New technology and criteria for PCOS and PCOM

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EVOLUTION OF DIAGNOSTIC CRITERIA FOR PCOS

- 1990 NIH
  - Anovulation
  - Hyperandrogenemia
  - No reference to ovarian morfology
- 2003. ESHRE/ASRM, Rotterdam
  - Chronic anovulation CA
  - Hyperandrogenism HA
  - Policystic ovaries on ultrasonography PCOM
  - Presence of two of the three criteria
- 2006. AEPCOS (Androgen Excess PCOS Society
  - PCOS is mainly a hyperandrogenic disorderer
  - Existance of hirsuitism/acne and/or hyperandrogenaemia constitutes a sine qua non for PCOS diagnosis
  - Second criterion either CA or PCOM
- 2011. Amsterdam ESHRE/ASRM sponsored 3rd PCOS consensus Workshop Group
  - Identified different phenotypes
  - Separeted most classic phenotype (HA and CA) from CA and PCOM
  - Major metabolic disorders should be adressed in the clinical workup

PCOS - incidence

- NIH criteria / AES

→ 6-8%

- Rotterdam criteria

→ 15-22%

~ 300 mill ♀

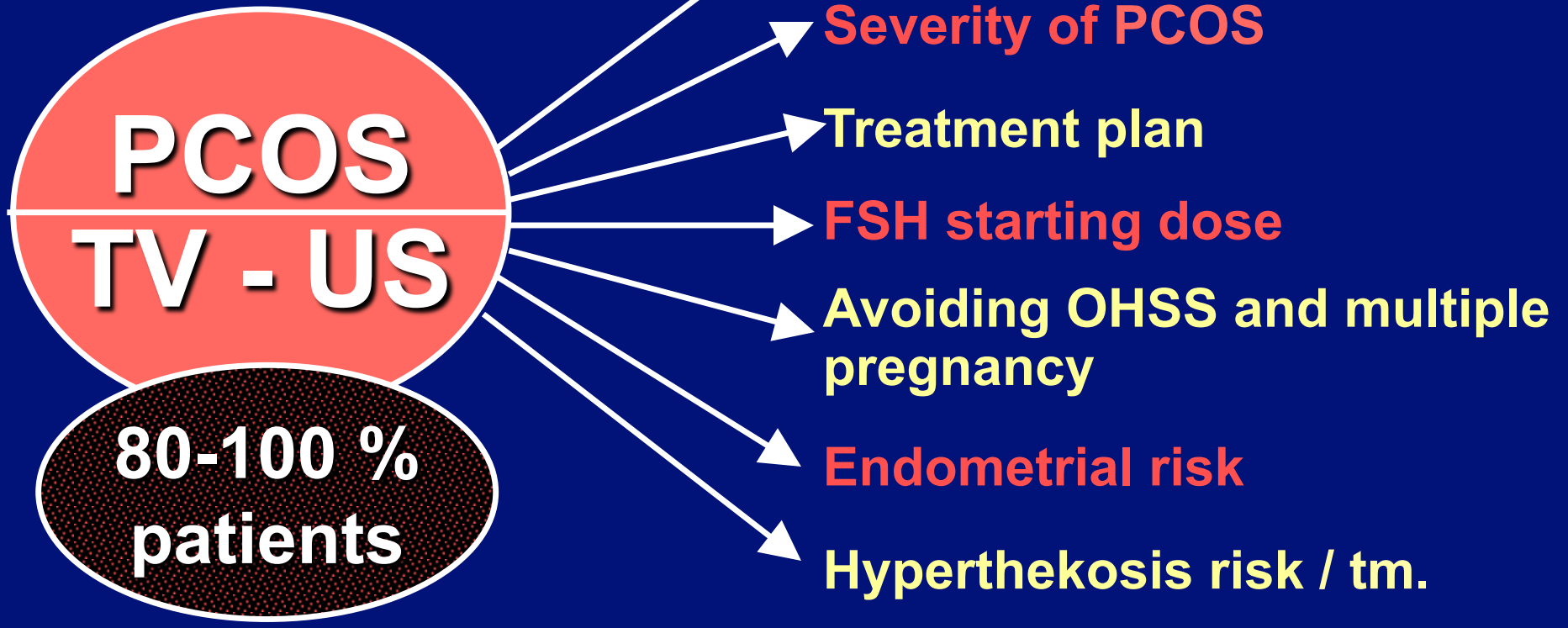
- Croatia

→ 18,4%

Šimunić et al.

