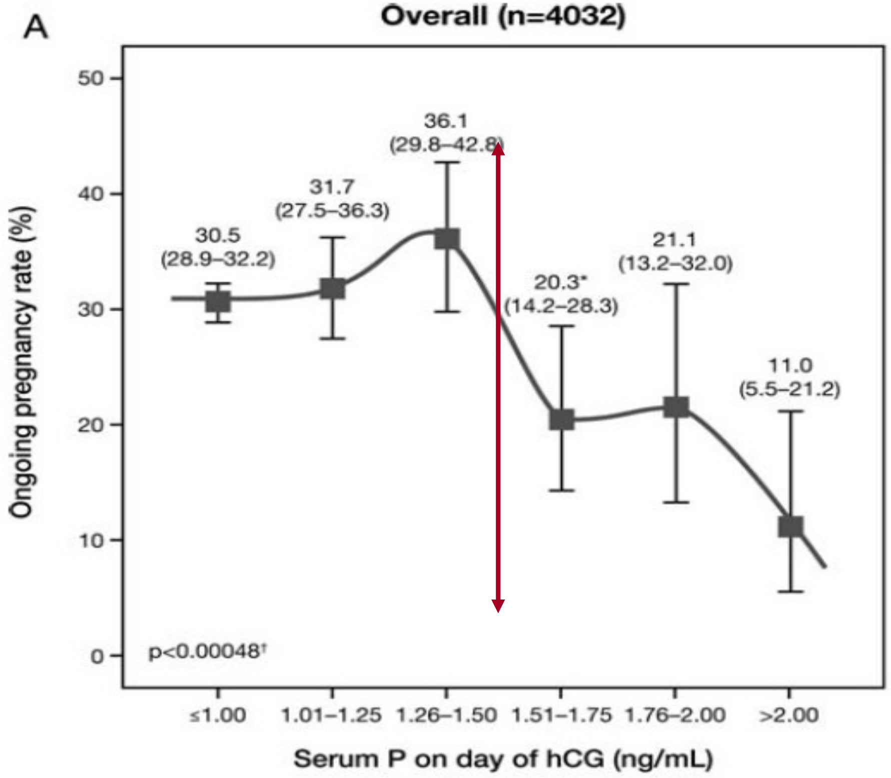
ARTICLE

A multi-centre international study of salivary hormone oestradiol and progesterone measurements in ART monitoring

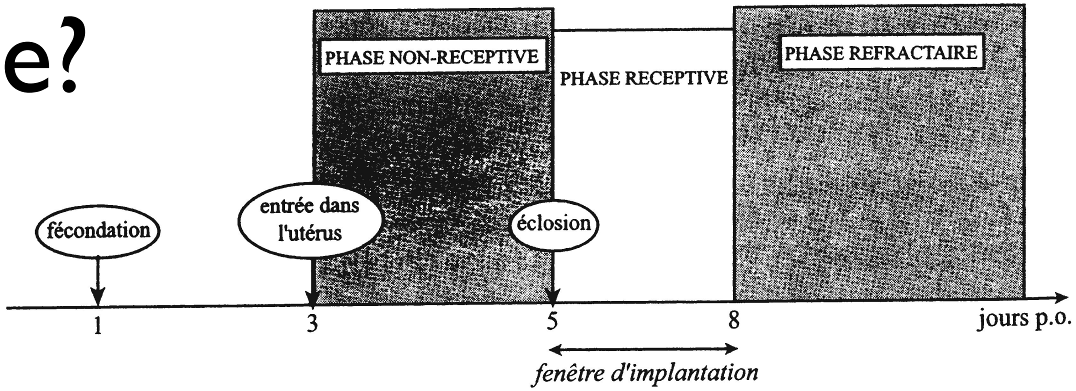
ELSEVIER
RBMO
CrossMark

- ➢ **Salivary estradiol hormone testing correlates well to serum-based assessment, whereas progesterone values, around the time of trigger, are not consistent from patient to patient.**

Et la progestéronémie?



Bosch et al, Hum Reprod 2010


PHASE NON-RECEPTIVE
PHASE RECEPTIVE
PHASE REFRACTAIRE
fécondation
entrée dans l'utérus
éclosion
1
3
5
8
jours p.o.
fenêtre d'implantation

- Pas d'études évaluant « qualité de la stimulation ovarienne » et progestéronémie ➔ pas recommandée pour évaluer ce paramètre!

- Mais impact d'une élévation prématurée de la progestérone en cours d'HSOC ➔ ↓↓ taux d'implantation en cas de TEF
  - ✓ *Incidence # 10 % des cycles (dépend du seuil choisi)*
  - ✓ *Publications récentes, seuil ≈ 1,5 ng/ml*

Sonigo et al. RBMO 2014

Human Reproduction Update, Vol.19, No.5 pp. 433–457, 2013
Advanced Access publication on July 4, 2013 doi:10.1093/humupd/dmt014

human reproduction update

Progesterone elevation and probability of pregnancy after IVF: a systematic review and meta-analysis of over 60 000 cycles

C.A. Venetis*, E.M. Kolibianakis, J.K. Bosdou, and B.C. Tarlatzis

- Corrélation très nette entre élévation de progestérone J-hCG et baisse des taux de grossesse
- Problème des seuils différents au sein des études (techniques de dosages différentes +++)
- Importance du « terrain » = type de « répondeuse » en FIV

