# Role of Doppler in Female Infertility

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## INTRODUCTION

Ultrasound has become the most widely used and important tool in the diagnosis and treatment of infertility. Whenever a patient presents with the complaints of infertility, ultrasound is one of the first steps in the evaluation which affects the management of the patient. It allows us to diagnose any uterine or adnexal pathology and when treatment begins it is used in almost every interaction with the patients. This is used for monitoring of follicular development and endometrial response as well as for oocyte retrieval and embryo transfer. Newer technology like (3D) ultrasound allows better imaging as well as more accurate volume rendering while Doppler modalities of ultrasound allow identification of the direction and magnitude of blood flow and calculation of velocity and thus it indicates the hypoxic status of the tissues. The Doppler Effect is defined as the observed changes in the frequency of transmitted waves when relative motion exists between the source of the wave and an observer. The phenomenon bears the name of its discoverer, Christian Andreas Doppler, an Austrian mathematician and physicist. The first medical applications of Doppler Sonography were initiated during the late 1950s and impressive technologic innovations have been continuing ever since. Shigeo Satomura from the Institute of Scientific and Industrial Research of Osaka University in Japan developed the first Doppler ultrasound device for medical diagnostic purposes and reported the recording of various cardiac valvular movements. Taylor and colleagues were the first to characterize Doppler waves from the ovarian and uterine arterial circulations utilizing pulsed duplex Doppler instrumentation. This work was followed by reports of transvaginal colour Doppler studies and transvaginal duplex pulsed Doppler studies of pelvic vessels. Through the late 1980s and early 1990s Doppler sonographic research in gynaecology steadily expanded.

## DOPPLER IN INFERTILITY

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. Transvaginal colour Doppler (TVCD) sonography provides an opportunity to visualize and quantify pelvic blood flow in relation to hormonal changes during the menstrual cycle. There is a complex relation between the concentration of ovarian hormones in peripheral blood and uterine artery blood flow parameters. Transvaginal Doppler sonography can be used to obtain flow velocity waveforms at any time during the menstrual period and thus it may be used as a noninvasive assay of uterine receptivity.

## UTERINE ARTERY DOPPLER

The endometrium is a key determinant in successful implantation. Endometrial receptivity is regulated by many factors including endometrial perfusion. The current assessment of the endometrium is restricted to measurement of its thickness and description of its appearance. These parameters are not specific and their value as prognostic indicators of implantation is limited. Doppler ultrasound assessment of uterine blood flow appears to be more informative and can be used as a noninvasive assay of uterine receptivity. It enables clinicians to cryopreserve the embryos if uterine conditions are adverse and reduce the number of transferred embryos if conditions are optimal. This noninvasive technique is rapid, easy to perform and may predict the likelihood of implantation.

The uterine artery spectral Doppler waveform in nongravid women has high impedance low diastolic flow with a characteristic notch during diastole. It is usually a high-resistance system. The flow changes periodically throughout the normal ovulatory menstrual cycle. There is a gradual yet continuous increase in blood flow velocity in association with a reduction in the resistance to flow through the menstrual cycle from the early follicular phase, maximal at the

## UTERINE ARTERY DOPPLER

mid-luteal phase. HCG administration induces significant increase in the resistance of uterine artery for 48 hours which can affect its evaluation on the day of follicular aspiration/rupture therefore Doppler study for uterine receptivity should be done on the day of HCG.Varying cut-off points for the maximum pulsatility index (PI) above which conception will not, or is highly unlikely to occur have been proposed, varying between 2.5 and 3.6(figure1).Using the 95th centile within successful conception cycles, Coulam et al. reported that a PI above 3.3 on the day of hCG administration had a negative predictive value of 88% for conception, with a sensitivity of 96% and a specificity of 26%.The scientific consensus implies cut-off values of 3.0 for the PI and 0.95 for the resistance index (RI) within the uterine artery. Embryo transfer in IVF cycle should be cancelled if the values are more.

Uterine Artery PI and RI are significantly increased in the unexplained infertility group. This can happen due to suboptimal endometrial angiogenesis or vasoconstriction or reduced vasodilatation.

## SUB ENDOMETRIAL BLOOD FLOW

The major compartment of uterus is the myometrium and not the endometrium and most of the blood passing through the uterine arteries may not reach the endometrium.A more logical approach is to evaluate the vascularization around the endometrium directly in order to assess endometrial receptivity in unexplained infertility. Functional maturity of the endometrium can be assessed by Doppler of spiral arteries. Spiral arteries undergo substantial changes during menstrual cycle. Endometrial Colour Doppler gives direct information about oestrogen and progesterone levels and also about functional maturity of the follicle and endometrium.Study of the endometrial perfusion can be done by either power 3-D Doppler or through the study of the vascularization of the sub endometrial area by conventional colour Doppler which is simple and is available in many radiological clinics.

On colour doppler the vascularity of the endometrium is classified by Apple Baum(figure 2) as follows :

**Zone I** : Blood vessels reaching myometrium surrounding the endometrium.
**Zone II** : Blood vessels reaching hyperechoic endometrial edge.
**Zone III** : Blood vessels reaching internal endometrial hypoechoic zone.
**Zone IV** : Blood vessels reaching endometrial cavity.