→ 199 042 ♀

PCOS: why US is necessary?



- The prevalence of PCOS –
  - Rotterdam criteria
    - GENERAL POPULATION 16.6%
    - INFERTILE POPULATION 20-25%
  - Criteria AFC >19 or AMH > 35 pmol/L
    - GENERAL POPULATION 6.3%
    - INFERTILE POPULATION 8%?

Lauritsen MP, HR 2014.

ULTRASOUND CRITERIA

- PCOM
  - Follicule number
  - Ovarian volume (OV)
  - Ovarian area

- UNIVERSAL CONSENSUS OF THE MAIN CRITERIA
  - FOLLICULAR EXCESS
  - OVARIAN ENLARGEMENT

Conway G, Dewailly D. et al.: The polycystic ovary syndrome: a position statement from the European Society of Endocrinology. European Journal of Endocrinology 2014 171 1-29.

CONTRAVERSY

- Normal values for FNPO (follicle number per ovary)?
- Normal values for OV (ovarian volume)?

US Rotterdam

P C O S

US

- ~~≥12 follicles~~ 2-9 mm in each ovary
- ↑ ovarian volume > 10 ml
- Only 1 ovary

⇨ **NO more** ⇒ stroma

distribution, UZV-CD

FNPO

- Rotterdam 2003 concensus treshold
  - ≥ 12 follicles 2-9 mm in diametar, mean in both ovaries

..met by more then 50% of normal young ovulatory women

Johnston EB et al.The polycystic ovary post-Rotterdam: a common, age-dependent finding in ovulatory women without metabolic signicance. Journal of Clinical Endocrinology and Metabolism 2010 95 4965-4972.

...73% of the control population would have met this definition

Christ JP et al: Follicule number, not assesments of the ovarian stroma, represents the best ultrasonografic marker of PCOS. Fertility Sterility 2014 101 280-287

Why variability and contraversy about the treshold for FNPO

- Method of counting follicles
- Observer variability
- Recent advancements in imagining technology

Unusually high rates of polycystic ovaries in healthy women of reproductive age using the ultrasound based criteria supported by the Rotterdam consensus

New criteria –NO CONSENSUS

≥19 follicles per ovary

- Dewailly D et al: Diagnosis of polycystic ovary syndrome (PCOS): revisitinig the threshold values of follicle count on ultrasound and of the serum AMH level for the definition of polycystic ovaries. Human Reproduction 2011 26 3123-3129.

≥ 26 follicles per ovary

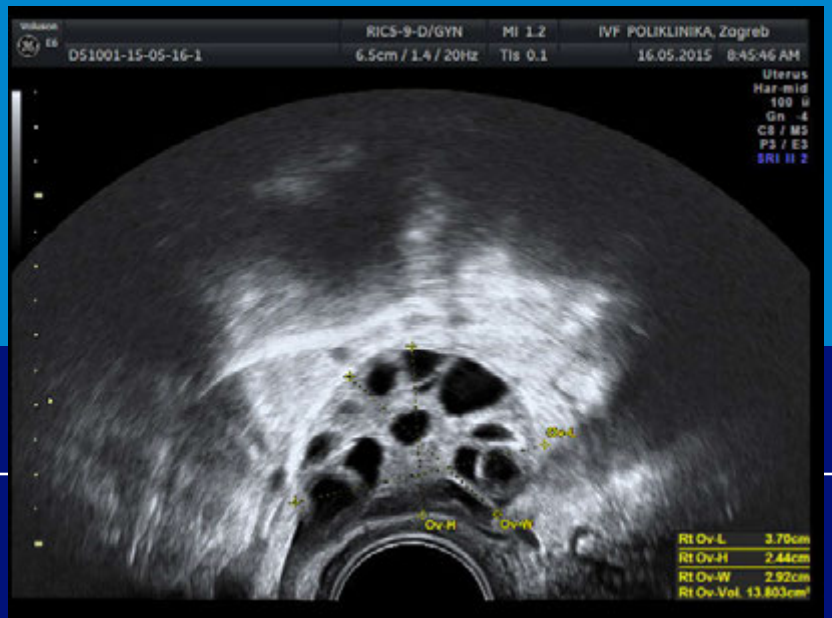
- Lujan ME et al: Updated ulatrasound criteria for polycistic ovary syndrome: reliable tresholds for elevated follicule population and ovarian volume. Human Reproduction 2013 28 1361-1368.