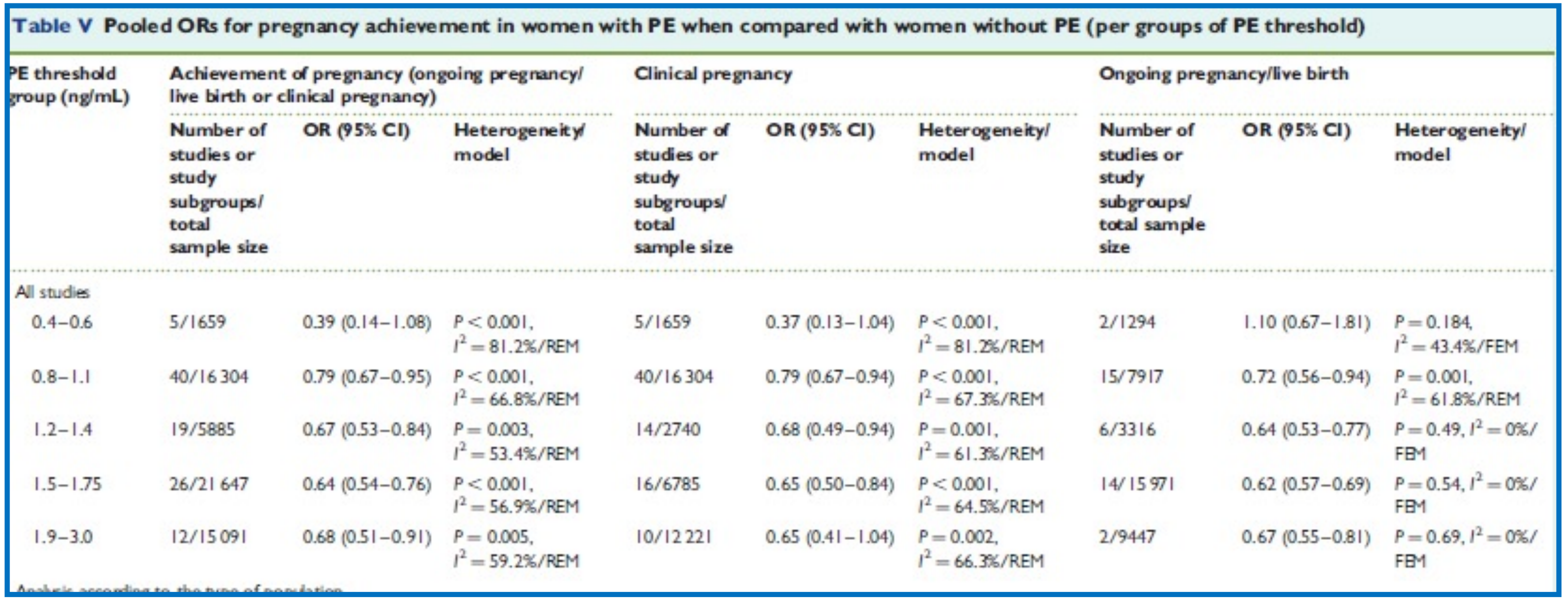
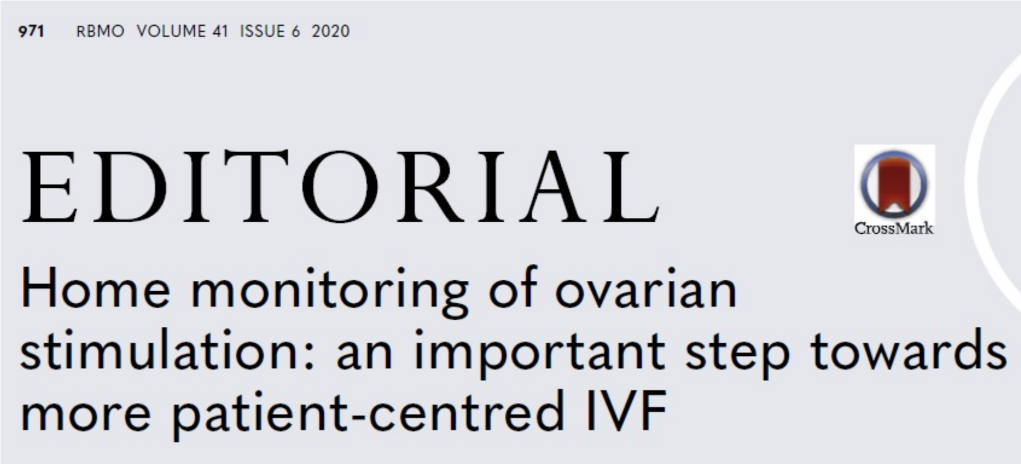


Table V Pooled ORs for pregnancy achievement in women with PE when compared with women without PE (per groups of PE threshold)

PE threshold group (ng/mL)	Achievement of pregnancy (ongoing pregnancy/live birth or clinical pregnancy)			Clinical pregnancy			Ongoing pregnancy/live birth		
	Number of studies or study subgroups/total sample size	OR (95% CI)	Heterogeneity/model	Number of studies or study subgroups/total sample size	OR (95% CI)	Heterogeneity/model	Number of studies or study subgroups/total sample size	OR (95% CI)	Heterogeneity/model
All studies									
0.4–0.6	5/1659	0.39 (0.14–1.08)	$P < 0.001$, $I^2 = 81.2\%$/REM	5/1659	0.37 (0.13–1.04)	$P < 0.001$, $I^2 = 81.2\%$/REM	2/1294	1.10 (0.67–1.81)	$P = 0.184$, $I^2 = 43.4\%$/FEM
0.8–1.1	40/16 304	0.79 (0.67–0.95)	$P < 0.001$, $I^2 = 66.8\%$/REM	40/16 304	0.79 (0.67–0.94)	$P < 0.001$, $I^2 = 67.3\%$/REM	15/7917	0.72 (0.56–0.94)	$P = 0.001$, $I^2 = 61.8\%$/REM
1.2–1.4	19/5885	0.67 (0.53–0.84)	$P = 0.003$, $I^2 = 53.4\%$/REM	14/2740	0.68 (0.49–0.94)	$P = 0.001$, $I^2 = 61.3\%$/REM	6/3316	0.64 (0.53–0.77)	$P = 0.49$, $I^2 = 0\%$/FEM
1.5–1.75	26/21 647	0.64 (0.54–0.76)	$P < 0.001$, $I^2 = 56.9\%$/REM	16/6785	0.65 (0.50–0.84)	$P < 0.001$, $I^2 = 64.5\%$/REM	14/15 971	0.62 (0.57–0.69)	$P = 0.54$, $I^2 = 0\%$/FEM
1.9–3.0	12/15 091	0.68 (0.51–0.91)	$P = 0.005$, $I^2 = 59.2\%$/REM	10/12 221	0.65 (0.41–1.04)	$P = 0.002$, $I^2 = 66.3\%$/REM	2/9447	0.67 (0.55–0.81)	$P = 0.69$, $I^2 = 0\%$/FEM
Analysis according to the type of population									



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EDITORIAL

Home monitoring of ovarian stimulation: an important step towards more patient-centred IVF

J.M.R. Gerris[1,*]
B.C.J.M. Fauser[2]

