Three-dimensional Ultrasound in Infertility

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Abstract: Moving forward from the first approach of three dimensional ultrasound, as a new gadget for technicians, the method makes proof of its use in an increasing number of medical fields.

Aim: The present paper, and its graphic back-up, are intended as a visual testimony of the fact that 3D ultrasound is much more than a simple generator of “nice”, commercial, images. Moreover, its use may be extended from obstetrics to gynecological pathology, especially in cases related to infertility.

Material and methods: we performed a review of the main local infertility causes and their perception by the three dimensional ultrasound, as compared to the conventional methods. General literature citations were completed with personal cases and images. In our research we used a Kretz – Voluson Expert 730 ultrasound machine with a full logistic equipment. Our database was completed over a period of 18 months and included various pathology, such as uterine anomalies, fibroids, polyps, ovarian cysts and many others.

Results: Three dimensional ultrasound represents the best tool in evaluating the uterine cavity, the endometrium, assessing its volume and vascularity pattern. It also offers a very good image of the uterine structure, the adnexal morphology and their relationship. It performs a thorough pelvic assessment by a single examination. Moreover, it may realize a histerosalpingography, which is as efficient as the radiological method, but easier and with less side effects.

Conclusions: Even though it is technically more difficult and time consuming, a good practice and a high quality ultrasound equipment offer a series of benefits over any other kind of investigation.

INTRODUCTION

Over the past decade there was a very important progress in digital technology, bringing along the development of the main diagnostic tool in most clinical fields, the ultrasound. With the increasing utility of the transvaginal ultrasound, the female pelvis became more and more accessible, a wider variety of gynecological pathology was open to diagnosis and treatment. Real time conventional scan and Doppler analysis are now part of the routine pelvic exam and an accurate evaluation allows gathering a number of anatomical and even histological details, in search for functional information, such as luteal phase deficiency or the implantation prognosis. In this field, the three dimensional ultrasound seemed a natural step. Initially regarded as an experimental investigation tool, with few clinical utilities, it soon developed into a complementary method for obstetrics, where the liquid environment surrounding the fetus makes it possible to achieve images that are mainly spectacular and commercial. On the other hand, three and four dimensional ultrasound (3D/4D) examination of the fetus offers a general surface image, with functional informations and even data about the internal organs, using the new technologies, such as STIC, minimum mode and reconstruction of the vascular structures. These technical acquisitions promoted 3D/4D ultrasound to a higher level, from a simple “gadget” for technicians, generator of “nice” images, to a useful diagnostic tool, with a very promising future.

Gynecological examination was initially doomed by the lack of a fluid environment. The first images obtained were at least disappointing. Only after the development of the new technologies and rendering modes it became possible to acquire valuable diagnostic images of the female genital organs. The most important advantage was the visualization of the coronal plane. It was a point of view completely new for pelvic examination, even though it is based on the well known fact that conventional ultrasound is a two-dimensional rendering mode of a three dimensional organ. Even with technical advances in gynecological 3D ultrasound, the coronal plane still remains the most important acquisition. The basis of the 3D examination in gynecology, derived straight from the surface rendering mode in obstetrics, consists in a progressive plane-by-plane two-dimensional scan, with digital image reconstruction. Starting from this point there are several possible rendering modes:

Thick-slice Rendering Mode

It represents the basic acquisition type, generated by a single scan of a limited number of planes that create a “slice” in the target organ, centered by a region of interest. The thinner the slice, the better the quality of the image. On the other hand, selecting a limited territory may leave outside investigational
area possible important diagnostic details. The key to a good, diagnostic image is a very good two-dimensional section. The main utility of this rendering mode in gynecology is the visualization of the endometrium. Better images are obtained with a thick, echogenic tissue, during the secretory phase. The acquisition should be in a perfect sagittal plane and the result is a coronal plane histogram.

Multiplanar Rendering Mode
(TUI – tomographic ultrasound imaging)

This rendering mode is derived from tomography and consists in sectioning the volume into a pre-determined number of slices, which are successively displayed. The final images are conventional, but the acquisition is three-dimensional. The main advantage is that from a single scan we can obtain data regarding structures at different levels. Moreover, the examination time is consistently reduced. The number and thickness of the slices may be subsequently modified, without further patient examination.²

Inversion and Minimum Mode

Inversion mode implies a photographic switch in the image aspect, such as transonic structures appear of solid consistency and the echogenic surrounding elements, appear as a liquid environment. The result is a better definition of the contours and relations with connecting structures in the region of interest. Moreover, by digital cutting, it is possible to alienate unwanted elements, rotate the section and create a very good anatomical image.³

Minimum mode enhances transonic structures, without changing their appearance in the final image. It shadows away solid organs, in order to visualize their fluid content.