28 follicles per ovary

- Christ JP et al: Follicule number, not assesments of the ovarian stroma, represents the best ultrasonografic marker of PCOS. Fertility Sterility 2014 101 280-287

Ovarian volume (OV)

- Good surrogate marker
- Less sensitivity compared with FNPO
- Recommendation when vaginal route is not feasible – adolescent girls
- **Treshold: ≥10 ml**



Ovarian stroma to total ovarian size ratio

- Cutoff value: 0.32
- Association with hyperandrogenemia
  - Fulghesu AM et al: Ultrasound in PCOS – the measuring of ovarian stroma and relationship with circulating androgens: results of multicentric study. Human reproduction 2007 22 2501-2508

There are few studies to corraborate the diagnostic potential of this parameter.

There is no additional value to include stromal size measurements in clinical practice

Doppler vascular indices

- Lack of uniform data
- Absence of cutoff values
- Impractical

Advantages of 3D ultrasound

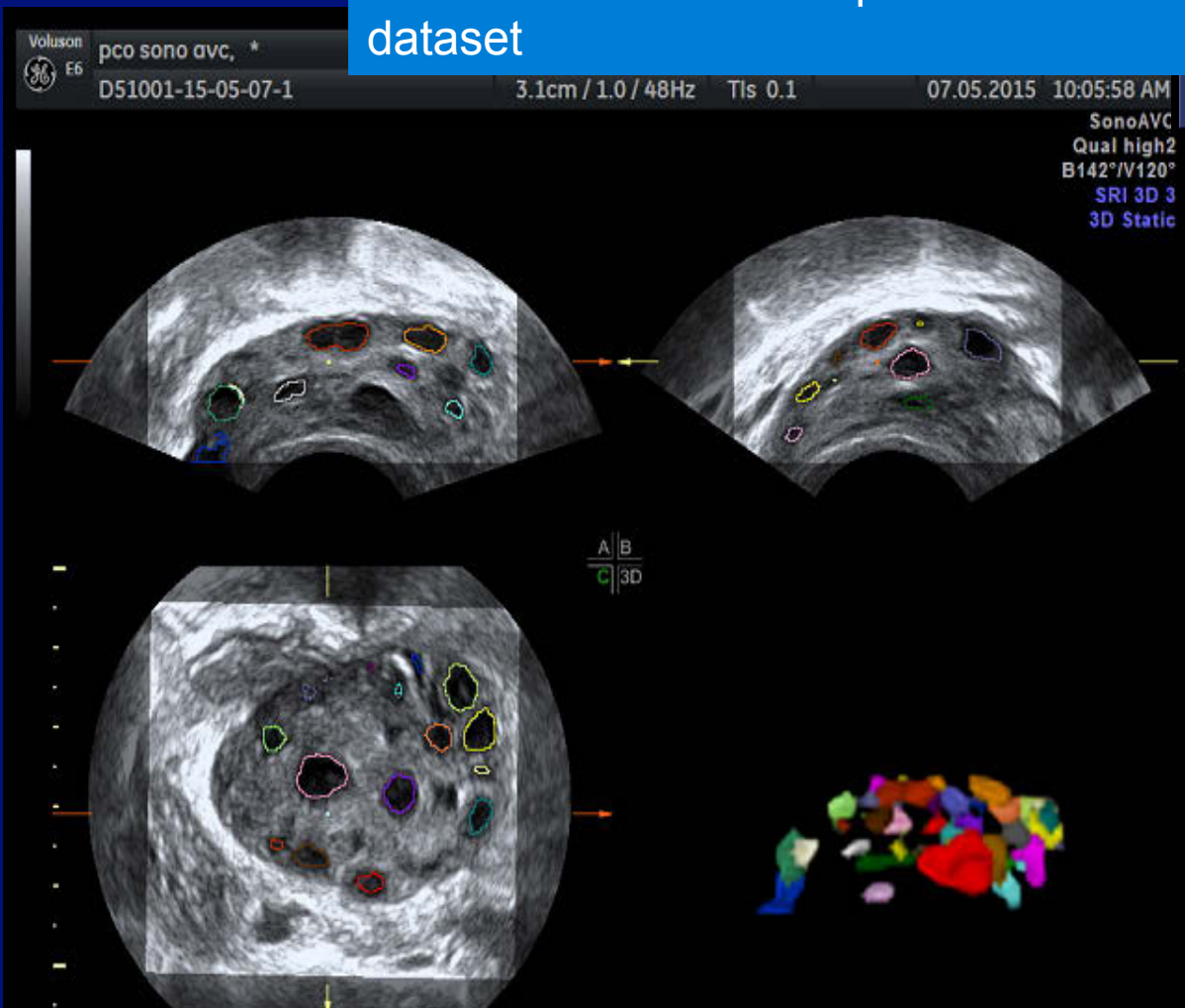
3D method seems to detect more follicles per ovary in subjects with PCOM

