

## Review Article

# Role of Color Doppler and Three-dimensional Ultrasound in Infertility

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### Abstract:

Color Doppler is emerging as a valuable diagnostic imaging modality in the field of medicine, primarily infertility. Reproductive disorders, including infertility and spontaneous abortions/miscarriages, have emerged as major public health problem(s) worldwide. Color Doppler energy imaging is a high throughput technology based on the total integral of energy frequency spectrum. Color Doppler is a high-throughput, sophisticated imaging technique for the assessment of uterine anomalies, intrauterine pathology, tubal patency, polycystic ovaries, ovarian follicular monitoring, endometrial receptivity, failed or an ectopic pregnancy, male infertility and uterine, endometrial and ovarian vascularity. Assessments of the utero-ovarian pulsatility indices (PIs), resistance indices (RIs), and endometrial color signals are important determinants of in vitro fertilization (IVF) cycles and pregnancy rates. With many clinical/scientific research experience in the field of reproductive medicine, I strongly believe that an overall public health model needs to be designed in managing infertility patients; therefore, major issues such as cost effectiveness and technical artifacts should address so as to achieve an accurate clinical diagnosis, successful IVF outcome/pregnancy, and overall patient satisfaction in a clinical rehearse setting. Simple, safe efficient and affordable diagnostic modalities should be incorporated at infertility clinics coupled with well-designed patient counseling sessions and community-based public health awareness campaigns conducted so as to reduce the morbidity and mortality rates associated with reproductive disorders.

Three dimension (3-D) ultrasound is a new imaging modality which is being introduced into clinical practice. It has been proved that 3-D ultrasound is a very highly reproducible technique. With 3-D ultrasound, a volume of a region of interest can be acquired and stored. This volume can be further analyzed in several ways, such as navigation, multiplanar display and surface rendering or volume calculation. Power Doppler ultrasound, in combination with 3-D ultrasound, allows for a whole assessment of relevant vessels and quantitative assessment of vessel density and perfusion within a specified area.

**Key words:** Color Doppler, Three Dimensional Ultrasound, Infertility.

### Introduction:

The emerging role of color Doppler as a valuable diagnostic imaging modality in the field of reproductive medicine, primarily infertility, reproductive disorders, including infertility and spontaneous abortions/miscarriages are major public health problems worldwide; therefore, cost-effective screening strategies with observational follow-up intervention and/or early identification of modifiable risk factors coupled with sophisticated clinical/molecular diagnostic modalities, for precise estimation of preventable proportion of miscarriage and/or infertility related gynecologic

pathologies are essential to significantly prevent the increasing burden of reproductive disorders in susceptible women. Mycobacterium tuberculosis is the major etiological agent for female infertility. Altered anti-Mullerian hormone levels are associated with diminished ovarian reserve, predisposing women of reproductive age to adverse pregnancy outcomes. Color Doppler energy imaging is a high throughput technology based on the total integral of energy frequency spectrum, it visualizes blood flow with the energy of moving reflectors and has advantage of high sensitivity to slow blood flow, while being less dependent on angles and providing a less cluttered image.

The development and clinical application of transvaginal probes have greatly enhanced sonographic depiction of the uterus and ovaries over that obtained

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with conventional trans-abdominal scans. The major factors that have contributed to this enhancement include a shorter probe-to-target distance, which allows use of higher-frequency transducers, and the use of multi-element phased linear arrays, which afford more tightly focused beams with higher line densities than conventional real-time probes. Ultrasound has actually become one of the indispensable diagnostic tools in the field of obstetrics and gynecology. Transvaginal probes have enhanced sonographic depiction of the uterus and ovaries over that obtained with conventional trans-abdominal scans. Cyclic variations of female pelvic hemodynamics and angiogenesis can be studied with Doppler ultrasound.

The power Doppler has a threefold increase in sensitivity compared with conventional color Doppler imaging at detecting low velocity flow. There have been numerous investigations on the applications of the assessment of uterine and perifollicular vascularity and their possible relation with the treatment of infertility. However, the main applications in infertility so far are follicular monitoring and endometrium measurement by traditional two-dimensional (2-D) ultrasound. Nowadays, sonography plays a vital role in tracking follicular development and endometrial assessment in patients receiving ovulation induction medication. The sonographic information can be coupled with estradiol values to provide an accurate assessment of the presence or absence and number of mature follicles. The maximal follicle size is the main point to consider giving human chorionic gonadotropin and ovum pick-up. In combination with 3-D ultrasound, the use of power Doppler in examining ovarian stromal blood supply still fails to prove its role in predicting ovarian response and pregnancy in the IVF treatment and in the intrauterine insemination treatment. Although 3-D ultrasound has probably not replaced 2-D ultrasound, it is being increasingly used in the clinical setting. 3-D ultrasound has become an indispensable and auxiliary tool, alongside with 2-D ultrasound.

