Ultrasound and Folliculogenesis

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ABSTRACT

Ultrasound as well as gynecologic endocrinology are two major advances which enabled revolution in assisted reproduction technology (ART). Today it is impossible to imagine ART without ultrasound.

Keywords: Assisted reproduction technology, Gynecologic endocrinology, Ultrasound.

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INTRODUCTION

No one disagrees that ultrasounds along with gynecologic Endocrinology have been two major advances in our specialty and that they have been the fundamental enablers of the revolution that has occurred in ART.^{1,2} Without ultrasound, ART as we now know it would be inconceivable. The main steps in this “revolution” were:

- Introduction of vaginal probes by Kratochwil in Vienna.
- Description of endometrial changes, folliculogenesis, and the diverse types of the endometrium by Hackelöer in Hamburg.
- The disappearance of laparoscopic follicular aspiration because of the introduction of ultrasound-guided transvaginal aspiration, developed by Feichtinger, also in Vienna.
- Three- (3D) and four-dimensional (4D) ultrasound have improved and eased folliculogenesis control.

Four-dimensional (4D) enables us to capture new planes of vision, improves image quality, and introduces new ultrasound modes (HDlive and silhouette, AVC, VOCAL, inverse mode, etc.) that allows great resolution and evaluation of pelvic organs.

In recent years, the spectacular advances with 4D ultrasonography have generated a new revolution in ART.

In spite of these advances, a review of the literature leads us to raise more questions:

- How can an evaluation of folliculogenesis be improved?
- How can we better evaluate existing antral follicles (AF)?
- How can we know the best moment to administer hCG for the induction of ovulation?
- What is the effect of the dominant follicle luteinization on growing follicles that remain?
- When should a luteal body be considered active, regressive, or luteinized and not broken?

Lastly, discussions related to ultrasound characteristics of the endometrium (thickness, morphology, vascularization, delimitation, and volume) are so ample that it is no simple matter to develop a protocol that guides to adequate evaluation of the concept of endometrial receptivity.

Commentary about the value of color Doppler and Doppler energy along with the recent advances in the varied modes of 3D/4D visualization (Figs 1 to 3) will merit a separate chapter.

ULTRASONOGRAPHIC NOTIONS FOR FOLLICULOGENESIS CONTROL

Among the available means for adequate control of folliculogenesis, only ultrasound is capable of showing the evolution of follicular growth over short time spans. Folliculogenesis starts 70–74 days before ovulation. That is two and a half cycles before its ovulatory cycle.

About 400–500 primordial and primary follicles initiate growth in a different ovarian area each time, with the mechanisms that control each area are still unknown.

- Why in this area?
- Why in this specific ovary?

These events take place independently of the action of hormones from the hypophysis (Figs 1 to 3).

Although the mechanism by which these cells start their growth is not known, it is known that there is an increase in local growth factors and an increase in follicular microvasculature. Furthermore, it is known that the layer of granulosa cells is functional and remains intact. The larger the number of cells in the granulosa layer will result in a greater number of gonadotropin (FSH and LH) receptors, and as a consequence, with a

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Fig. 1: (Top) Nowadays used new US modes for follicle genesis monitoring which are more definitive than the 2D vaginal ultrasound used today. Above and left the three-orthogonal planes and histogram doing the total ovarian volume calculation which is of interest when looking to the ovarian reserve. To the right Doppler energy and tomography ovarian cuts. This modes increases the findings by using only color Doppler. (Below) 2D in orthogonal planes and AVC from the existing antral follicles. Each follicle is shown in a different color. It is easy to count and measure each follicle. The dominant follicle is clearly depicted in blue color

greater probability of follicular. Ovarian folliculogenesis has three well-established phases (Fig.4).

The end of the vast majority of antral and preantral follicles will be their atresia by apoptosis (Fig. 4).

ANTRAL FOLLICLES

There are two basic exploratory ultrasound applications during these events: visualization and antral follicle (AF) count in the basal state.