- Semiauthomatic method
- Time saving
- Reproducibility of results

sonoAVC

(authomatic volume counting)

detects and quantifies anechoic structures within an acquired 3D dataset



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Date of Exam: 07.05.2015 Page 1 / 6

Exam Type:

Name: pco sono avc | DOB: | Sex: Female

Pat. ID: D51001-15-05-07-1 | Perf. Phys.:

Ref. Phys.:

Indication: | Sonogr.:

LMP: | Day of Cycle: | Gravida: | AB:

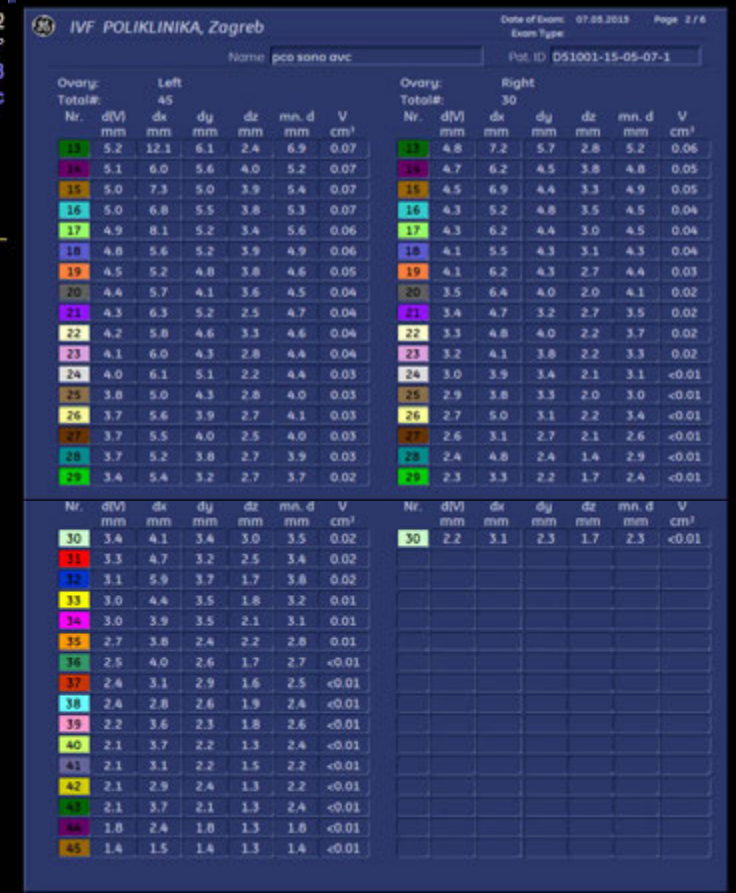
Day of stim.: | Expected Ovul.: | Para: | Ectopic:

