# PREOPERATIVE THREE-DIMENSIONAL POWER DOPPLER ULTRASONOGRAPHIC EVALUATION OF ADENOMYOSIS AND UTERINE LEIOMYOMA

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The purpose of this study was to evaluate whether 3D power Doppler ultrasonography is capable of accurately differentiating between uterine leiomyoma and adenomyosis prior to surgery. This study comprised 95 women with a benign uterine mass admitted for a total abdominal hysterectomy. All subjects underwent a trans-abdominal 3D power Doppler ultrasonographic examination prior to surgery. The examination evaluated tumor size, tumor volume, vascular location (location), vascular index (VI), flow index (FI), and vascular-flow index (VFI). Results reveal that patients with uterine leiomyoma had significantly higher VI ($U = 375.50$, $p < 0.001$), FI ($U = 386$, $p < 0.001$), and VFI ($U = 374.5$, $p < 0.001$) levels than did patients with adenomyosis. A significant difference in vascular location was also noted between cases of uterine leiomyoma and adenomyosis (Fisher exact test, $p < 0.001$). The results suggest that 3D power Doppler ultrasonography could be used to more effectively differentiate between uterine adenomyosis and leiomyoma, with potential widespread applicability in the near future.

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## 1. Introduction

Adenomyosis is a common disorder that affects women during their reproductive years. It can induce clinical symptoms such as menorrhagia, dysmenorrhea, chronic pelvic pain, with adverse effects on fertility [1]. In clinical practice, misdiagnosing adenomyosis as uterine leiomyoma is easy, due to their similarity in clinical symptoms and signs [2]. Unfortunately, the treatment methods for these two conditions differ widely. Uterine leiomyoma is identified as a well-circumscribed mass, sharply demarcated from the surrounding myometrium by a pseudocapsule, the surgical removal of which is relatively straightforward [3]. In contrast, adenomyosis appears as an ill-defined area in which the myometrium is interspersed with endometrial glands and stroma, making complete removal through surgery difficult or even

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impossible. Thus, the definitive treatment for adenomyosis is hysterectomy [4]. Accurate preoperative distinction between these two conditions is crucial to patients wishing to retain fertility or to those for whom a myomectomy [5] would be appropriate. To date, however, it has been necessary to wait for postsurgical histological findings to make a definitive diagnosis.

Among the latest technological advances in the evaluation of vascular flow and vascular flow patterns is 3D power Doppler sonography, which provides a histogram to quantify blood flow and vascularization. The associated histogram software analyzes frequency shifts in blood velocity using the power Doppler signal as the amplitude component of the received signal to reveal the number of moving blood cells [6-7]. This enables the visualization of small vessels and blood flow of lower volume [8]. Such features make this approach an optimal method for the 3D reconstruction of vessels. The recent advent of 3D power Doppler ultrasonography has made feasible the quantification of the total blood flow in the uterine mass.

The ability to reveal differences in vascularity could provide an additional parameter with which to differentiate between leiomyoma and adenomyosis. However, a correlation between 3D power Doppler ultrasonography and the angiogenesis patterns of uterine tumors has yet to be established. The purpose of this study was to investigate the value of 3D power Doppler ultrasonography in the differentiation of uterine adenomyosis and leiomyoma.

## 2. Materials and methods

### *2.1. Participants*

The subjects of the study included women with a benign uterine mass, admitted to National Cheng Kung University Hospital for a total abdominal hysterectomy. All subjects received a trans-abdominal 3D power Doppler (Voluson 530D®, Medison-Kretz, Zipf, Korea-Austria) ultrasonographic examination prior to surgery. All quantitative measurements were performed by one of the authors (Y-M, Cheng). The ultrasonographic examination provided data related to tumor size, tumor volume, vascular location (location), vascular index (VI), flow index (FI), and vascular-flow index (VFI). During the serial examination, the Doppler settings were not altered. The region of interest included the entire region of the uterine mass. After evaluating the total color percentage and flow amplitude for the volume of interest,[9] the virtual organ computer aided analysis (VOCAL) software (Medison-Kretz) for the analysis of 3D power Doppler histograms was then used with computer algorithms to form indices of blood flow and vascularization. The 3D power Doppler settings were as follows: Angio : cent, FRQ: Mid, Frame filter: 3, Line density; 254, Enhance: 3, Far gain: max 62, persist: 0.3/0.4, Quality: 12, Density: 6, Enhance: 3, Balance: G>192, Reject: 79. Subjects were enrolled from July to September 2011. Prior written informed consent was obtained and, in adherence to the Helsinki Principles, all procedures were previously reviewed and approved by the ethics board at Chang Jung Christian University, Taiwan.