The number of existing antral follicles in basic ultrasound and, although in lesser magnitude, the ovarian volume, is of great importance for knowledge about the ovarian reserve. To develop an evaluation protocol, it is agreed that the count of antral follicles must be done during the first days of the menstrual cycle. Nevertheless, antral follicle count can be carried out at any phase of the menstrual cycle. Small follicles (2–3 mm) can be seen and measured with vaginal probes. Visualization is much simpler using the different 3D modes: inverse, AVC, VOCAL, and silhouette (Figs 5 and 6).

FOLLICULOGENESIS CONTROL

Vaginal 2D or 3D ultrasound allows optimal evaluation (daily or at short intervals) of follicular growth. When farmers want to determine the best time to pick their oranges they do not need to check on them daily.

They must wait several days to notice size and color changes that indicate when picking must be done. It is the same with follicles. It is advisable to have the first ultrasound evaluation on the second or third day of the cycle. Subsequent evaluations in induced cycles will be done six days after the administration of gonadotropins or four to five days after administration of clomiphene.

We are of the opinion that ultrasound evaluation is sufficient for adequate folliculogenesis control in natural cycles as well as in ART cycles. Additional evaluation of estradiol concentrations has not proven to add additional information that is crucial for adequate control of ovarian stimulation cycles for IVF/ICSI. In the vast majority of cases, ultrasound is enough. In this way laboratory, overwork and unnecessary additional charges are avoided.

FOLLICULOGENESIS IN NATURAL CYCLE

Folliculogenesis varies depending on whether it is spontaneous or induced. As mentioned above, the first (or basal) ultrasound should be performed on the second or third day of the cycle. This would provide approximate knowledge of ovarian reserve.

Follicles between 2 mm and 9 mm are part of the cohort of small antral follicles that are starting the process of maturation. Shortly after, a dominant follicle,

Fig. 2: Follicle genesis. Vascular image around each follicle obtained with 3D angiography and color power Doppler. It is clearly depicted that only preovulatory follicles dispose of a great vascularity located around the whole follicle which will allow fluid transvasation to the follicular fluid without increasing its internal fluid pressure. It can be observed that only antral preovulatory follicles dispose of this enormous perifollicular vascularization. In the above picture, the same follicles observed with AVC mode

Fig. 4: Human folliculogenesis schema. Estimate follicular development (in weeks) from primordial to preovulatory follicle (1): Recruitment of the follicular cohort; Selection of 20–25 antral follicles during the peak of intercycle FSH during the previous cycle; Dominance and maturation of one, and exceptionally, more than one follicle

Fig. 3: Spontaneous folliculogenesis. The new US mode “silhouette” shows a better delimitation of the structure profile and allow a clear delimitation of each antral follicle

distinguished by greater size and faster growth, will appear. The remaining antral follicles will cease to grow or become atretic. It is from this moment that, if so desired, hormonal determinations and ultrasound controls every 48 hours can be done.

Follicle growth and 17β -estradiol production occur in parallel. The follicle is considered to be mature when it produces ~ 250 pg/mL of 17β -estradiol.

Since in natural cycles the relation of follicular growth to estradiol production occurs in a linear manner up to the tenth day of the cycle, these determinations can be avoided. Follicle growth after the tenth day is not linear, but exponential. The closest the follicle gets to ovulation, the fastest is its growth. The follicle grows between 1 mm and 1.2 mm/day up to the tenth day and a mean growth of 1.8 mm/day at the end of the proliferative phase.

Before ovulation the dominant follicle measures 22–25 mm (occasionally, between 18 and 36 mm), and this growth is the only marker that will predict with certainty ovulation (Figs 7 to 10).

A very approximated summary would be (Table 1).

There are other US images that predict an approaching ovulation, but they are not always visible.

