Quantification of blood perfusion using 3D power Doppler: an in-vitro flow phantom study

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Three-dimensional (3D) power Doppler data is increasingly used to assess and quantify blood flow and tissue perfusion. The objective of this study was to assess the validity of common 3D power Doppler ‘vascularity’ indices by quantification in well characterised in-vitro flow models. A computer driven gear pump was used to circulate a steady flow of a blood mimicking fluid through various well characterised flow phantoms to investigate the effect of the number of flow channels, flow rate, depth dependent tissue attenuation, blood mimic scatter particle concentration and ultrasound settings. 3D Power Doppler data were acquired with a Voluson 530D scanner and 7.5MHz transvaginal transducer (GE Kretz). Virtual Organ Computer-aided Analysis software (VOCAL) was used to quantify the vascularisation index (VI), flow index (FI) and vascularisation-flow index (VFI). The vascular indices were affected by many factors, some intuitive and some with more complex or unexpected relationships (e.g. VI increased linearly with an increase in flow rate, blood mimic scatter particle concentration and number of flow channels, and had a complex dependence on pulse repetition frequency). Use of standardised settings and appropriate calibration are required in any attempt at relating ‘vascularity indices’ with flow.

1. Introduction
Three-dimensional (3D) power Doppler angiography provides a novel tool to study blood flow to a whole tissue or organ and subjectively assess vessel pattern and distribution. The power Doppler signal may also be quantified to give objective information about blood flow. The potential medical applications are numerous and this is reflected in the increasing number of recent publications [1-5].

Many of these studies report an improved diagnostic capability, with power Doppler ultrasound able to differentiate between patient populations and disease states. Some of our own clinical studies have looked at power Doppler applications in liver disease [6, 7] and our current interest is focussed on the application of 3D power Doppler for assessing perfusion in the human endometrium [8, 9].

Whilst there are several computer models available to quantify the power Doppler signal, the most popular and most widely reported within the clinical setting, particularly in obstetrics and gynaecology research studies is the ‘histogram facility’ available within 3D View Virtual Organ Computer-aided Analysis software (VOCAL) (GE Kretz, Zipf, Austria). This system, integrated into the Kretz Voluson 530D ultrasound scanner utilises specific algorithms to quantify the relative proportion of colour pixels and their signal intensities within a user-definable area [1]. However, the relationship of these 3D vascular indices to the true in-vivo blood flow characteristics (volume flow, speed, perfusion) is uncertain. A comprehensive review of various techniques and considerations for the estimation of...
blood perfusion using ultrasound is provided elsewhere [10]. Many of the considerable pitfalls and limitations associated with the quantification of the power Doppler signals have also been recognized [11-13].

One way to experimentally assess perfusion estimation techniques is to use a well characterised Doppler test device or ‘ultrasound flow phantom’. These dedicated systems have been used to assess various established and new ultrasound flow measurement techniques [14]. To date very few studies have considered three-dimensional data [15, 16] and none (to our knowledge) have assessed the most widely used clinical system (currently the vascular indices provided by VOCAL, GE Kretz, Austria).

The objective of this study was to assess the validity of these common 3D power Doppler ‘vascularity’ indices by quantification in well characterised in-vitro flow models. This paper describes some initial results of work in progress.

2. Methods

2.1. Equipment and data collection

A computer driven gear pump (Integra series micropump (EG130-0036), Micropump Corporation, Vancouver, WA, USA) was used to circulate a steady flow of a blood mimicking fluid through various well characterised flow phantoms (Figure 1). The ‘true flow rate’ was calculated by measurement of the weight of BMF collected into a measuring cylinder over a set amount of time and correcting for the known density of the BMF. The BMF consisted of (%weight): water (83.86%); glycerol (10.06%); dextran (3.36%); 5 micron Orgasol™ (1.82%) and Synperonic N surfactant (0.9%). The well characterised BMF is described elsewhere [17, 18].

![Figure 1. Photograph of a test tank and schematic diagram of the experimental set-up.](image)

Three different test tanks were used to complete the full range of experiments. The first test tank used for the majority of experiments consisted of a Perspex box with a 0.8 mm thick C-flex™ tube of 4 mm in diameter (Cole-Palmer, IL, US) running horizontally through the centre of the tank and fixed at a constant depth. This test-tank was used for assessment of the effect of velocity, blood-mimic concentration and change in ultrasound settings. The second test tank consisted of an identical C-flex tube fixed at an inclined position (45°) relative to the surface. This tank was used to test for the effect of depth dependent attenuation by moving the transducer relative to the C-flex tube in a series of 5mm steps. Both of these test tanks were filled with a well characterised agar-based tissue-mimicking material (TMM) [19, 20]. The TMM consisted of (%weight): water (82.97%); glycerol (11.21%); benzalkoniumchloride (0.46%); 400 grain SiC powder (0.53%); 3 micron Al₂O₃ powder (0.94%); 0.3 micron Al₂O₃ powder (0.88%) and agar 3.00%. The third test tank contained nine 2.4 mm silastic
tubes arranged in a three-by-three matrix, held in position by two rotatable manifolds, constructed such that each tube could be removed and the opening sealed to modify the number of vessels within the system. This test tank was filled with a 10% glycerol solution to allow access to the tubes so that the number of vessels within the system could be altered to assess the effect of vascularity.