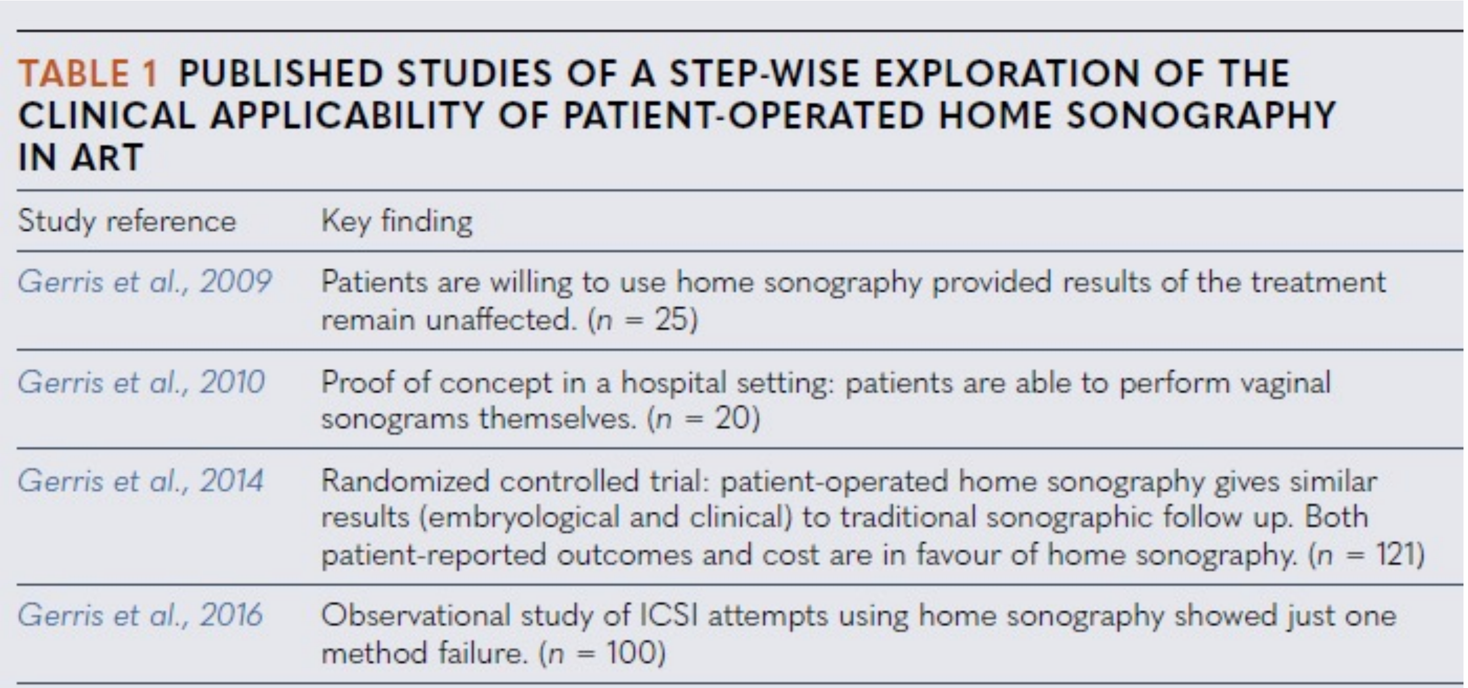


TABLE 1 PUBLISHED STUDIES OF A STEP-WISE EXPLORATION OF THE CLINICAL APPLICABILITY OF PATIENT-OPERATED HOME SONOGRAPHY IN ART

Study reference	Key finding
Gerris et al., 2009	Patients are willing to use home sonography provided results of the treatment remain unaffected. (*n* = 25)
Gerris et al., 2010	Proof of concept in a hospital setting: patients are able to perform vaginal sonograms themselves. (*n* = 20)
Gerris et al., 2014	Randomized controlled trial: patient-operated home sonography gives similar results (embryological and clinical) to traditional sonographic follow up. Both patient-reported outcomes and cost are in favour of home sonography. (*n* = 121)
Gerris et al., 2016	Observational study of ICSI attempts using home sonography showed just one method failure. (*n* = 100)

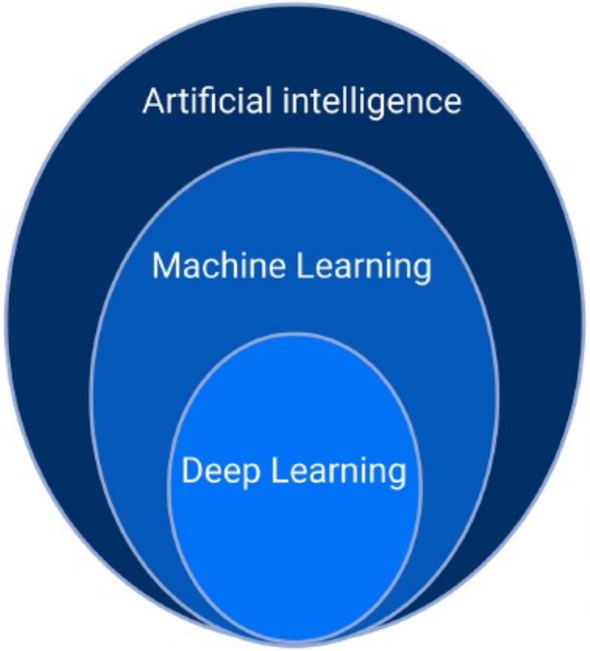
Reproduction & Fertility | D J X Chow *et al.* | Does AI have a role in the IVF clinic? | 2:3 | **C29**–C34