Ovary: Left — Total#: 45

Nr.	d(V) mm	dx mm	dy mm	dz mm	mn. d mm	V cm³
1	7.9	11.5	9.7	4.9	8.7	0.26
2	6.5	12.2	7.2	4.5	8.0	0.14
3	5.9	7.6	6.2	4.8	6.2	0.11
4	5.8	9.0	6.2	3.9	6.3	0.10
5	5.7	9.0	6.4	3.4	6.3	0.10
6	5.6	11.1	5.0	3.6	6.6	0.09
7	5.6	9.9	5.6	3.4	6.3	0.09
8	5.5	7.5	6.5	3.6	5.9	0.09
9	5.5	7.7	5.8	3.8	5.8	0.09
10	5.5	7.0	5.9	4.2	5.7	0.09
11	5.4	7.8	6.0	3.8	5.8	0.08
12	5.2	7.7	6.7	3.2	5.9	0.08

Ovary: Right — Total#: 30

Nr.	d(V) mm	dx mm	dy mm	dz mm	mn. d mm	V cm³
1	17.6	30.8	24.6	12.7	22.7	2.86
2	13.5	20.3	16.4	11.1	15.9	1.29
3	6.6	9.6	7.7	4.2	7.2	0.15
4	6.4	10.1	7.2	3.8	7.0	0.14
5	6.3	9.1	7.3	4.3	6.9	0.13
6	6.1	9.5	6.8	3.6	6.6	0.12
7	5.8	6.9	6.3	4.8	6.0	0.10
8	5.6	7.7	6.0	3.9	5.9	0.09
9	5.5	8.5	5.8	3.7	6.0	0.09
10	5.3	7.7	6.6	3.2	5.8	0.08
11	5.0	5.6	5.3	4.4	5.1	0.06
12	4.9	5.8	5.3	3.9	5.0	0.06



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Date of Exam: 07.05.2015 Page 2 / 6

Exam Type:

Name: pco sono avc | Pat. ID: D51001-15-05-07-1

Ovary: Left — Total#: 45

Nr.	d(V) mm	dx mm	dy mm	dz mm	mn. d mm	V cm³
13	5.2	12.1	6.1	2.4	6.9	0.07
14	5.1	6.0	5.6	4.0	5.2	0.07
15	5.0	7.3	5.0	3.9	5.4	0.07
16	5.0	6.8	5.5	3.8	5.3	0.07
17	4.9	8.1	5.2	3.4	5.6	0.06
18	4.8	5.6	5.2	3.9	4.9	0.06
19	4.5	5.2	4.8	3.8	4.6	0.05
20	4.4	5.7	4.1	3.6	4.5	0.04
21	4.3	6.3	5.2	2.5	4.7	0.04
22	4.2	5.8	4.6	3.3	4.6	0.04
23	4.1	6.0	4.3	2.8	4.4	0.04
24	4.0	6.1	5.1	2.2	4.4	0.03
25	3.8	5.0	4.3	2.8	4.0	0.03
26	3.7	5.6	3.9	2.7	4.1	0.03
27	3.7	5.5	4.0	2.5	4.0	0.03
28	3.7	5.2	3.8	2.7	3.9	0.03
29	3.4	5.4	3.2	2.7	3.7	0.02
30	3.4	4.1	3.4	3.0	3.5	0.02
31	3.3	4.7	3.2	2.5	3.4	0.02
32	3.1	5.9	3.7	1.7	3.8	0.02
33	3.0	4.4	3.5	1.8	3.2	0.01
34	3.0	3.9	3.5	2.1	3.1	0.01
35	2.7	3.8	2.4	2.2	2.8	0.01
36	2.5	4.0	2.6	1.7	2.7	<0.01
37	2.4	3.1	2.9	1.6	2.5	<0.01
38	2.4	2.8	2.6	1.9	2.4	<0.01
39	2.2	3.6	2.3	1.8	2.6	<0.01
40	2.1	3.7	2.2	1.3	2.4	<0.01
41	2.1	3.1	2.2	1.5	2.2	<0.01
42	2.1	2.9	2.4	1.3	2.2	<0.01
43	2.1	3.7	2.1	1.3	2.4	<0.01
44	1.8	2.4	1.8	1.3	1.8	<0.01
45	1.4	1.5	1.4	1.3	1.4	<0.01

