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● *Original Contribution*

3-D ULTRASOUND SEGMENTATION OF THE PLACENTA USING THE RANDOM WALKER ALGORITHM: RELIABILITY AND AGREEMENT

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Abstract—Volumetric segmentation of the placenta using 3-D ultrasound is currently performed clinically to investigate correlation between organ volume and fetal outcome or pathology. Previously, interpolative or semi-automatic contour-based methodologies were used to provide volumetric results. We describe the validation of an original random walker (RW)-based algorithm against manual segmentation and an existing semi-automated method, virtual organ computer-aided analysis (VOCAL), using initialization time, inter- and intra-observer variability of volumetric measurements and quantification accuracy (with respect to manual segmentation) as metrics of success. Both semi-automatic methods require initialization. Therefore, the first experiment compared initialization times. Initialization was timed by one observer using 20 subjects. This revealed significant differences ($p < 0.001$) in time taken to initialize the VOCAL method compared with the RW method. In the second experiment, 10 subjects were used to analyze intra-/inter-observer variability between two observers. Bland–Altman plots were used to analyze variability combined with intra- and inter-observer variability measured by intra-class correlation coefficients, which were reported for all three methods. Intra-class correlation coefficient values for intra-observer variability were higher for the RW method than for VOCAL, and both were similar to manual segmentation. Inter-observer variability was 0.94 (0.88, 0.97), 0.91 (0.81, 0.95) and 0.80 (0.61, 0.90) for manual, RW and VOCAL, respectively. Finally, a third observer with no prior ultrasound experience was introduced and volumetric differences from manual segmentation were reported. Dice similarity coefficients for observers 1, 2 and 3 were respectively 0.84 ± 0.12, 0.94 ± 0.08 and 0.84 ± 0.11, and the mean was 0.87 ± 0.13. The RW algorithm was found to provide results concordant with those for manual segmentation and to outperform VOCAL in aspects of observer reliability. The training of an additional untrained observer was investigated, and results revealed that with the appropriate initialization protocol, results for observers with varying levels of experience were concordant. We found that with appropriate training, the RW method can be used for fast, repeatable 3-D measurement of placental volume. (E-mail: gordon.n.stevenson@gmail.com) © 2015 World Federation for Ultrasound in Medicine & Biology.

Key Words: **3-D ultrasound, Random walker, Placenta, Volume, Virtual organ computer-aided analysis (VOCAL), Repeatability, Agreement, Intra-class correlation coefficient.**

INTRODUCTION

Placental size at birth has long been considered an indicator of fetal outcome. Large studies have reported a significant relationship between fetal outcome and a small placenta at term (Kloosterman 1970). As a result, this correlation raises the question of whether measurement of the volume of the placenta *in utero* could be an indicator of fetal health or a predictor of pregnancy outcome.

Before the advent of 3-D ultrasound, many studies reported correlations between placental volume and pregnancy outcome with respectable levels of specificity and sensitivity (Bleker et al. 1977; Hoogland et al. 1980; Wolf et al. 1989a, 1989b). These studies used multiple 2-D scans to attempt to reconstruct the overall 3-D volume, which limited the adoption as a way to predict pregnancy outcome as part of clinical practice for a number of reasons. The quality of the reconstruction is dependent on the operator's choice of analysis planes, which can lead

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to errors when consistently repeatable planes are chosen in a large population. Additionally, the extra time required to measure organ volume in 3-D compared with existing 2-D biometric measurements, as well as the lack of machines capable of multiplanar reconstruction, has limited the adoption of placental volume measurement as a serious diagnostic tool.

With the increasing use of commercial 3-D ultrasound systems with software for 3-D image analysis, studies on organ volumetry are being seen more frequently in the literature. Many publications have investigated the use of the virtual organ computer-aided analysis (VOCAL, General Electric Healthcare, Milwaukee, WI, USA) imaging tool packaged within the 4D View (Version 9.1, GE Kretz, Zipf, Austria) image viewer for volume estimation. This method calculates organ volume based on interpolation of a number of 2-D contours that are drawn at intervals defined by angle of rotation (12°, 15°, 18° or 30°) around a user-defined axis. After the contours are traced, the method generates a final 3-D volume by interpolation around the axis. The interpolative method is purely geometric and does not consider the underlying image data. As a result, irregularly shaped organs are less likely to be accurately segmented than organs with smoothly varying shapes.