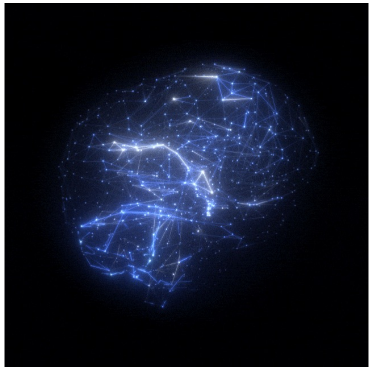
2021

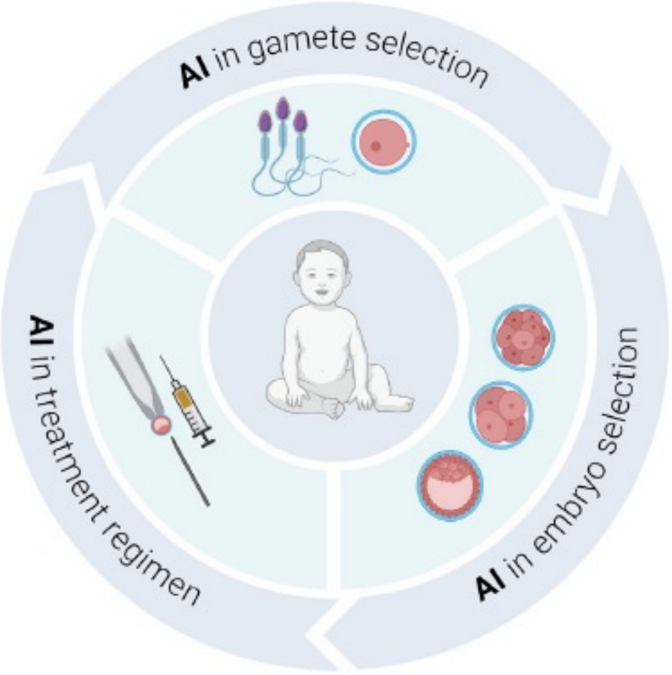
COMMENTARY

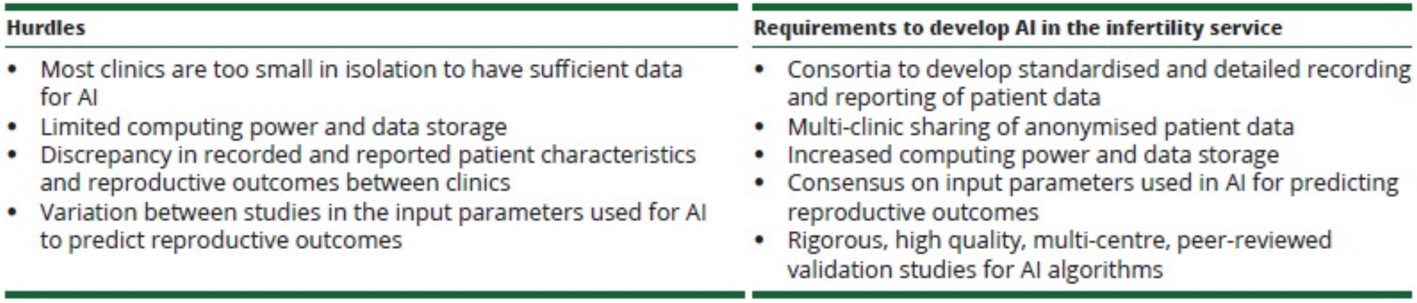
Does artificial intelligence have a role in the IVF clinic?

Darren J X Chow[1,2,3], **Philip Wijesinghe**[4], **Kishan Dholakia**[3,4,5,6] and **Kylie R Dunning**[1,2,3]

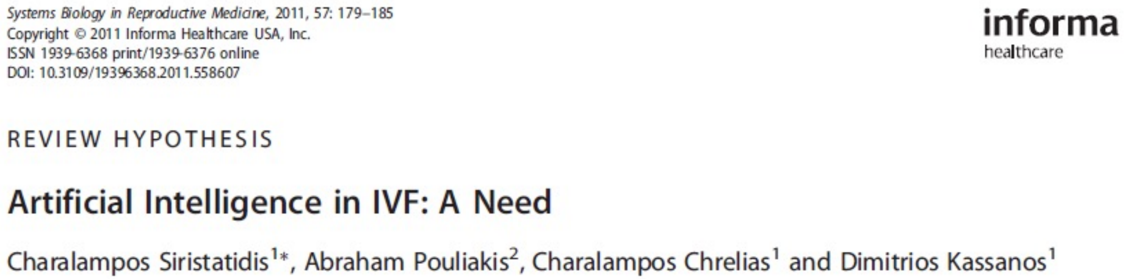

Artificial intelligence
Machine Learning
Deep Learning




AI in gamete selection
AI in embryo selection
AI in treatment regimen



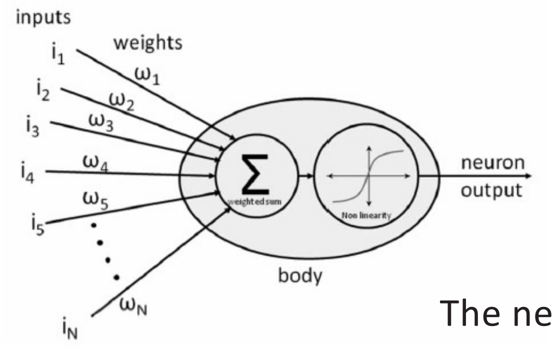
Hurdles	**Requirements to develop AI in the infertility service**
• Most clinics are too small in isolation to have sufficient data for AI • Limited computing power and data storage • Discrepancy in recorded and reported patient characteristics and reproductive outcomes between clinics • Variation between studies in the input parameters used for AI to predict reproductive outcomes	• Consortia to develop standardised and detailed recording and reporting of patient data • Multi-clinic sharing of anonymised patient data • Increased computing power and data storage • Consensus on input parameters used in AI for predicting reproductive outcomes • Rigorous, high quality, multi-centre, peer-reviewed validation studies for AI algorithms


Systems Biology in Reproductive Medicine, 2011, 57: 179–185
Copyright © 2011 Informa Healthcare USA, Inc.
ISSN 1939-6368 print/1939-6376 online
DOI: 10.3109/19396368.2011.558607

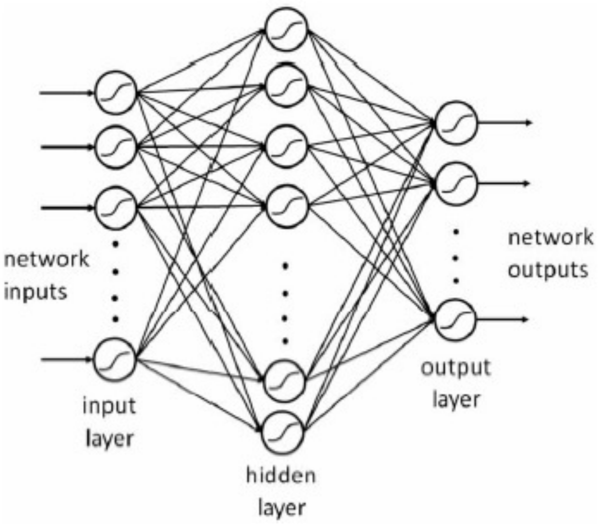
REVIEW HYPOTHESIS

Artificial Intelligence in IVF: A Need

Charalampos Siristatidis[1]*, Abraham Pouliakis[2], Charalampos Chrelias[1] and Dimitrios Kassanos[1]