This rendering mode is best employed for fluid structures such as ovarian cysts or follicles, as well as the uterine cavity during the saline infusion sonohysterography. The shape, the volume, as well as the print created by submucous myomas or polyps are easily detected.

Volume Contrast Imaging (VCI)

Employed statically, as well as dynamically, this rendering mode is based on enhancing contrast and underlying the shape of solid structures. It can offer images in two planes:

- plane A (VCI-A), the conventional section plane, with limited use
- plane C (VCI-C), an image of the coronal plane. It offers a direct view of the coronal plane, with a contrast enhancement.⁴

VOCAL II (virtual organ computer aided analysis)

One of the newest ultrasound technologies, it was created for accurate volume calculations of solid or fluid structures. It starts with a basic static acquisition of the interest region, followed by a contour trace in two planes, while the volume is rotated in the third plane with a predetermined angle. The actual volume calculation is computer generated after the volume is completely traced.⁴ The acquisition may be improved by adding Doppler analysis, thus creating a vascular volume. There are a number of vascular parameters that can be digitally detected. This tool is extremely useful in generating an implantation prognosis in stimulated cycles, according to the type and degree of endometrial vascularity.⁵

3D and 4D Angiography

It consists of a highly spectacular rendering mode of the vascular structures, either statically or dynamically. The acquisition is based on power Doppler or high density flow (HD flow). The diagnostic informations are strictly anatomical, descriptive, no functional data can be provided.

The image may be viewed as a simple angiography or integrated in the surrounding solid structure, as a “glass body” image, with very little details about the relations with the organ (Fig. 1).

There is a particular investigation in which 3D angiography is very useful, that is the saline infusion hysterosalpingography, when the fluid passage through the tubes may be perceived and rendered as a 3D Doppler image.

MATERIAL AND METHOD

In order to assess the benefit of 3D/4D ultrasound examination over different conventional methods, we used a Kretz – Voluson Expert ultrasound machine with full logistic equipment. Our selection of cases was completed over a period of 18 months, from October 2005, until March 2007. The purpose of this study was to achieve a wide variety of uterine and ovarian pathologies, documented with complementary diagnosis methods.

![Fig 1: Three dimensional angiography of the iliac artery and the uterine artery origin. The image represents both 3D vascular rendering modes, angiography and “glass body”](image-url)
We focused mainly on young women with local causes of infertility, as it represents a more and more important category, where prompt and accurate diagnosis is essential.

We considered the standard definition of infertility as failure to conceive after 12 months of unprotected regular intercourse. Statistically, it affects almost 10% of the couples, with 40% of the cases related to female pathology. Male infertility is involved in a similar percentage and in 20% of the situations, the etiologies are intricate. Traditionally, infertility causes may be divided into cervical, uterine/endometrial, tubal and peritoneal infertility, and, finally, anovulation. All these territories will consist in targets for sonographic evaluation, conventional, as well as three dimensional. It is worth mentioning that over the past 20 years there has been a shift in the causes of infertility, passing from the ovarian and uterine anomalies, to tubal and male infertility factors. Mostly, this is due to the increasing frequency of tubal and pelvic surgery, ectopic pregnancies, use of intrauterine contraceptive devices, and, not to mention the more and more frequent pelvic inflammatory disease. Thus, there is a consequent increase in the number of couples which present with tubal infertility. Obstruction and damage of the fallopian tubes account for almost 35% of all infertility cases.

The study included a total number of 124 patients, aged between 25 and 38 years. Without aiming for an accurate statistics, we selected for presentation only the most representative cases for different local pathologies associated with infertility. Most of our patients were secondary infertility (86 cases – 69.3%), following miscarriages (42 cases – 48.8%), terminations (16 cases – 18.6%) or deliveries (28 cases – 32.5%). Among them, we selected only those patients with uterine, tubal or ovarian anomalies, creating a study group of 92 women. Severe male infertility and chronic anovulation associated with endocrine anomalies represented exclusion criteria.

We performed a systematic review of the main local infertility causes, with comparison to similar data found in literature. Without aiming for an accurate statistics, we divided the cases according to the anomaly type and selected for presentation only the most representative cases for different local pathologies associated with infertility. The paper, along with its graphics, is meant as a visual testimony of the fact that 3D/4D sonography represents a useful tool for the diagnosis and prognosis of uterine and ovarian pathology associated with infertility.