In early pregnancy, before the placenta develops into the typical discoid shape observed at birth, placental shape can appear irregular on ultrasound (Aye et al. 2015; Yampolsky et al. 2013). Segmentation of the placenta is also difficult for a number of other reasons. In early pregnancy there is a lack of differentiation between uterine tissue and placenta, which makes determination of the placental border challenging as only weak edges delineate the anatomical boundary. Finally, hypo-echoic placental lakes can be present, leading to a heterogeneous appearance of the placental tissue. An additional technical challenge is that the VOCAL method does not provide a voxelwise comparison of results. As a result, we are forced to compare only the total volumetric result statistically rather than compare differences in binary volumes produced by different segmentation techniques. The latter option would provide a far greater understanding of how to optimize these computerized methods to reduce measurement error.

Despite these potential drawbacks, VOCAL studies have successfully correlated placental volume to pathology such as abnormal uterine artery Doppler indices, chromosomal abnormality, malarial infection, pre-eclampsia and small-for-gestational age (SGA) status (Collins et al. 2013; Odeh et al. 2011; Plasencia et al. 2011; Rijken et al. 2012; Rizzo et al. 2009; Wataganara et al. 2005; Wegrzyn et al. 2005). In particular, a recent study of 600 patients looking at a variety of biochemical and imaging markers (β subunit of human chorionic gonadotropin [β-HCG] and uterine artery Doppler) found that placental volume was the only independent marker for SGA (Law et al. 2009), indicating the potential utility of the volumetric method for clinical use.

Here we propose an image segmentation method that, as we illustrate, provides better results than VOCAL. This is achieved by avoiding segmentation of regions as placenta that by VOCAL segmentation would be labeled as placenta, but actually, based on image appearance, should not. This situation is especially prevalent for placental volumes that are highly irregular in shape. Automation would also reduce the time taken to estimate placental volume and provide more consistent measurements between observers. This work presents an implementation of a new method of placental volume segmentation based on an existing image segmentation technique, random walker (RW) (Grady 2006). To the best of our knowledge, there is no algorithm or software that is publicly available and independent of ultrasound manufacturer for segmentation of the placenta using 3-D ultrasound. The random walker algorithm was selected because of its inherent advantages in dealing with weak image boundaries, noise robustness and ambiguous seeded region features (Grady 2006) that are typical in 3-D ultrasound acquisitions of the placenta.

Previous studies have reported reproducibility as intra-class correlation coefficients (ICCs) for intra- and inter-observer variability. High ICCs have been reported by Nowak et al. (2008) (intra-/inter-observer >0.99) and Huster et al. (2010) (intra-observer: 0.95, 0.84; inter-observer: 0.88). However, other authors have obtained conflicting results. Cheong et al. (2010) describe excellent intra-observer repeatability (ICC $>$ 0.999) using VOCAL, but report poor reproducibility measured by ICC when compared with multiplanar (MPR) measurements (VOCAL 18° vs. MPR 0.757, VOCAL 12° vs. MPR 0.878). For the purposes of this work, we define excellent reproducibility as an ICC >0.90 (Kottner et al. 2011).

This work extends our previous publication (Stevenson et al. 2010) by illustrating that the method can feasibly be initialized in a short amount of time to be a clinically useful tool. In the experiments performed, we found that the algorithm provides rapid 3-D segmentation of the placenta, with reproducibility values in line with or better than those provided by the current technique, VOCAL, and it is concordant with manual segmentation. This was performed on a subset of the overall data that were acquired as part of a larger clinical study investigating imaging biomarkers in the placenta. By testing using observers with varying levels of expertise in ultrasound image analysis, we also illustrate that the RW method can be used with relatively little user