The neuron model



Multilayer neural networks

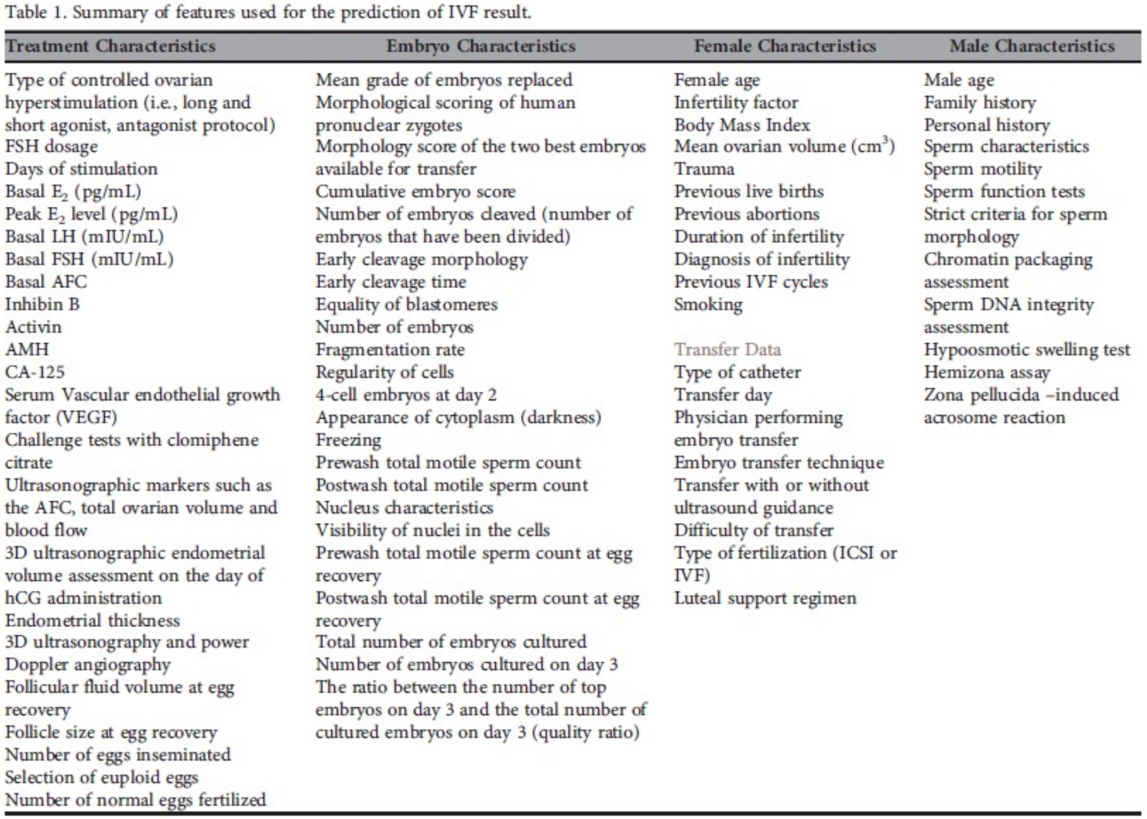


Table 1. Summary of features used for the prediction of IVF result.

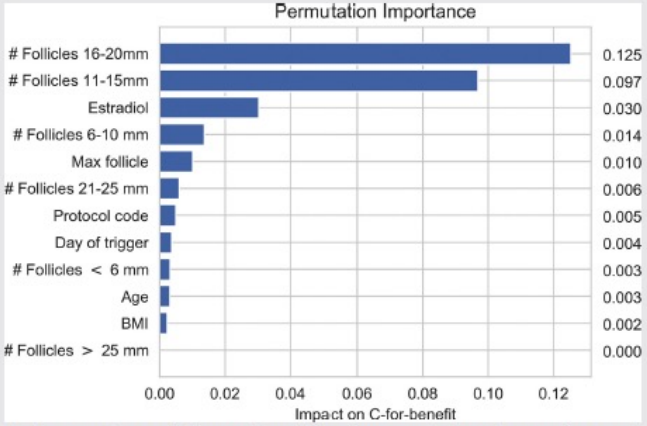
Treatment Characteristics	Embryo Characteristics	Female Characteristics	Male Characteristics
Type of controlled ovarian hyperstimulation (i.e., long and short agonist, antagonist protocol)	Mean grade of embryos replaced	Female age	Male age
FSH dosage	Morphological scoring of human pronuclear zygotes	Infertility factor	Family history
Days of stimulation	Morphology score of the two best embryos available for transfer	Body Mass Index	Personal history
Basal E_2 (pg/mL)	Cumulative embryo score	Mean ovarian volume (cm^3)	Sperm characteristics
Peak E_2 level (pg/mL)	Number of embryos cleaved (number of embryos that have been divided)	Trauma	Sperm motility
Basal LH (mIU/mL)	Early cleavage morphology	Previous live births	Sperm function tests
Basal FSH (mIU/mL)	Early cleavage time	Previous abortions	Strict criteria for sperm morphology
Basal AFC	Equality of blastomeres	Duration of infertility	Chromatin packaging assessment
Inhibin B	Number of embryos	Diagnosis of infertility	Sperm DNA integrity assessment
Activin	Fragmentation rate	Previous IVF cycles	Hypoosmotic swelling test
AMH	Regularity of cells	Smoking	Hemizona assay
CA-125	4-cell embryos at day 2		Zona pellucida –induced acrosome reaction
Serum Vascular endothelial growth factor (VEGF)	Appearance of cytoplasm (darkness)	Transfer Data	
Challenge tests with clomiphene citrate	Freezing	Type of catheter	
Ultrasonographic markers such as the AFC, total ovarian volume and blood flow	Prewash total motile sperm count	Transfer day	
3D ultrasonographic endometrial volume assessment on the day of hCG administration	Postwash total motile sperm count	Physician performing embryo transfer	
Endometrial thickness	Nucleus characteristics	Embryo transfer technique	
3D ultrasonography and power Doppler angiography	Visibility of nuclei in the cells	Transfer with or without ultrasound guidance	
Follicular fluid volume at egg recovery	Prewash total motile sperm count at egg recovery	Difficulty of transfer	
Follicle size at egg recovery	Postwash total motile sperm count at egg recovery	Type of fertilization (ICSI or IVF)	
Number of eggs inseminated	Total number of embryos cultured	Luteal support regimen	
Selection of euploid eggs	Number of embryos cultured on day 3		
Number of normal eggs fertilized	The ratio between the number of top embryos on day 3 and the total number of cultured embryos on day 3 (quality ratio)		

Fertility and Sterility® Vol. 116, No. 5, November 2021

A machine learning algorithm can optimize the day of trigger to improve in vitro fertilization outcomes

Eduardo Hariton, M.D., M.B.A.,[a] Ethan A. Chi,[b] Gordon Chi,[b] Jerrine R. Morris, M.D., M.P.H.,[a] Jon Braatz, B.S.,[b] Pranav Rajpurkar, Ph.D.,[b] and Mitchell Rosen, M.D., H.C.L.D.[a]