### *2.2. Data Analysis*

The Mann-Whitely U test was used to determine whether the data related to continuous ultrasonographic parameters (e.g., VI, FI, VFI) differed between groups. Differences in ultrasonographic parameter category variables (e.g., location) were examined using Fisher's exact test.

Sensitivity, specificity, positive predictive value (PPV), and negative predictive value were calculated for ultrasonographic vascular location in the detection of myoma and adenomyosis. The effects of the ultrasonographic parameters on final pathological diagnosis were assessed through logistic regression. All data were analyzed using SPSS Version 15.0 (SPSS Inc., Chicago, IL). A p value of $< 0.05$ was used as a measure of statistical significance.

## 3. Results

### *3.1. Higher VI, FI and VFI values in myoma than did women with adenomyosis*

A total of 95 patients with a mean age of 43.4 years (SD = 5.2; range= 32-58) were enrolled in the study. Demographic and health characteristics are shown in Table 1. Among the patients, three had breast cancer and one had cecal cancer. Menorrhagia was the most common

symptom (51/95). Preoperative 3-D Doppler ultrasound diagnosis indicated myoma in 56 patients, adenomyosis in 39 patients (Table 1), and a mix type (myoma + adenomyosis) in one woman (data not shown). Eighty-five percent (n=82) of the patients underwent hysterectomy surgery; 13.5% (n=13) underwent myomectory surgery. Pathological examination revealed 56 cases of myoma (58.3%), and 40 cases of adenomyosis (41.7%).

**Table1: Demographic and health characteristics of patients**

| | Total (95) | Myoma (56) | Adenomyosis (39) |
|---|---|---|---|
| **Age, mean(SD)** | 43.4(5.2) | 43.96(5.741) | 42.67(4.325) |
| | | n(%) | n(%) |
| **Parity** | | | |
| 0 | 14 | 13(22.8) | 1(2.6) |
| 1 | 9 | 6(10.5) | 3(7.7) |
| 2 | 33 | 17(29.8) | 16(41.0) |
| ≧3 | 40 | 21(36.9) | 19(48.7) |
| **Health history** | | | |
| Normal | 91 | 53(93.0) | 38(97.4) |
| Breast tumor | 3 | 3(5.3) | 0 |
| Cecal cancer | 1 | 1(1.8) | 0 |
| Hypertension | 1 | 0 | 1(2.6) |
| **Symptoms** | | | |
| Menorrhagia | 51 | 35(61.4) | 16(41.0) |
| Dysmenorrhea | 17 | 3(5.3) | 14(35.9) |
| Palpable abdominal mass | 11 | 11(19.3) | 0 |
| Multiple symptom | 17 | 8(14.0) | 9(23.1) |
| **Phase** | | | |
| Follicular phase | 83 | 46(80.7) | 37(94.9) |
| Luteal phase | 13 | 11(19.3) | 2(5.1) |
| **Preoperation diagnosis** | | | |
| Myoma | 56 | 56(98.2) | 0(.0) |
| Adenomyosis | 39 | 0(.0) | 39(100) |
| Myoma+Adenomyosis | 1 | 1(1.8) | 0 |
| **Surgery** | | | |
| Hysterectomy | 82 | 45(78.9) | 37(94.9) |
| Myomectomy | 13 | 12(21.1) | 1(2.6) |
| Biopsy | 1 | 0(.0) | 1(2.6) |

A comparison of 3D power Doppler ultrasonographic parameters between women with myoma and women with adenomyosis is provided in Table 2. Women with myoma had

significantly higher VI (U = 375.50, p < 0.001), FI (U = 386, p < 0.001), and VFI (U = 374.5, p <0.001), values than did women with adenomyosis. A significant difference in vascular location was also observed between myoma and adenomyosis (Fisher exact test, p < 0.001). The proportion of peripheral location in the myoma group was higher (92.9%; n = 52) than that found in the adenomysis group (15.0%; n = 6). By contrast, the proportion of central location in the adenomyosis group (85%; n = 34) was higher than that in the myoma group (7.1%; n = 4).