VISUALIZATION OF THE CUMULUS OOPHORUS

The cumulus oophorus can be seen 20% of the times with transvaginal ultrasound. However, with 3D/4D/HD Live it can be seen 50% of the times as well as follicles larger than 18 mm always (Figs 11 to 13).

The cumulus oophorus appears less than 24 hours before ovulation. What we are really observing are the more mature follicles which are likely to contain meta-phase II oocytes, and therefore, ideal for fertilization (or for aspiration in cases of cycles induced for IVF/ICSI).

Fig. 5: Silhouette mode of a normal ovarian section showing three growing and various atretic follicles. Below: Antral follicles count with AVC, in colors and silhouette modes. Thanks to these new modes our knowledge and the calculation form of the antral follicles for the ovarian reserve have dramatically changed in the last years

Fig. 6: Automatic volume calculation using VOCAL mode. We observe the whole ovarian surface and, indoor, the follicles. This calculation, recommended by the Rotterdam classification in cases of polycystic ovaries is, in our opinion, less valuable than the simple AF count

UNCOUPLING OF THE GRANULOSA

- It occurs in 5–12 hours before ovulation (Fig. 14).
- It occurs when the theca becomes edematous under the effect of hyaluronidase.
- It appears as an irregular, dark halo.

As is the case with the previous sign, it is difficult to observe with transvaginal sonography. But with 3D/4D/HDlive it can be seen 50% of the times in ovulatory follicles. As is the case with visualization of the cumulus, it is a sign that indicates a potential for follicular maturation.

Fig. 7: Dominant also called De Graaf follicle. Next to the follicle various small antral follicles. The arrow shows a part of the granulosa sheet uncoupling, an US sign of imminent ovulation

APPEARANCE OF THE “ROSEBUSH THORNS”

In these cases, the granulosa layer is already irregular, it is undulating, breaking apart, and indentations appear towards the interior of the follicle (Fig. 14). These last two images coincide with the onset of luteinization. As was the case with the two last images, it is difficult to observe with transvaginal ultrasound (18%) and should be looked for with 3D and HDlive (60%).

OVULATION

Upon rupture of the wall of the follicle follicular fluid escapes, a phenomenon that is not explosive, but that may take from a few seconds to 30–45 minutes.

Fig. 8: Ripe preovulatory follicle. We are visualizing the whole follicle cavity. 2D/3D ultrasound is visualized in a case of spontaneous ovulation. The size arrive 21–25 mm

Fig. 9: Mature follicle in a proliferation phase HDlive US with various light focus orientations

Fig. 10: Mature follicle. HDlive. This mode allows to see the whole inner part of the follicle observed from different light angles appearing lights and shadows which increase the vision quality, Also maximal luminescence can be employed (below right)

Table 1: US characteristics mature preovulatory or de-graaf follicle

Size ≥ 21 –25 mm, in the spontaneous cycle.
Size ≥ 18 mm, in stimulation with clomiphene and/or hMG
Size ≥ 15 mm, in stimulation with gonadotropins
Production above 250 pg/mL of 17β estradiol
Visualization of the cumulus oophorus
Visualization of the rosebush thorns sign or irregular contour
Visualization of the uncoupling of the granulosa

- Sudden follicle disappearance (a not very useful indirect sign. It is more important if it is accompanied by a simultaneous appearance of fluid in Douglas's sac).
- The appearance of the typical corpus luteum images: After a few minutes, the follicular antrum fills partially or totally with blood with the simultaneous appearance of the typical image of "hemorrhagic" corpus luteum, of irregular shape, internal echoes, and frequently, thickened wall.

This is the first really pathognomonic image and it is found in practically 100% of cases (Fig. 15).

After the appearance of this, the corpus luteum takes one of the three US presentation forms, all absolutely pathognomonic of ovulation.

Many ultrasound signs have been described, both with transabdominal and transvaginal ultrasound, but we will list the ones we consider to be of clinical interest.