FIGURE 2

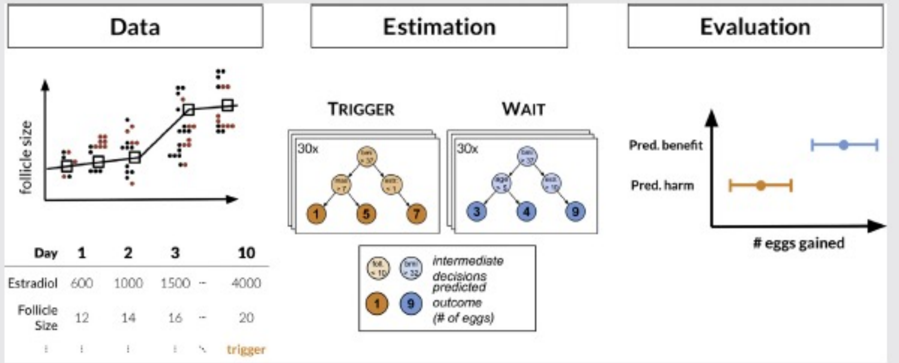


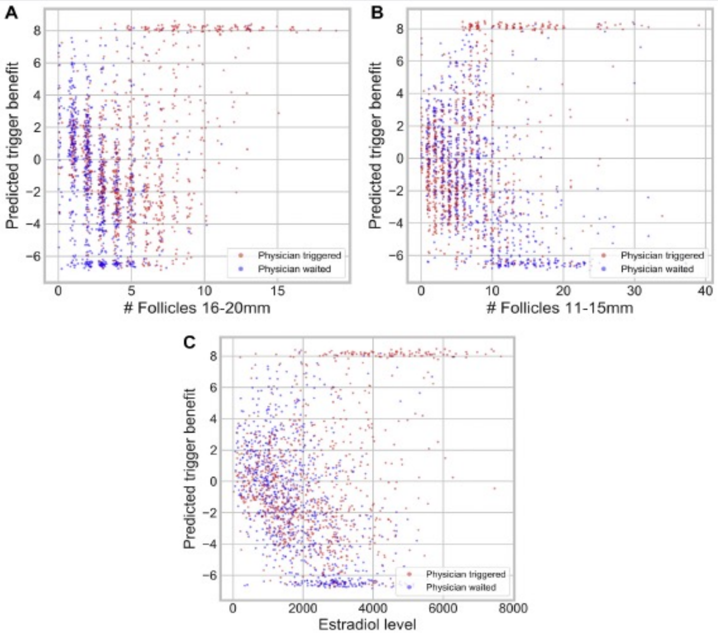
Feature importance bar chart. Removing a specific figure results in a drop in performance, with the most important features at the top, implying that those features are considered most when is the optimal day for trigger. It is important to note that feature importance is not designed to explain how important a given feature is to the outcome independently, but rather to explain our model's predictive capacity, as some features may be correlated. BMI = body mass index.

- Patients undergoing IVF-ICSI from 2008 to 2019 (n = 7,866).
- Result(s): The machine learning algorithm is more effective than physician's decision :
  - ✓ 3.015 (95% CI 2.626, 3.371) more 2PNs.
  - ✓ 1.515 (95% CI 1.134, 1.871) more usable blastocysts.

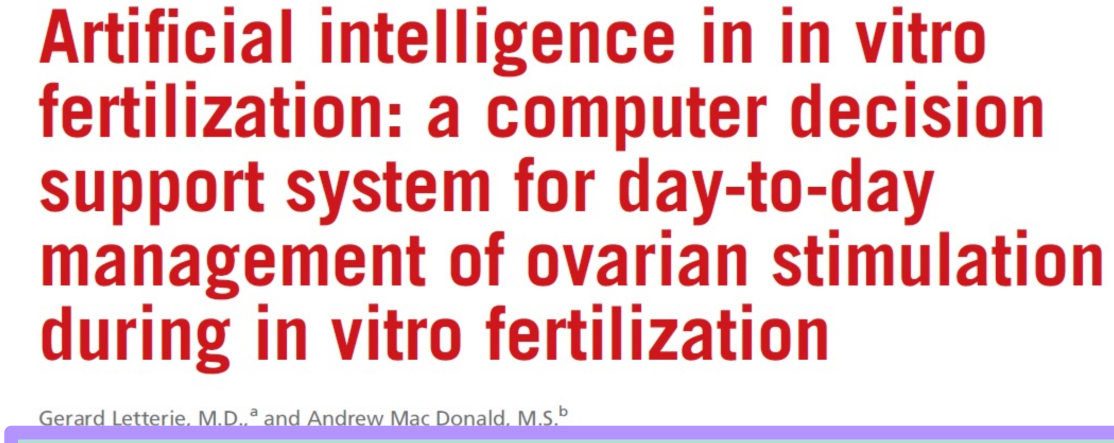
➔ Future research is required to confirm these findings prospectively.

FIGURE 1


Data
Estimation
Evaluation
follicle size
Day 1 2 3 10
Estradiol 600 1000 1500 4000
Follicle Size 12 14 16 20
trigger
TRIGGER
WAIT
30x
30x
1
5
7
3
4
9
intermediate decisions
predicted outcome (# of eggs)
Pred. benefit
Pred. harm
# eggs gained

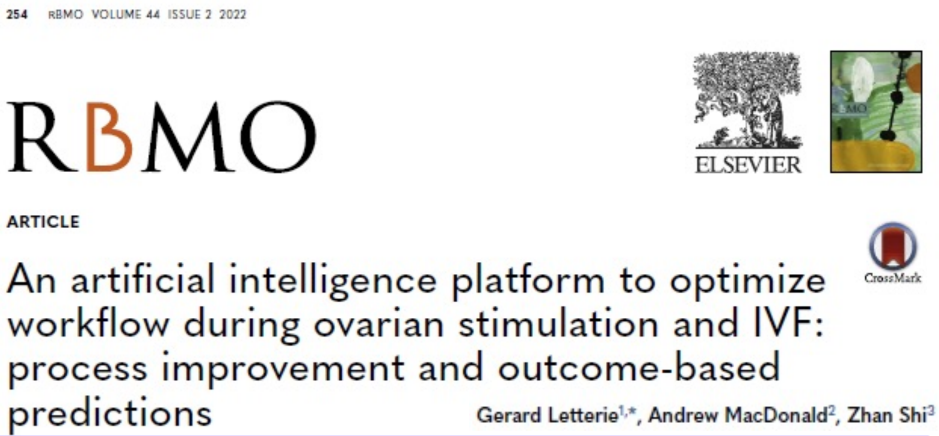


Points are colored red if a physician decided to trigger the given patient at that time and blue if otherwise.