**Table2: Comparison of 3D power Doppler ultrasonographic parameters between myoma and adenomyosis**

| | Myoma n=56 Mean(SD) | Adenomyosis n=39 Mean(SD) | U value | *p* |
|---|---|---|---|---|
| VI | 2.16(1.37) | 0.85(0.86) | 375.500 | .000 |
| FI | 51.55(6.72) | 41.30(8.63) | 386.000 | .000 |
| VFI | 1.33(0.84) | 0.47(0.54) | 374.500 | .000 |
| | **n (%)** | **n (%)** | **Fisher Exact** | *p* |
| Location | | | | |
| Peripheral | 52 (92.9) | 6 (15.0) | | .000 |
| Central | 4 (7.1) | 34 (85.0) | | |

Bivariate logistic regression was conducted to determine whether the parameters for 3D ultrasonography are capable of predicting with significant accuracy the patterns of uterine masses (Table 3). As expected, the parameters of location (b =4.3, p <0.001 ), VI (b =- 1.46, p <0.001 ), FI (b = -.17, p <0.001 ), and VFI (b =-2.23, p < 0.001), were sufficient to significantly predict the patterns in the uterine masses. Note, that the parameter of location accounted for 67% of the variance.

**Table3: logistic regression of 3D power Doppler ultrasonographic parameters**

| Variables | Coefficient | S.E. | Wald | OR | 95%CI | $R^2$ |
|---|---|---|---|---|---|---|
| Location | 4.300 | .682 | 39.729 | 73.667 | 19.348-280.483 | .671 |
| VI | -1.460 | .316 | 21.326 | .232 | .125-.431 | .398 |
| FI | -.168 | .036 | 22.280 | .845 | .788-.906 | .404 |
| VFI | -2.225 | .481 | 21.421 | .108 | .042-.277 | .407 |

Because vascular location proved the most powerful among the ultrasonographic parameters, we examined its effectiveness as a diagnostic method to differentiate between uterine myoma and adenomyosis (Table 4). In the detection of uterine myoma, the location of the peripheral vessel had a sensitivity of 92%, a specificity of 85%, a positive predictive value of 89.66%, and a negative predictive value of 89.47%. In the detection of adenomyosis, the location of the central vessel had a sensitivity of 85%, a specificity of 92.86%, a positive predictive value (PPV) of 89.47%, and a negative predictive value (NPV) of 89.66%. These results indicate the effectiveness of 3D power Doppler ultrasonography as a preoperative method to accurately differentiate between uterine leiomyoma (Figure 1A), and adenomyosis (Figure 1B).

**Table 4: Diagnostic accuracy of ultrasonographic vascular location in the detection of myoma and adenomyosis**

| | Sensitivity(%) | Specificity(%) | PPV(%) | NPV(%) |
|---|---|---|---|---|
| **Myoma** | 92 | 85 | 89.66 | 89.47 |
| **Adenomyosis** | 85 | 92.86 | 89.47 | 89.66 |