#### **Overview of Color Doppler in Infertility:**

Color Doppler is a high-throughput, sophisticated imaging technique for the assessment of uterine anomalies, intrauterine pathology, tubal patency, polycystic ovaries, ovarian follicular monitoring, endometrial receptivity, failed and/or ectopic pregnancy, male infertility, and uterine, endometrial, and ovarian vascularity<sup>1-6</sup>. Human chorionic gonadotropin (hCG) three dimensional power Doppler assessment of the follicle was implicated in improving pregnancy rates in intrauterine in seminal cycle<sup>7</sup>. Three dimensional volume reconstruction by the virtual organs computer-aided analysis (VOCL) technique allows ovarian volume calculation, and automatic

volume calculation software provides the follicular count and mean volumetric calculation<sup>8</sup>. Color Doppler producing ovarian vascular mapping allows the realization of a new functional approach of ovarian hyperstimulation syndrome (OHSS); local vascular factors, namely, ovarian angiogenesis and/or increase in capillary permeability released by hCG injection have a role in this syndrome.

Color Doppler imaging has indeed proved to be a valuable diagnostic imaging modality during pregnancy and embryonic development, where in an optimal blood supply toward the endometrium is essential for normal implantation. Ectopic and multiple pregnancies are emerging as one of the leading causes of morbidity and mortality in women of childbearing age and untreated, ectopic pregnancy can lead to massive hemorrhage and infertility, eventually resulting in death;<sup>9</sup> the advent of high-resolution color Doppler imaging is a boon for early prevention of pregnancy related deaths in women worldwide. An elegant report highlighted the public relevance of sophisticated uterine artery Doppler imaging as the possible valuable predictive factor governing pregnancy outcomes, including prediction/prevention of miscarriage in women of ethnically disparate population. The hemodynamic parameters in stimulation cycles are different from those in natural cycles and the precise values of these parameters in predicting pregnancy are also different. Intra-scrotal abnormalities detected by CD imaging aid in the management of male infertility; vascular channels and reflux flow in varicocele, testicular microlithiasis, testicular tumors, epididymal cyst, testicular cyst, and intra-scrotal hemangioma may be accurately diagnosed using the modern, high-throughput Doppler imaging technique.

#### **Assessment of Neovascularization with Color Doppler and Power Doppler:**

It has been suggested that neovascularization may be of prime importance in the growth and selection of ovulatory follicles. Several studies have examined the cyclic variations of female pelvic hemodynamics and angiogenesis using Doppler ultrasound<sup>10,11</sup>. Since then, transvaginal pulse Doppler has been used quite extensively to assess uterine and ovarian blood flow patterns in ART (assisted reproductive technique) cycles<sup>12,13</sup>. Power Doppler or color angio-ultrasound has aroused attention since its introduction. The power Doppler has a threefold increase in sensitivity compared with conventional color Doppler imaging at detecting low velocity flow<sup>14,15</sup>. There has been reports about application in relation to assessment of uterine and perifollicular vascularity<sup>16-18</sup> and outcome of IVF. Similar application were reported of perifollicular vascularity and uterine perfusion and outcome of intrauterine insemination (IUI)<sup>19-21</sup>.

### The era of Three-dimensional Ultrasound:

The advent of 3-D ultrasound has widened the field of clinical application. With this technique, any desired plane through an organ can be obtained. With 3-D ultrasound, a volume of region of interest can be acquired and stored. This volume can be further analyzed in several ways, such as navigation, multiplanar display and surface rendering or volume calculation. Power Doppler ultrasound, in combination with 3-D ultrasound, allows for whole assessment of relevant vessels and quantitative assessment of vessel density and perfusion within a specific area. A whole evaluation is then possible for endometrial and sub-endometrial vascularization and also for ovarian stromal vascularity<sup>22-27</sup>.

It has been postulated that increased ovarian stromal vascularity may lead to a greater delivery of gonadotropin to the granulosa cells of the developing follicles. Ovarian stromal vascularity can be assessed by color or power Doppler ultrasound. Power Doppler is better applied to the study of ovarian stromal vascularity as it is more sensitive to lower velocities and essentially angle-independent<sup>28</sup>. Ovarian stromal vascularity has been measured by 2-D power Doppler ultrasound and there was no predictive value for the ovarian response in combination with 3-D ultrasound<sup>29</sup>. The use of power Doppler in examining ovarian stromal blood supply still fails to prove its role in predicting ovarian response and pregnancy in IVF treatment and IUI treatment<sup>30</sup>.

### Future Perspectives:

Future research and development efforts in the field of reproductive medicine are warranted to further provide more meaningful interpretation of the sophisticated color Doppler-based diagnostic imaging, thereby significantly increasing the success rates of IVF among infertile patients. Moreover, multicentric and/or multinational research and development efforts may incorporate case-control/gene epidemiology, animal model, in vitro cell-based assays, and clinical trials for biomarker development utilizing genomics, proteomics, transcriptomics, and metabolic approaches for efficient management of infertility patients of ethnically disparate populations worldwide.

### Conclusion:

Ultrasound has actually become one of the indispensable diagnostic tools in the field of obstetrics, gynecology and the clinical application in infertility as well. Color Doppler is a high-throughput sophisticated

imaging technique for the assessment of uterine anomalies, intrauterine pathology, tubal patency, polycystic ovaries, ovarian follicular monitoring, endometrial receptivity, failed and/or ectopic pregnancy, male infertility, and uterine, endometrial, and ovarian vascularity. Three dimensional ultrasound is a very highly reproducible technique for the clinical stage of infertility, however, the main actor still remains as the 2-D ultrasound. Although 3-D ultrasound has probably not replace 2-D ultrasound. It is being increasingly used in the clinical setting. 3-D ultrasound has become an indispensable and auxiliary tool, alongside with 2-D ultrasound.

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