Fig. 11: Cumulus oophorus marked with yellow arrows and observed with 4D, HDlive and VOCAL (above). Below three cuts of the same cumulus oophorus using HDlive

Fig. 12: Cumulus oophorus

Fig. 13: Cumulus oophorus, in his upper part we see the uncoupling of a part of the granulosa (arrow)

It is important to emphasize that two of the ultrasound images, the reticular, and especially the eco-gray, may be unnoticed with 2D transvaginal ultrasound, especially if Doppler is not used Fig 16).

CORPUS LUTEUM

The three ultrasound images of the corpus luteum are:

- Three-layered corpus luteum

The corpus luteum reveals an external hyper-refrangent layer with transvaginal 2D, due to thickening of the theca wall, an intermediate gray layer, due to the refringence of the luteinized theca granulosa, and an internal and central dark layer that is due to blood accumulation. This is the most common image. It is present in 90% of cases (Figs 16 and 17).

Fig. 14: Rosebush thorns (red arrow)

Corpus Luteum with a Reticular Pattern

This image usually appears 48–72 hours after ovulation.

It is produced by a clot, reticulin fibers, collagen, and disseminated luteinized cells that they confer a reticular aspect to the corpus luteum (Fig. 18).

Eco-gray Corpus Luteum

This image is difficult to differentiate from ovarian stromal but very simple to observe with Doppler, since the characteristic intense peripheral vascularization of very low resistance that is known as "ring of fire," appears (Fig. 19). Without Doppler, it may remain unnoticed and be confused with ovarian stromal. With 3D Doppler diagnosis is very easy (Fig. 19).

Fig. 15: Hemorrhagic corpus luteum depicted with 3D tomographic and HDlive views

This image is produced by the luteinized granulosa-theca that is occupying the entire follicular cavity without the presence of blood or clots. It is typical after day 21 of the cycle (Figs 19 and 20).

Given the enormous vascularization that is produced by the invasion of vessels from the luteinized theca-granulosa, Doppler study is of extraordinary help.

The corpus luteum attains a 2–3 cm size, but it can easily grow to 5 cm and may be confused with pathologic cysts or other tumors.

This image disappears with menstruation.

All of these ovarian changes will be accompanied by corresponding endometrial changes that we will address further ahead.

Follicles that persist after day 14 without presenting corpus luteum imaging, and naturally, without Doppler effect changes are unruptured luteinized follicles (ULF).

These are not unusual (they are observed in 6% of induced cycles).

DOPPLER IN A NATURAL CYCLE

Except for 24 hours prior to ovulation when perifollicular vascularization can be detected, Doppler has no application in spontaneous folliculogenesis.

Neither does it predict hyperstimulation in induced cycles.

During the 24 hours before ovulation, the dominant follicle is surrounded by low resistance, a thin vascular layer that occupies 50–75% of the follicular periphery (Fig. 21).

CORPUS LUTEUM FUNCTIONALITY

Doppler study evaluates corpus luteum function, which becomes an exceptional application of ultrasound.

Fig. 16: Three-layered corpus luteum visualized with three-orthogonal planes and power Doppler. The central part is clearly depicted as eco-negative image (blood). At its around, an eco-gray sheet, the luteinized granulosa-theca sheet, and in the outer part and with numerous vessels showing the typical image of "the ring of fire" a more white sheet

Fig. 17: Three sheet HDlive corpus luteum. The yellow arrow shows the cavity, the green the granulosa and the red one the theca layer. The above left part of the figure shows the “fire ring” power Doppler, typical image, as well as the corpus luteum in maximum luminescence (above right)

The luteinized granulosa-theca is rich in thick, very low resistance blood vessels.

Because of this the “ring of fire” above mentioned that is formed by all the vessels that surround the corpus luteum periphery are pathognomonic of a mature follicle and subsequently, of the corpus luteum. It is present in all cases, independently of the type of corpus luteum that appears (Figs 16, 19 and 21).