3D Power Doppler data were acquired with a Voluson 530D scanner and 7.5MHz transvaginal transducer (GE Kretz, Zipf, Austria). The transducer was held perpendicular to the surface of each test tank by a retort stand (Figure 1) to give a central two-dimensional view of the vessel(s). Power Doppler was then applied and the volume mode activated to generate a truncated sector defining the area of interest. The angle was set to 90° to ensure that a complete volume was obtained and a three-dimensional dataset acquired using the medium sweep mode, as this is used in the clinical setting. The acquired volume was then stored to magnetic optical disk and subsequently sent to a personal computer via a dedicated DICOM link (Digital Imaging and Communications in Medicine). The power Doppler settings were specifically maintained for all experiments examining the effect of external parameters including flow rate, BMF concentration, vessel number and attenuation. These were as follows: medium central frequency, quality 9, density 8, reject 82, signal rise 0.4, signal persistence 0.4, frame rate 12.9, wall motion filter 141, pulse repetition frequency 2.4, power 4 dB and colour gain 36.8. These settings were chosen as they reflected those used in our clinical studies. During the experiments examining the effect of the Doppler ultrasound settings, a single parameter was changed while the rest were kept constant. This was not always possible, however, as variation in several of the parameters induced an automatic and irreversible change in related settings.

2.2. Data Analysis
Quantification of the 3D power Doppler signal was performed using the ‘histogram’ facility, within 3D View VOCAL. This allows the user to define an orthogonal volume of interest (VOI) to quantify the power Doppler signal within any given volume of interest defined by the user. VOCAL is based on the detection and weighting of colour voxels, relative to the total volume being considered and various indices have been defined [1]. The Vascularisation Index (VI) reflects the relative proportion of colour voxels within the user-defined area and the Flow Index (FI) their mean signal intensity. The Vascularisation Flow Index (VFI) represents a combination of these two measurements. These indices are described elsewhere [1]: Vascularisation Index (VI) = colour values / (total voxels - background values); Flow Index (FI) = weighted colour values /colour values; Vascularisation Flow Index (VFI) = weighted colour values / (total voxels – background values).

Figure 2. Example of data analysis technique using VOCAL software. This generated a 3D ‘rectangular sampling box’ that was applied over the mid-point of the vessel, as indicated by a central point on screen. The resultant ‘histogram’ and Vascular Indices generated are shown to the right.
3. Results

Some of the experimental results are summarised in Figure 3.

![Graphs illustrating the effect of scatter particle concentration, attenuation, pulse repetition frequency (PRF), wall motion filter, flow rate and the number of vessels on the vascular indices.](image-url)
The VI, FI and VFI indices were affected by ultrasound power and gain settings, and had a significant but complex relationship with pulse repetition frequency and wall filter settings. The VI increased linearly with an increase in flow rate, blood mimic scatter particle concentration and number of flow channels. The FI increased rapidly with blood mimic concentration and then plateaued. The FI had a cubic relationship with volume flow and a complex relationship with the number of channels.

4. Metrological significance
Advances in ultrasound technology and new flow measurement techniques facilitate the clinical assessment of blood flow and tissue perfusion. This study highlights important metrological challenges in the assessment of perfusion quantification techniques. In addition to our single and multi-vessel phantoms, more sophisticated perfusion phantoms are required.

5. Conclusion
This study examined the relationship between the three-dimensional indices of vascularity, generated through the application of the histogram facility within 3D View, and machine settings and external confounding factors including volume flow rate, attenuation, blood mimic scatter concentration and degree of vascularity. The vascular indices were affected by many factors, some intuitive and some with more complex or unexpected relationships. To examine why these relationships were seen, it is necessary to consider both the algorithms behind these indices and the principles of power Doppler. Use of standardised settings and appropriate calibration are required in any attempt at relating ‘vascularity indices’ with flow. The results highlight limitations of power Doppler flow quantification and some of the issues that need to be clarified if power Doppler flow quantification is to have an effective clinical role.

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