Ovary: Right — Total#: 30

Nr.	d(V) mm	dx mm	dy mm	dz mm	mn. d mm	V cm³
13	4.8	7.2	5.7	2.8	5.2	0.06
14	4.7	6.2	4.5	3.8	4.8	0.05
15	4.5	6.9	4.4	3.3	4.9	0.05
16	4.3	5.2	4.8	3.5	4.5	0.04
17	4.3	6.2	4.4	3.0	4.5	0.04
18	4.1	5.5	4.3	3.1	4.3	0.04
19	4.1	6.2	4.3	2.7	4.4	0.03
20	3.5	6.4	4.0	2.0	4.1	0.02
21	3.4	4.7	3.2	2.7	3.5	0.02
22	3.3	4.8	4.0	2.2	3.7	0.02
23	3.2	4.1	3.8	2.2	3.3	0.02
24	3.0	3.9	3.4	2.1	3.1	<0.01
25	2.9	3.8	3.3	2.0	3.0	<0.01
26	2.7	5.0	3.1	2.2	3.4	<0.01
27	2.6	3.1	2.7	2.1	2.6	<0.01
28	2.4	4.8	2.4	1.4	2.9	<0.01
29	2.3	3.3	2.2	1.7	2.4	<0.01
30	2.2	3.1	2.3	1.7	2.3	<0.01

Name pco sono avc DOB Sex Female

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Day of stim. Expected Ovul. Para Ectopic