Measurement of resistive and pulsatility indexes provide us with knowledge of its functional activity. We can also evaluate whether there is corpus luteum insufficiency if impedance remains high or if there is an increase in impedance during the secretory phase.

FOLLICULOGENESIS IN AN INDUCED CYCLE

Any protocol of medical ovulation induction is “antiphysiological.”

All of these protocols (clomiphene and letrozole included) produce hyperstimulation as a consequence, by selecting a greater number of follicles that develop faster and in a shorter time.

Although this effect seems to be theoretically counter-productive, it really isn't, because humans have millions of primordial and primary follicles to be used from the seventh month of intrauterine life on.

At puberty, between 11 years and 13 years of age, the ovary has 350,000 follicles that will produce 400–450 ovulations during reproductive life.

In other words, the ovarian reserve is high.

Medical induction of multiple follicles with subsequent ovulation will not end their supply prematurely.

This knowledge is fundamental for ultrasound control and evaluation of the differences between spontaneous and induced folliculogenesis.

In induced folliculogenesis a base ultrasound should be done to evaluate ovarian reserve.

The following ultrasound should be done 5 or 6 days after stimulation with gonadotropins or 3–4 days of finishing clomiphene or letrozole induction.

It does not make sense to evaluate earlier with ultrasound. Neither should estradiol levels be done in those days.

Follicular growth is not synchronic. Existing antral follicles initiate their growth, but they initiate it at different times and at different speeds.

This lack of synchrony is one of the basic problems of ovulation induction.

The growth rate is faster than with spontaneous ovulation.

Follicles grow exponentially and much faster.

Once hCG is administered to liberate ovulation with a follicular diameter of 17–18 mm, follicles continue growing for about 40 hours.

Follicle growth does not occur in parallel with 17 β -estradiol production.

The global level represents the total production of all follicles.

Fig. 18: Corpus luteum reticularis. Observe how well the reticulum is visualized using HDlive and maximum luminescence

Fig. 19: An eco-gray corpus luteum with the characteristic "ring of fire" produced by the enormous quantity of vessels which are surrounding the pre-ovulatory follicle as well as the corpus luteum. We are showing the "ring" with color and Doppler energy. In the image center, and in red color, the volume of the corpus luteum is calculated with VOCAL

Fig. 20: Gray corpus depicted with HDlive (yellow arrow). This image is difficult to differentiate from ovarian stromal, but very simple to observe with Doppler, since the characteristic intense peripheral vascularization of very low resistance that is known as "ring of fire"

But since growth is not synchronic, that is, production by follicles of different sizes and growing at different speeds, and they will produce different quantities of estradiol.

The global level must be divided by the total number of follicles observed to estimate the approximate production of each one.

The number obtained is therefore only an approximation.

There are some follicles that produce much estradiol and others a scant amount.

The value obtained from this division presupposes that all follicles produce identical amounts of hormone, which is not true.

The largest follicle does not always contain the most mature oocyte, neither is it always the one with the highest hormonal production.

For this reason, it is advisable to aspirate all follicles that exceed 14 mm and all those that show an oocyte-cumulus complex.

As it may be noticed, ultrasound is a basic need for adequate control of a cycle by ovarian stimulation.

The cycle will be canceled when more than 10 antral follicles are observed and/or estradiol is above 2,500 pg/mL.

An exception, of course, will be when ovulation induction is done with a subcutaneous agonist, the so-called "agonist bolus."

Fig. 21: Hyperstimulation showed with Doppler energy. Many ovulatory follicles all showing “ring of fire” are depicted. We also show the 3D angio-Doppler vascularity (below right)

DOPPLER IN AN INDUCED CYCLE

Although there was an expectation that with ultrasonography it would be possible to avoid the potentially grave complication of ovarian hyperstimulation syndrome, we believe that neither 2D nor 3D angiography can effectively prevent it (Fig. 21).

This complication can occur independently of the size or number of ovarian perifollicular or medullar vessels existent.