RESULTS

Uterine Pathology

Normal Uterus

Normal uterus is easily assessed using 3D ultrasound, where the coronal plane gives a good image of the endometrial cavity, the surrounding myometrium and of the uterine external contour, a fact of most importance. Conventional ultrasound, with a thorough scan in both in sagittal and transverse sections, offers an almost complete description of the uterus, endometrial thickness and vascularisation pattern. Three dimensional ultrasound does not substitute, but completes the examination by offering a complete image of the uterine cavity in one single acquisition, static rendering mode or VCI-C (Fig. 2), calculating the endometrial volume with VOCAL II, as well as vascularity indices (Fig. 3).

In some cases there is necessary to complement a simple sonography with saline infusion hysterography (SIS). A very handy technique, cheap, with minimum patient discomfort, and very important diagnostic data. The endometrial cavity is easily visualized, the contrast is greatly enhanced, it is helpful in differentiating between polyps and submucous myomas. It also facilitates the differential diagnosis between endometrial hyperplasia and carcinoma, along with the Doppler analysis. It may visualize and, up to some point, treat uterine adhesions. Technically speaking, it is easy to perform, as a short outpatient procedure, does not require any kind of anesthesia, it is safe, avoids X-ray exposure, is well tolerated and performed
at a minimal cost.\textsuperscript{10} The procedure is scheduled during the follicular phase, between days 5 and 10. It requires a sonohysterography catheter, such as the Goldstein Catheter (Cook ObGy), or a pediatric no.8 Foley catheter, which has the advantage of a very low cost, but is more difficult to position, as the balloon should be inflated at the internal os and not in the uterine cavity. Under transvaginal continuous evaluation, small amounts of saline solution are being injected in a pulsed manner. The sonographer gently slides the probe from one cornua to the other, then from the cervix to the fundus, reconstructing the uterine anatomy. 3D acquisition may be performed at any time, in a sagital or transverse section (Fig. 4). The image may be modified according to necessities, using inversion mode, rotation and digital cutting.

The Endometrial Polyp

Conventional ultrasound presents the endometrial polyp as a focal, unequal thickening of the endometrium, of higher echogenicity than the myometrium, with an easily detectable single feeding vessel. Large polyps may appear as diffuse endometrial thickening, being difficult to differentiate from simple hyperplasia. Three dimensional sonography may facilitate diagnosis, using static acquisition, direct or inversion mode during SIS (Fig. 5). The differential diagnosis from a submucous myoma in questionable cases is easily set. Also, the shape, the dimensions, the origin and the impact on the endometrial cavity are clearly visualized, guiding the therapeutic procedure.

An alternative diagnostic method is hysteroscopy. With a 100\% reliability it has the advantage of offering a therapeutic solution in one step. But it is an invasive procedure, it requires a very skilled practitioner, it may be associated with complications as uterine perforation, infection, hemorrhage and it may require general anesthesia.

Uterine Myoma

Most frequent tumors of the feminine genital tract, uterine myomas may be generators of infertility by obstructing the fallopian tubes, distorting the endometrial cavity and causing subendometrial ischemia, thus interfering with gamete transport and implantation.\textsuperscript{11} Sonographically, they present as focal enlargements of the uterus, with a texture similar to the myometrium and posterior shadowing. The appearance greatly depends upon the presence of calcification or necrosis. Doppler ultrasound visualizes circular surface vessels, sometimes detecting the main feeding vessel. The resistance index is always relatively high, an average on 0.55.\textsuperscript{12} The exact position, the impact on the ostium tubae and the uterine cavity may be difficult to assess by conventional ultrasound. A very easy
The exact incidence of congenital uterine anomalies is difficult to determine since many women with such anomalies are not diagnosed, especially if they are asymptomatic, but it seems to be around 2 to 4% of live births. The prevalence is higher among women with adverse reproductive outcomes. As an example, the incidence of Müllerian anomalies among women with recurrent first trimester miscarriage or late first trimester - second trimester miscarriage/preterm delivery was 5 to 10% and greater than 25%, respectively, in another study. The most common type of Müllerian anomalies are uterine anomalies, with a distribution as follows: septate/arcuate uteri (90%), bicornuate uterus (5%), and didelphic uterus (5%).

There is a special mention regarding the association with spontaneous first trimester abortions. Among all types of congenital uterine anomalies, the septate uterus presents the highest rate of miscarriage. Clinically, this is of greatest importance, as septate uterus is considered a “mild” anomaly and the differential diagnosis with bicornuate uterus, anomaly with a better fertility prognosis, is difficult.