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7	5.8	6.9	6.3	4.8	6.0	0.10
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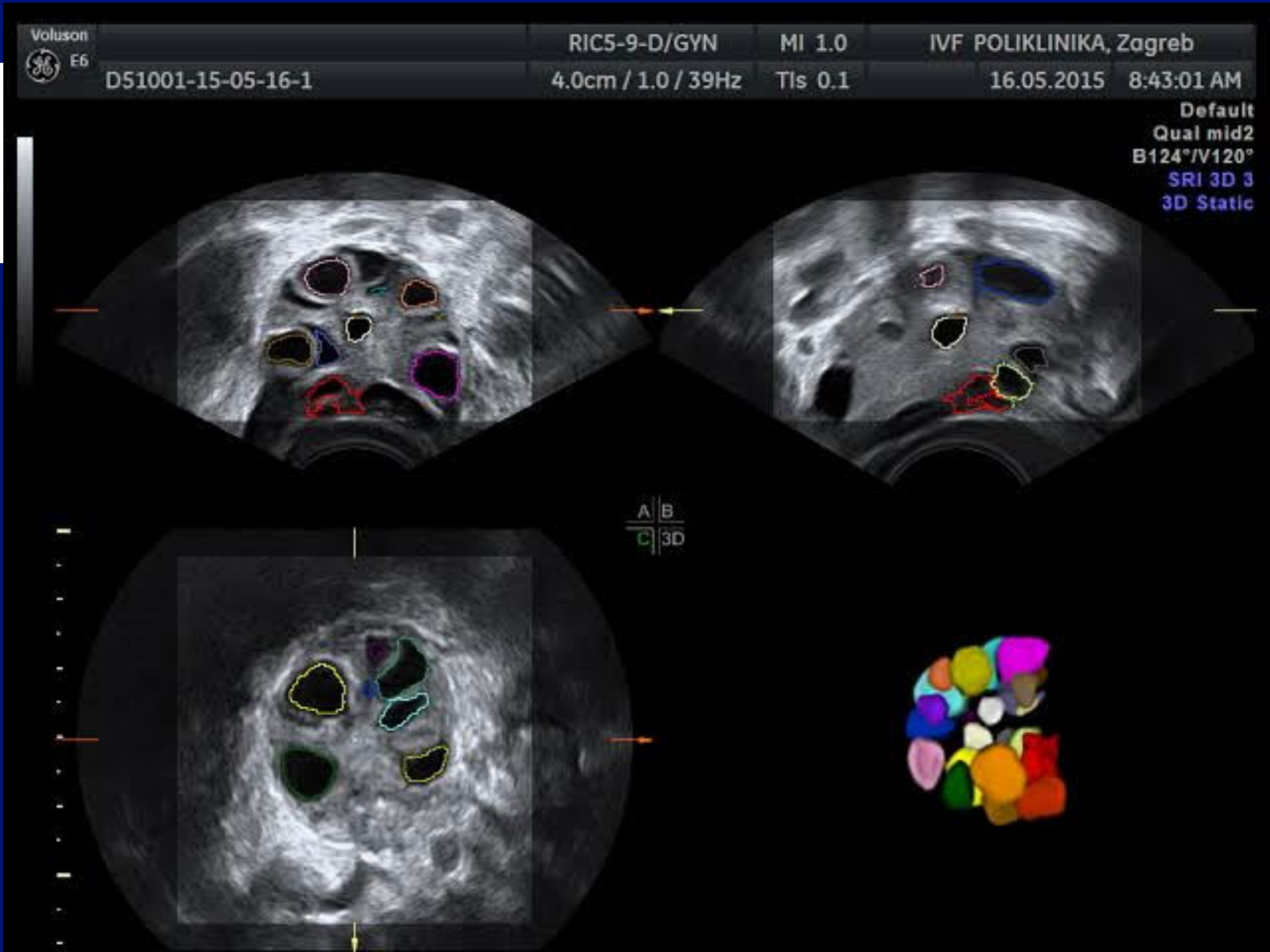
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E6
RIC5-9-D/GYN
MI 1.0
IVF POLIKLINIKA, Zagreb
D51001-15-05-16-1
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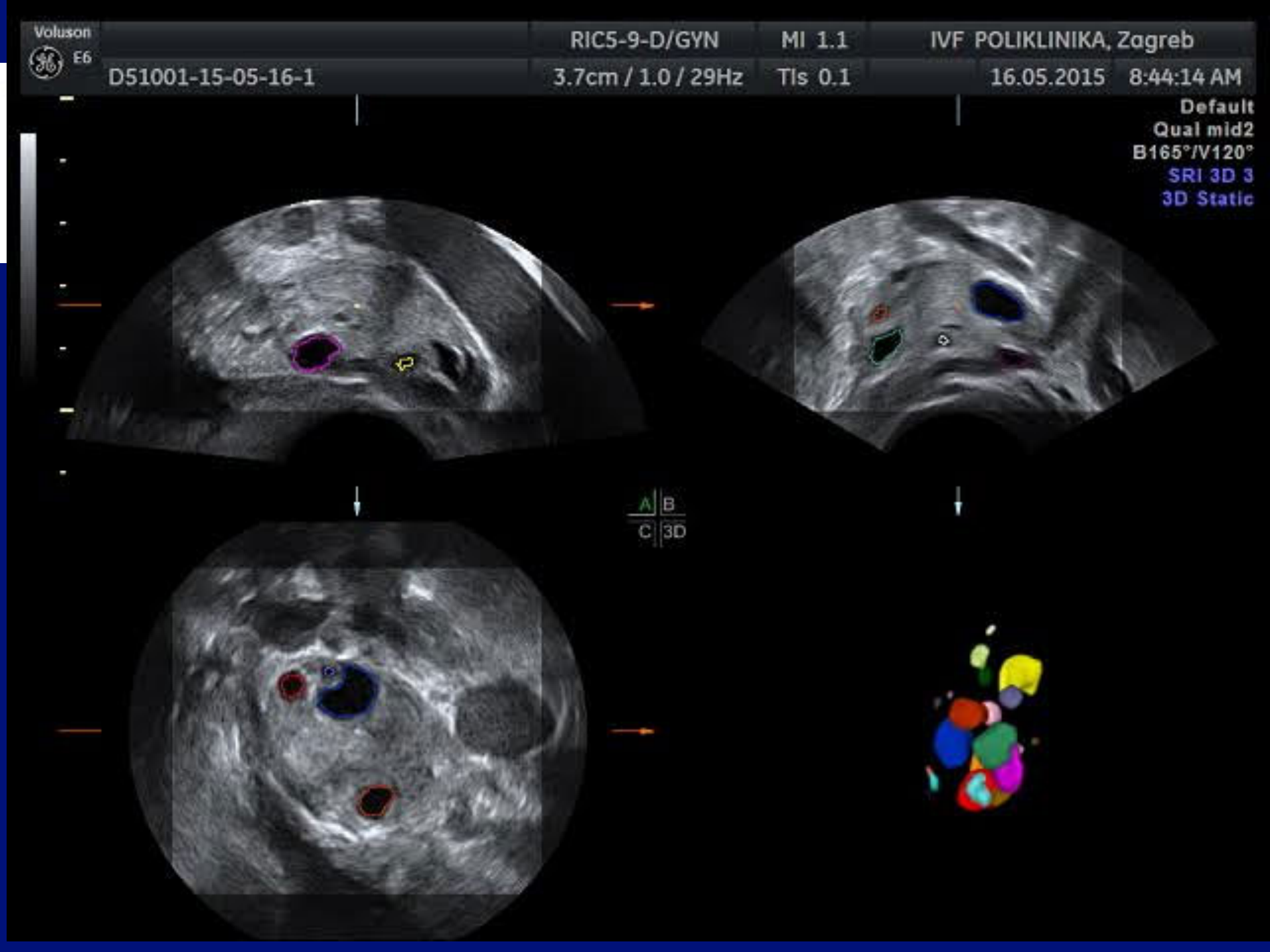
16.05.2015 8:43:01 AM
Default
Qual mid2
B124°/V120°
SRI 3D 3
3D Static
A
B
C
3D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RIC5-9-D/GYN
MI 1.1
IVF POLIKLINIKA, Zagreb
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TIs 0.1
16.05.2015 8:44:14 AM
Default
Qual mid2
B165°/V120°
SRI 3D 3
3D Static
A
B
C
3D