The follicular growth and number must be monitored while stimulation is underway.

NEW ULTRASOUND MODES

Ultrasound should guide the moment of hCG administration for:

- The collection of the greatest number of best quality oocytes
- Obtaining in this way good embryos, and,
- Increasing the rate of gestations.

The new ultrasound modes, applied to ovulation induction, are contributing relevant data in relation to the actual modes used in reproduction: AVC, inverse mode, VOCAL, HD Live, and Silhouette.

AVC and VOCAL

Advantages provided

Semiautomatic evaluation of antral follicle number, their diameters and the volume of their follicular fluid

in a much more precise way than was up to now done (Figs 22 to 25).

This is of utmost importance for prediction of ovarian response and selection of stimulation protocol.

Volumetric appraisal of each antral follicle.

This has allowed us to find out that:

- A 1 mL volume corresponds with a diameter >12 mm.
- A 4 mL volume corresponds with a diameter >18 to 20 mm.
- A 7 mL volume corresponds with a diameter > 24 mm.

The value obtained with this technology correlates better with the degree of oocyte maturation observed after aspiration.

From all this we have deduced something very important for clinical care:

- The dominant follicle will not affect the fertilization of smaller antral follicles that are also aspirated for IVF procedures.
- Aspiration of follicles larger than 12–14 mm allows recovery of phase II oocytes.
- Following hCG administration, the greatest number of mature oocytes are obtained from follicles between 18 and 20 mm. It is not necessary to wait for larger follicles. Because of this more than only larger antral follicles can be aspirated with a likelihood of obtaining oocytes.
- The VOCAL mode is especially interesting in the volumetric evaluation either of the wall ovary as well as for each AF (Figs 6, 19 and 26). Ovarian volume is nowadays considered diagnostic criteria in polycystic ovarian syndrome.

Fig. 22: Image of a low ovarian reserve. AVC and surface mode are showing very few follicles in the cortical part of the ovary (AVC, above left, surface 3D mode above right and below left, and inverse mode below right)

Fig. 23: Low ovarian reserve image. Only four AFs are shown with 2D but also, and very specially, when using AVC (below right)

INVERSE MODE

This is a very interesting mode for evaluation of the number and volume of antral follicles (Figs 26 and 27). It is useful for calculating ovarian reserve.

By applying this mode, the ovarian parenchyma is not seen. The echo-negative follicles become echo-positive.

Recently, the use of this mode has come into question because it seems that small antral follicles are not seen (Fig. 28).

Fig. 24: Excellent answer to gonadotropins due to existing a very good ovarian reserve. 2D/3D, HDlive, inverse mode and AVC, of an hyperstimulated ovary. The existing AF, better observed than in 2D, appears in different colors. The computer calculates automatically the number, their measurements and volume

Fig. 25: AVC mode. High response to ovulation induction, risk of hyperstimulation. Newly each AF appear with a different color and the software will calculate its volume. In this way the follicles to be punctured can be selected

HDLIVE AND SILHOUETTE MODES

As we have insisted repeatedly, HD Live has been the first ultrasound mode, following the introduction of high-frequency vaginal probes that have improved image quality (Fig. 29).

Silhouette mode has been introduced recently. It helps define more neatly the images (Fig. 30). We allude to this mode in several figures.

STUDY OF THE ENDOMETRIUM

In folliculogenesis, almost as important as the impact on oocytes is the effect on the endometrium, also known as endometrial receptivity.

Ultrasound parameters associated with reproductive results in IVF/ICSI cycles

- Endometrial thickness
- Endometrial pattern (echogenicity and homogeneity)
- Volume, and
- Vascularization findings with 3D/4D

Endometrial thickness

Although still a controversial subject, we considered >8 mm an adequate endometrial thickness. However, we recognize that gestations are possible with lesser thicknesses, even <4–5 mm.

Echogenicity and Homogeneity

The best reproductive results are obtained in IVF/ICSI cycles when the trilaminar line is observed during the periovulatory period.