An accurate diagnosis in all cases implies a very good visualization of the uterine cavity, with focus on the fundus, and a delineation of the uterine external contour. So far, the most commonly used diagnostic method was hysterosalpingography (HSG). It provides excellent view of the uterine cavity and cervical canal, informations related to tubal patency, but no data regarding the fundal shape. Moreover, it exposes the patient to ionizing radiation and requires an X-ray laboratory. Alternative method for external visualization of the uterus is laparoscopy. Expensive, invasive, gives no information regarding the endometrial cavity. MRI may be employed in certain cases, with very good results, but at high costs.

**Arcuate/Sepatate Uterus**

The septate/arcuate uterus develops from a defect in canalization or resorption of the midline septum between the two müllerian ducts. The degree of septation varies from a small midline septum to total failure in resorption resulting in a septate uterus with longitudinal vaginal septum. Partial and complete uterine septa are defined by the proximity of the septum to the internal os; the presence or absence of a complete or partial vaginal septum is not relevant to the classification. A septate or arcuate uterus has a normal external surface, but two endometrial cavities, in contrast to a bicornuate uterus which has an indented fundus and two endometrial cavities. The distinction between arcuate and septate uterus is rather difficult and up to some point, subjective. It is accepted that the arcuate uterus has a slight midline septum with a broad, fundal basis and normal external surface, while the septate uterus presents a more important septum and sometimes may have a small indentation that does not exceed 10 mm depth.
Sonographically, the two uterine cavities are seen as split endometrial echoes, best visualized during secretory phase. The degree of septation may be assessed by conventional scan or, much better, by three dimensional sonography, thick slice or VCI-C. The coronal plane offers a very good diagnostic image of the endometrial cavity, as well as the fundal contour. In unclear cases, saline infusion gives a perfect image of the uterine cavity. 3D acquisition with inversion mode creates a hysterosalpingogram sometimes of better quality than the radiological image (Fig. 6).

In our study it was the most common Müllerian anomaly, with a total of 18 patients, confirmed by HSG or laparoscopy. All sonographic images were diagnostic, there were no false negative results. As a conclusion, apart from further pelvic evaluation, there is no need for more invasive testing.

Bicornuate Uterus

A bicornuate uterus refers to a uterus in which the fundus is indented (arbitrarily defined as ≥1 cm) and the vagina is generally normal. This anomaly results from only partial fusion of the müllerian ducts. This leads to a variable degree of separation of the uterine horns that can be complete or partial. Characteristically, there is only one cervix. Thus, the diagnosis depends on the very good visualization of the two endometrial cavities and the cervix. From a theoretical point of view, it is easy to obtain a good coronal plane, but, sometimes, it may turn out to be quite difficult, due to some degree of uterine rotation. In our study group we had 3 patients with bicornuate uterus. We had a sonographic diagnosis in two cases. The third one was diagnosed as a septate uterus, rectified after the HSG. Saline infusion remains a very good method of clearing up a diagnosis, when necessary.

Didelphic Uterus

Uterine didelphys, or double uterus, occurs when the two müllerian ducts fail to fuse, thus producing duplication of the reproductive. Generally the duplication is limited to the uterus and cervix (uterine didelphys and bicollis [two cervices]) although duplication of the vulva, bladder, urethra, vagina, and anus may also occur. A complete vaginal septum, generating an obstructed hemivagina, may be associated with ipsilateral renal agenesis.

Women with a didelphic uterus and bicollis often have good reproductive outcomes. A septated vagina occurs in 75% of cases and may cause difficulty with sexual intercourse or vaginal delivery.

We encountered the anomaly in two of our patients, in one case associated with incipient pregnancy (Fig. 7). A correct diagnosis was stated in both cases using 3D ultrasound, with the remark that sonography cannot evaluate vaginal septum.

The Ovaries

Sonographic evaluation of the ovaries is directed towards their number, size, location, presence of dominant follicle; correlates follicle size to endometrial appearance and measurements; evaluates the cul-de-sac; assesses the corpus luteum, as a very important prediction factor for early pregnancy outcome; notes the presence of persistent follicular cysts. The ovarian volume is age dependent, as well as the follicular size and number and the degree of stromal vascularity. All these parameters may are easily assessed by 3D sonography, using the VOCAL II program. Their importance increased during the last decade,
replacing the older hormonal parameter, such as the estradiol (E2) level, as predictor of follicular development and maturity. The follicular size may be expressed as a two-dimensional data, varying from 16-18 mm (gonadotropin stimulation) to 20-24 mm (clomiphene citrate stimulation), or as a volume of 3 to 7 ml. The stromal vascularization indices are calculated using the VOCAL II program after the follicular volume is taken out from the total ovarian volume. Resistance to ovarian artery blood flow begins to decline in the dominant ovary during the phase of rapid follicular growth, in association with rising serum estradiol concentrations, and reaches a nadir at the time of ovulation. Thereafter, it does not change for four to five days, and then gradually increases to a level slightly lower than that in the early follicular phase. This represents an important monitoring tool for stimulated cycles.