Artificial intelligence in in vitro fertilization: a computer decision support system for day-to-day management of ovarian stimulation during in vitro fertilization

Gerard Letterie, M.D.,[a] and Andrew Mac Donald, M.S.[b]



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RBMO

ARTICLE

An artificial intelligence platform to optimize workflow during ovarian stimulation and IVF: process improvement and outcome-based predictions

Gerard Letterie[1],*, Andrew MacDonald[2], Zhan Shi[3]

Conclusions : a first-iteration algorithm is described designed to improve workflow, minimize visits and level-load embryology work. This algorithm enables decisions at three interrelated nodal points for IVF workflow management to include monitoring on the single best day, assign trigger days to enable a range of 3 days for level-loading and estimate oocyte number.

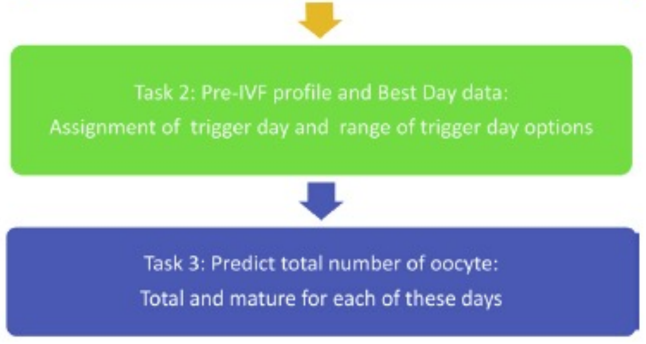
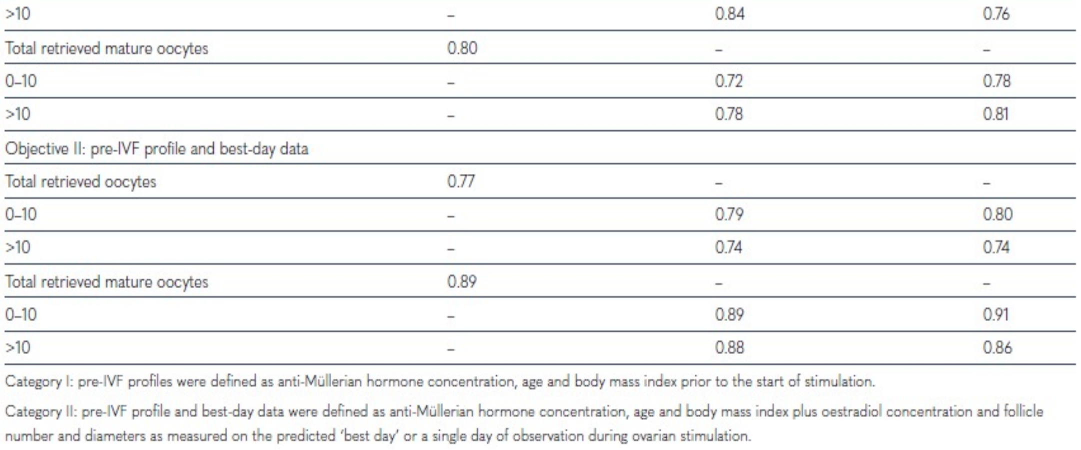

Task 2: Pre-IVF profile and Best Day data:
Assignment of trigger day and range of trigger day options
Task 3: Predict total number of oocyte:
Total and mature for each of these days

FIGURE 1 Model for progressive data accumulation to predict outcomes and schedule the single best day, assign a trigger day and retrieval options and estimate the number of expected oocytes.



>10	–	0.84	0.76
Total retrieved mature oocytes	0.80	–	–
0–10	–	0.72	0.78
>10	–	0.78	0.81
Objective II: pre-IVF profile and best-day data			
Total retrieved oocytes	0.77	–	–
0–10	–	0.79	0.80
>10	–	0.74	0.74
Total retrieved mature oocytes	0.89	–	–
0–10	–	0.89	0.91
>10	–	0.88	0.86

Category I: pre-IVF profiles were defined as anti-Müllerian hormone concentration, age and body mass index prior to the start of stimulation.

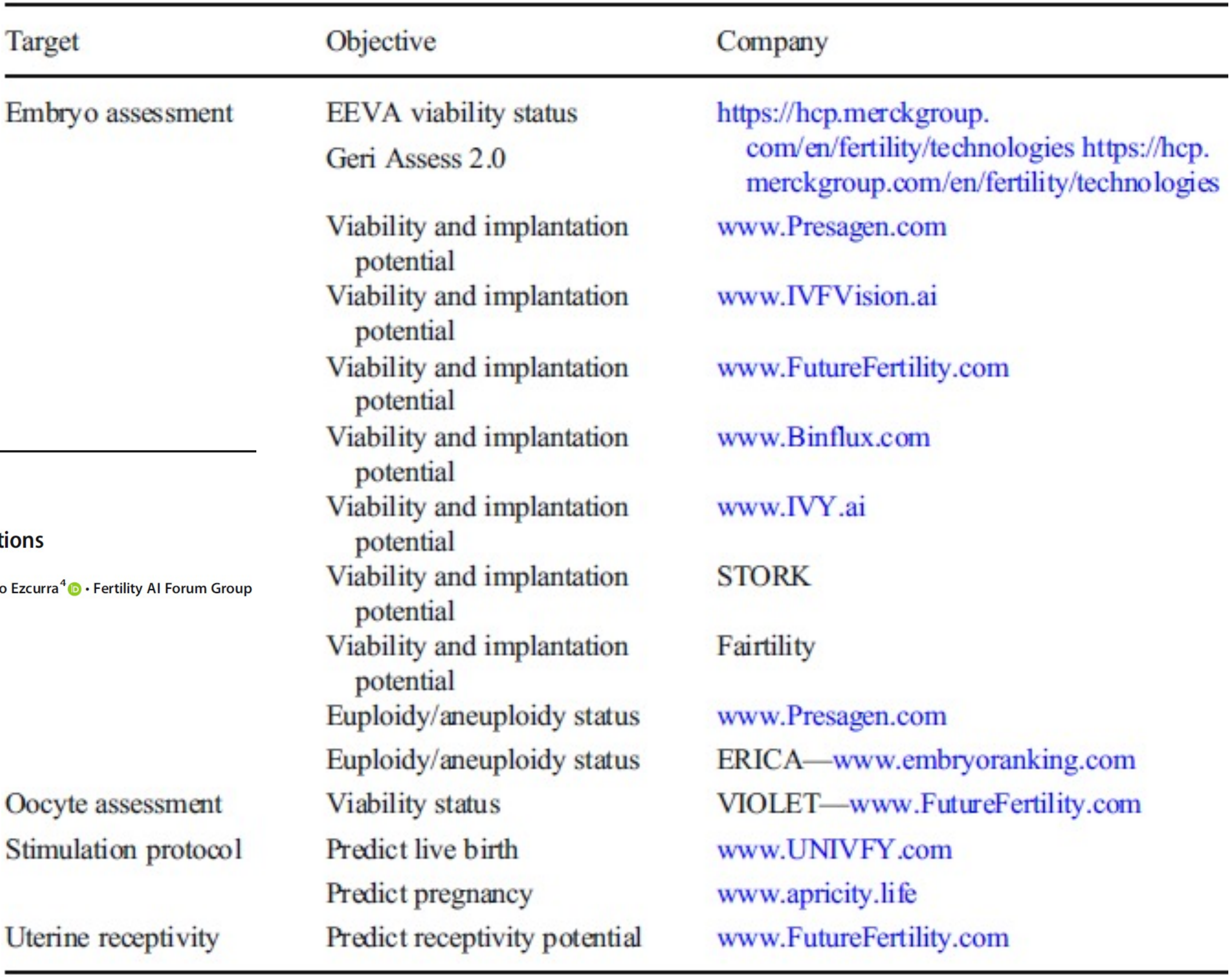
Category II: pre-IVF profile and best-day data were defined as anti-Müllerian hormone concentration, age and body mass index plus oestradiol concentration and follicle number and diameters as measured on the predicted 'best day' or a single day of observation during ovarian stimulation.