- Manual correction of follicle number
- Technology developed for folliculometry
- Resolution for follicules < 10 mm?
  - further studies are required before recommending its routine use

AMH

- New marker of polycistic ovaries in PCOS
- Serum AMH levels highly corelate with the number of AF
- AMH concentracion high in women with PCOS
- Age related decline in the AFC is also reflected in AMH concentrations
- Treshold ? (>35 pmol/L? , 28 pmol/L)

AMH

- Easier to reproduce then the FC (quality of ultrasound, operator skill)
- Need for single AMH assay
- Simplification of the diagnosis of PCOS
- 15% PCOS - AMH < 30 pmol/L

Lauritsen MP. HR, 2014.

Dewailly D. HR, 2011.

High response ⇒AMH and PCOM / PCOS

- HR incidence 15-20%
- PCOM/PCOS 18-30%

→ same oocyte quality

	Population	AMH pmol/L	top Q embryos
	General / NR	15 – 20	37,3%
	PCOM	40 – 60	38,6%
HR	PCOS • normal cycle	50 – 60	
	PCOS • oligomenorrhoea	70 – 80	34,5%
	PCOS • amenorrhoea	90 - 120	

Sigala,FS,2015.

- 15% PCOS → AMH < 30 pmol/L
- AFC ≥ 25 per ovary
- AF produces more AMH in PCOS

Pigny,HR,2006.
Homburg,HR,2013.
Dewailly,HR,2014.
Bhide,FS,2015.

PCOM/PCOS: the problem of high responders in IVF

- AF in PCOS > AMH production
- US:
  - 12 or 20 follicles - same prediction of HR
    - same prediction for OHSS

    >12 FNPO ~ AFC 25, AMH 30 pmol/L

    >19 FNPO ~ AFC 40, AMH 60 pmol/L

    HR

  Today HR and high oocite number has different approach in IVF/ICSI treatment

PCOM/PCOS dg criteria - IVF

- US
- AMH
- Younger age
- Hyperandrogenism
- Long MC
- Olygomenorhea
- Amenorhea

- FSH starting dose
- Antagonists
- Monitoring E2/P4

OHSS risk

- Agonist trigger
- Freeze all
- Blastocyst culture

CONCLUSION

- Standardization of the follicle counting technique
- The need for regularly updating the thresholds used to define follicle excess
- Serum AMH concentration generated great expectations as a surrogate marker for the follicle excess of PCOM
- The siginificance of PCOM in ovulatory women not showing clinical or biochemical androgen excess