The most important ovarian event of luteal phase is represented by the development of the corpus luteum. Traditionally, a cystic structure of variable size, but less than 4 cm, it can actually have many forms and the definitive element is the rich peripheral vascularization, described as a “fire ring”. Sonographically, the corpus luteum is easily accessible. For a long time it was believed that progesterone levels were correlated with size and appearance of the corpus luteum, that is the proportion of the fluid component. Later it was proved that luteal function is related to the degree of thecal vascularization, characterized by a very low resistivity index (RI), which returns to normal 7 to 10 days after the ovulation in the absence of fecundation. Abnormal vascularization, with increased RI in the dominant ovary is a marker of luteal phase defect and a poor pregnancy outcome.

The solitary ovarian cyst benefits of a correct volume calculation using 3D ultrasound and a graphic representation of the structure, its shape and relations. A cyst offers a fluid environment, facilitating the view of inner structures, such as intracystic papillae or vegetations, clearing the etiology and the prognosis. It interferes with fertility whenever a great proportion of ovarian substance is destroyed, but it represents one of the most frequent sonographic findings. The VOCAL II associated with Doppler acquisition offers informations about peripheral vascularization, as a supplementary prognosis index.

The Fallopian Tubes

Evaluating the tubal patency represents a key step in the assessment of the infertile couple, especially in situations with risk factors for tubal damage. Over the past 20 years there has been a shift in the causes of infertility, passing from the ovarian and uterine anomalies, to tubal and male infertility factors, obstruction and damage of the fallopian tubes accounting for almost 35% of all infertility cases. Normally, the fallopian tubes are not accessible to ultrasound evaluation, unless their diameter is increased by a pathological process, such as hydrosalpinx, pyosalpinx, ectopic pregnancy, tubal carcinoma or torsion. The diagnosis of tubal patency has changed very little during time, laparoscopy with chromo per tubation being still considered the “gold standard”, as it was 20 years ago, along with radiological HSG. Even though it is not possible in all situations we consider that 3D ultrasound may represent a very good diagnostic tool, in cases with dilated tubes and a good image of the female pelvis. The most representative rendering mode is inversion mode, very spectacular and easy to handle, especially in patients with an amount of fluid in Douglas pouch.

A special remark has to be made regarding the evaluation of tubal patency in patients with non-dilated salpingae. Even though very little related to 3D ultrasound, saline infusion hysterosalpingography may beneficiate from its techniques. A variable amount of saline solution is injected in pulses, under continuous vaginal scan. Power Doppler permits a good image of the tubal passage (Fig. 8) and it may be combined with 3D acquisition, creating a graphic representation of the fallopian tube. In some cases during the saline passage the tube is dilated such as a static acquisition with inversion mode is possible, but this is rather accidental, as it requires a long saline pulse and an important tubal diameter.

With all its disadvantages, such as case-to-case variability, time consuming technique, high rate of false positive results,
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the ultrasound evaluation of the fallopian tubes still represents the main developing direction for future tubal investigation.

CONCLUSIONS

Even though it seems the handiest diagnostic method, easily employed in out-patient clinics, an accurate investigation, especially in patients with minimal pathology, implies a lot of medical energy and time.

The first condition for a good image is a very performant ultrasound machine. Secondly, training and experience bring along more and more diagnostic details. It is difficult to talk about a learning curve, as acquisition and investigational techniques differ greatly from one case to another, one type of pathology to another. Definitely, a large experience with conventional ultrasound in female pelvis pathology is required, as well as a good acquaintance with 3D/4D technology. As in the obstetrics field, further technical development is expected to bring along easier and more comfortable ultrasound diagnostic methods. Until then, we can still conclude that sonography, in the hands of a skilled practitioner, with a good technological basis, is one of the best diagnostic tools in gynecology, successfully replacing more invasive methods.

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Technical Details
Paper size 8.5 x 11.5 inches
Print size 7 x 10 inches
Digital file format EPS on CD (at 300 dpi resolution)
Printed on art paper using offset printing.

Schedule
Issues are published in the months of January, April, July and October.

Payment Details
- Payment should favour “Jaypee Brothers Medical Publishers Pvt (L) ” and should be payable at New Delhi, India
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