Journal of Assisted Reproduction and Genetics (2020) 37:2817–2824
https://doi.org/10.1007/s10815-020-01950-z

OPINION

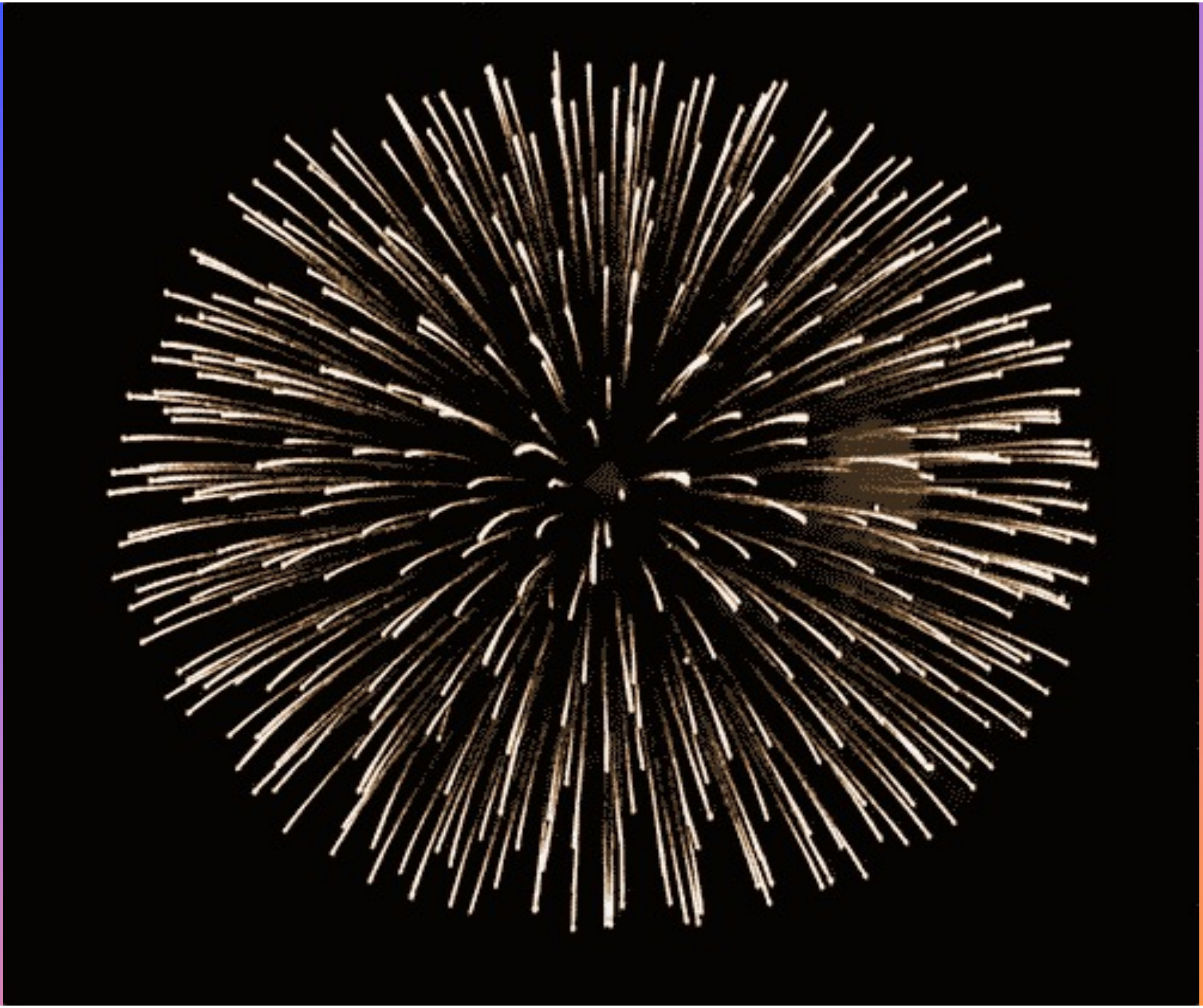
AI in the treatment of fertility: key considerations

Jason Swain[1] • Matthew Tex VerMilyea[2] • Marcos Meseguer[3] • Diego Ezcurra[4] • Fertility AI Forum Group



Target	Objective	Company
Embryo assessment	EEVA viability status	https://hcp.merckgroup.com/en/fertility/technologies
	Geri Assess 2.0	https://hcp.merckgroup.com/en/fertility/technologies
	Viability and implantation potential	www.Presagen.com
	Viability and implantation potential	www.IVFVision.ai
	Viability and implantation potential	www.FutureFertility.com
	Viability and implantation potential	www.Binflux.com
	Viability and implantation potential	www.IVY.ai
	Viability and implantation potential	STORK
	Viability and implantation potential	Fairtility
	Euploidy/aneuploidy status	www.Presagen.com
	Euploidy/aneuploidy status	ERICA—www.embryoranking.com
Oocyte assessment	Viability status	VIOLET—www.FutureFertility.com
Stimulation protocol	Predict live birth	www.UNIVFY.com
	Predict pregnancy	www.apricity.life
Uterine receptivity	Predict receptivity potential	www.FutureFertility.com

Conclusion

- Intelligence Artificielle : des progrès majeurs en perspective !
- Gain de temps
- Efficience croissante
- Optimiser la personnalisation de la prise en charge en AMP de chaque patiente / chaque couple