For good implantation to occur the vascularity should cover 5 mm area of zone 3 and 4 of endometrium. By 3D power Doppler no pregnancy have been reported if vascularization index (VI) < 1.0,flow index (FI) < 31 and vascularization flow index (VFI) < 0.25.

Studies by Yange et al and Zaidi et al found that patients with higher vascular signals in the sub endometrial area onthe day of HCG had a better chance of pregnancy and its absence was associated with failure of implantation in stimulated cycles in IVF. It has also been observed that when pregnancy is achieved in absence of endometrial and sub endometrial flow on the day of embryo transfer, more than half of pregnancies end as spontaneous miscarriage.

## PERIFOLLICULAR VASCULARITY

Adequate vascular supply to provide endocrine and paracrine signals plays a key role in the regulation of follicle growth.Colour Doppler imaging facilitates detection of small vascular areas in the ovarian stroma and follicular rim and the onset of the ovulatory process prior to follicular rupture can be detected.Thus it helps in timed coitus and timing of HCG injection in IUI patients.

Blood flow from the follicle can be seen when the follicle reaches 10 to 12 mm in diameter and is a hemodynamic parameter of its growth, maturation and ovulation. A mature follicle is a rounded 16-18mm sized follicle with thin walls and no internal echogenicity.A sonolucent halo appears surrounding the follicle. On color Doppler vascularity is seen surrounding 3/4th of the follicular circumference. At the time of presumed ovulation there is increased

## PERIFOLLICULAR VASCULARITY

vascularity on the inner wall of the follicle and a coincident surge in blood velocity just before eruption. On pulse Doppler, the vessels show a PSV>10 cms/sec. Rising PSV with steady low RI means that the follicle is close to rupture. Vascularization of maturing follicle is graded as follows depending on the percentage of follicular circumference seen to be vascularized - Grade I <25% ; Grade II <50% ; Grade III < 75% ;Grade IV >75%. Follicles with vascularity>50% (figure 3) has higher Oocyte retrieval rate and fertilization rate. If the follicular vascular indices are not in the defined range it means that the follicle is not yet physiologically mature and therefore stimulation still needs to be continued. Fertilization of a follicle with a PSV of less than 10cms/sec (hypoxic follicle) have high chances of embryo with chromosomal abnormality. Steady or decreasing PSV with rising RI suggests that the follicle is proceeding towards LUF.

## CONCLUSION

Doppler study of uterine hemodynamics should be considered in infertility work-up. Even if TVCD of follicle is normal, endometrial and the uterine artery indices should be within normal limits on the day of HCG for implantation. Women with suboptimal uterine perfusion may be offered therapy aimed at improving uterine blood flow. Embryo cryopreservation and subsequent endometrial preparation can be considered in IVF patients with poor endometrial perfusion.

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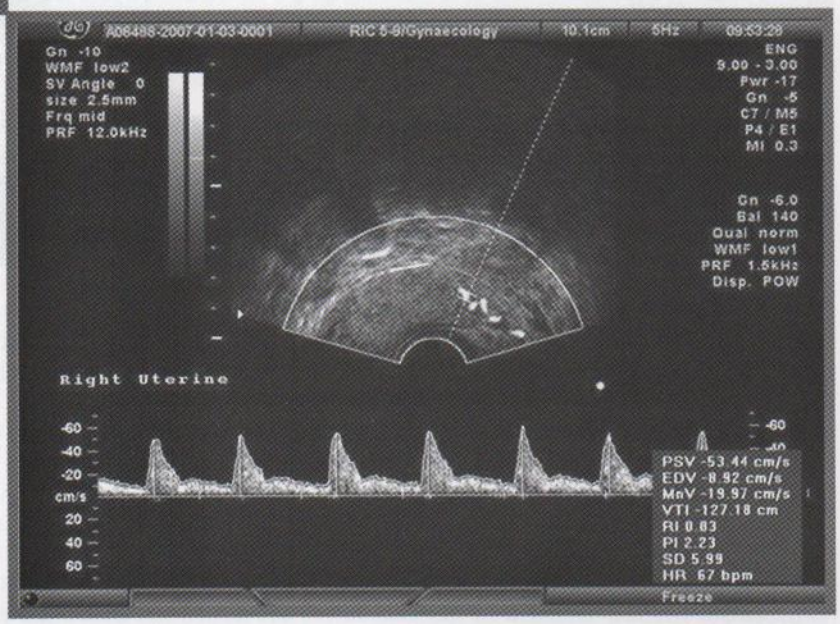
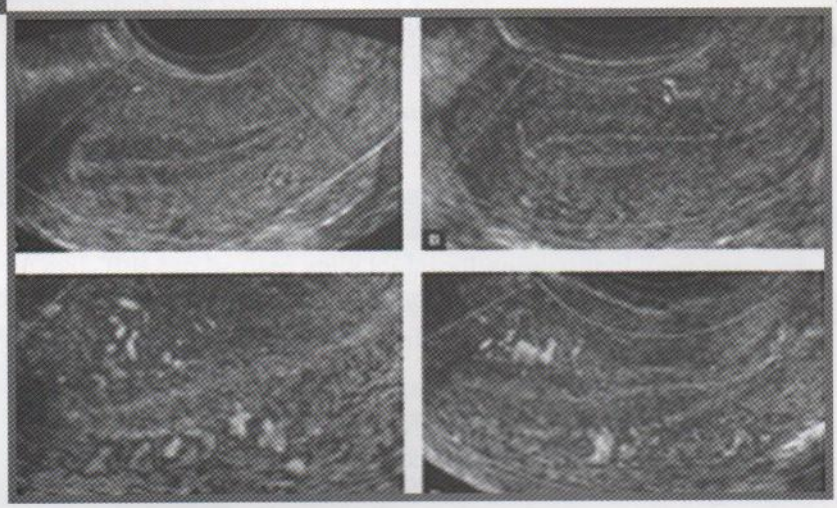
## FIGURE 1: UTERINE ARTERY DOPPLER