Fig. 26: Inverse mode of an ovary with an excellent reserve

Fig. 27: AF calculation using inverse mode in a case of hyperstimulation

Endometrial Volume

Not one woman became pregnant when the endometrial volume was <2 mL. Gestation occurred only in 5% of women with a 2–3 mL volume, and in all cases where gestation was achieved the volume was >6 mL (Figs 31 and 32).

Endometrial Vascularization

Angio-power 3D Doppler must be used for this evaluation. There is a significant correlation between vascular indexes and reproductive success (Fig. 33).

Ovarian Endocrinologic Pathologies

Polycystic ovarian syndrome (PCOS) is the most common endocrinopathy in the reproductive age, affects the 12–21%, and after the advanced age, the second cause of infertility in women.

It's a complex endocrine situation due to its heterogeneity and the existing doubts about its etiology.

Various groups of investigators suggest that the origin of PCOS is genetic (polygenic) and/or one

Fig. 28: Inverse mode of an ovary with excellent reserve. Each follicle appears in yellow color

androgenic medium Ambiental is effected during the fetal live, which involves the programation of the metabolic/endocrine axis, more specifically metabolism of carbohydrates and the adrenal secretion

Due to that, its diagnosis is based in clinical, biologic and morphologic criteria its definition has suffered various revisions:

In the Consensus Conference of the National Institute of Health (NIH) in 1990 the PCOS was defined as:

- Chronic anovulation with clinic and/or biochemical hyperandrogenism, excluding other etiologies which are clinically similar such as thyroid or adrenal dysfunction.

Fig. 29: 3D, HDlive and AVC in an hyperstimulated ovary. Look at the quality of the obtained images. Compare with the 2D vaginal images (below left) in orthogonal planes

Fig. 30: Mode 3D HDlive, and using magic cut, of the cavity. Silhouette of a normal endometrium

Fig. 31: VOCAL mode. This is the ideal technique to evaluate the ovarian response as well as the uterine receptivity. To the left the picture shows how we are measuring the follicular volume. To the right the endometrial volume which appears very well defined from the myometrium

Fig. 32: 3D, VOCAL and reconstruction from modes (below left). We see an ovary with scarce reserve and its corresponding volume automatically calculated with the VOCAL mode. The ovary is very small and the US machine brings electronically volume values (above and right, yellow color)

Fig. 33: VOCAL of a normal uterus also with 3D-Doppler-angiography. A clear endometrial, subendometrial and myometrium vascularization is depicted

In the year 2003, the Rotterdam consensus of the la European Society for Human Reproduction/ American Society of Reproductive Medicine (ESHRE/ASRM) proposed that the diagnosis must include two of the following criteria:

- Oligo and/or anovulation,
 - Clinic and/or biochemical Hyperandrogenism, and
 - Polycystic ovaries using the US
- Also excluding other etiologies as above mentioned. This syndrome is ultrasound characterized by:
- Numerous small same sized peripheric antral follicles
 - With an increased medullary tissue
 - Monotonous and persistent ovarian central vascularization without cyclic changes.

Fig. 34: 3D, 4D and HDlive of typical PCOS

Fig. 35: VOCAL, left, and inverse mode, right, of a PCOS

Fig. 36: Transvaginal 2D US, left, and the new silhouette mode, right, in typical PCOS

The US is nowadays an essential part of the diagnostic criteria, and 3D, HDlive (Fig. 34) VOCAL, inverse mode (Fig. 35) and silhouette (Fig. 36) show more definitive images than transvaginal 2D.

The size of the ovarian medullaris is not considered in the Rotterdam Criteria. We considered this part important for the diagnosis due to a bigger size. Only

using this new technology (Fig. 37) the real medullaris size can be estimated.

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Fig. 37: Double niche section of the ovarian medulla is shown in red and yellow color.
The computer calculates its real size (yellow arrows)

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