## FIGURE 2: SUBENDOMETRIAL BLOOD FLOW



## FIGURE 3: PERIFOLLICULAR VASCULARITY

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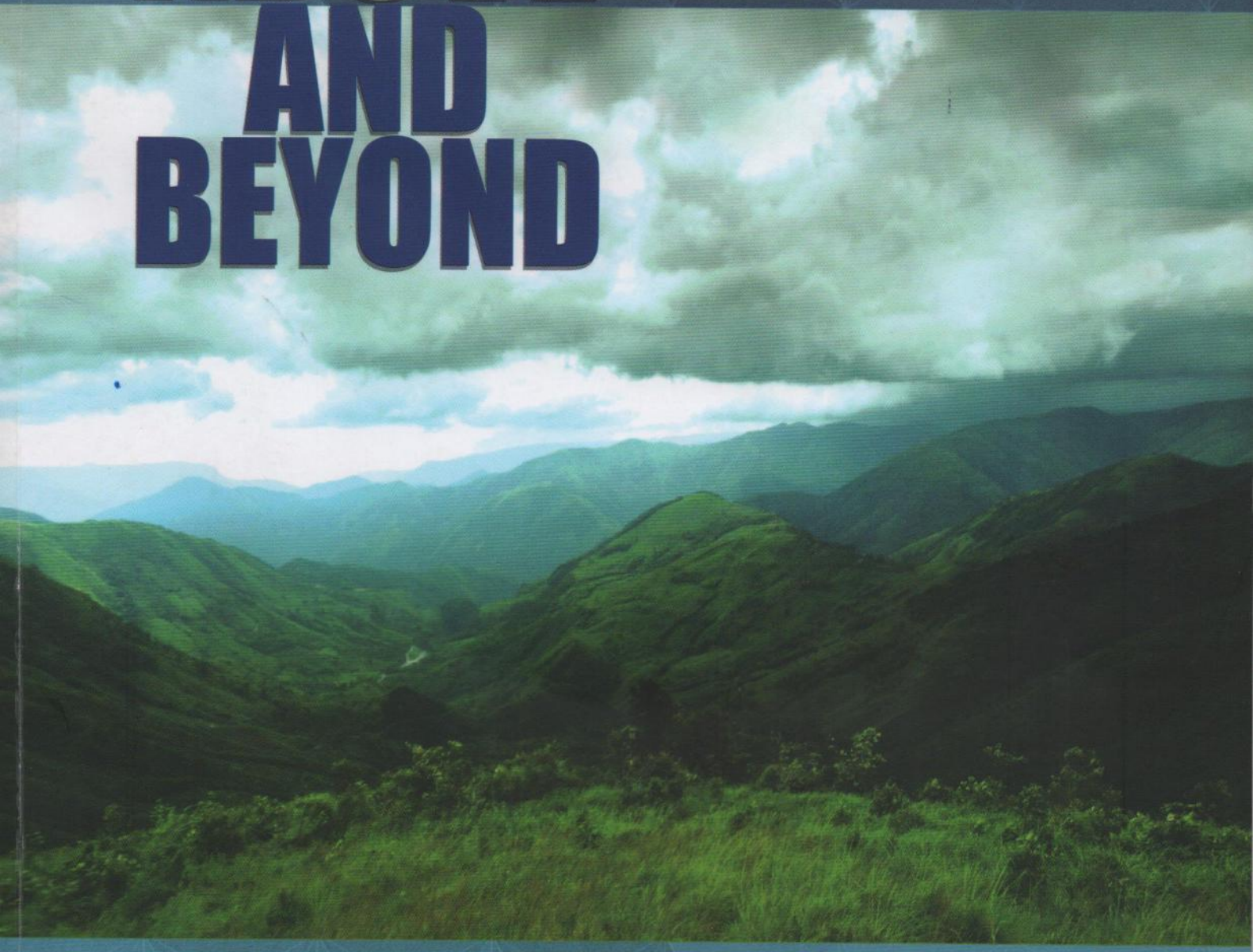
Theme

# ABOVE AND BEYOND



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