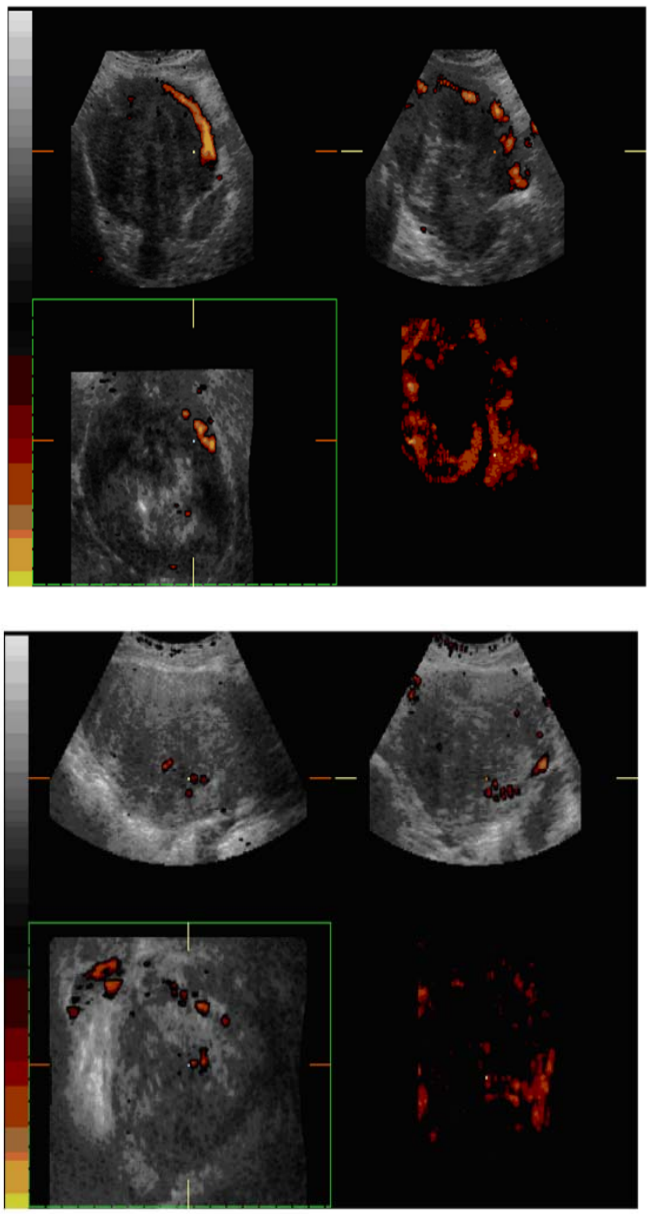

*Fig. 1. (A). 3D power Doppler ultrasonography of a leiomyoma, illustrating the vascular flow located on the peripheral surface of the uterine mass. (B) 3D power Doppler ultrasonography of adenomyosis, illustrating the vascular flow located on the central part of the uterine mass.*

## 4. Discussion

Adenomyosis is a common gynecologic disease that affects women. Unfortunately, diagnosis based on clinical methods is usually hindered by nonspecific symptoms.[10] Leiomyoma is the most common uterine tumor, with clinical presentations similar to those of adenomyosis [11]. Non-invasive diagnostic techniques, such as magnetic resonance imaging (MRI), have been employed to improve the accuracy of differentiating between adenomyosis and leiomyoma [12]; however, this approach can be compromised by the variety of morphological patterns [13].

Angiogenesis is the process of generating capillary blood vessels leading to neovascularization. It occurs under a variety of physiological and pathological conditions [14]. Quantitative morphometric studies in disease have shown that vascular volume, length, and surface area increase during the early stages of growth [15].

Several methods have been developed to diagnose adenomyosis [16]. Hystero-salpingography (HSG) and trans-abdominal sonography (TAS) lack the specificity required for the diagnosis of adenomyosis [16]. Grimbizis et al., reported that the diagnosis of adenomyosis, adenomyoma, and leiomyoma by transvaginal sonography (TVS) provides an acceptable degree of accuracy [17]. Previous studies have shown that the diagnosis of adenomyoma by transvaginal ultrasonography provides sensitivity of 80% and specificity of 94.3%. In the diagnosis of leiomyoma it provided sensitivity of 94.3% and specificity of 80% [18]. Although emerging data has indicated that magnetic resonance imaging (MRI) has a higher degree of sensitivity and specificity than TVS [19], the costs associated with this type of diagnostics are high. Moreover, one study demonstrated that TVS could be as accurate as MRI in the diagnosis of adenomyosis [20].

The recent availability of color Doppler sonography (CDS) has provided gynecologists with a sophisticated method for investigating uterine morphologic and physiologic features [21]. Pulsed Doppler sonography and CDS, have enabled the recording of vascular patterns and the measurement of changes in blood flow resistance and flow velocity [22]. Investigators have reported their findings related to adenomyosis and leiomyoma using color Doppler ultrasound [23-24]; however, that study employed 2D color Doppler ultrasound the results of which revealed that 87% of adenomyosis cases had vessel distributions different from those found in leiomyoma cases, in addition to a high pulsitility index (PI) [24]. In the early 1990s, color Doppler sonography [25] with a higher degree of sensitivity became available. Now, transvaginal color Doppler ultrasound, in combination with B-mode imaging, is increasingly used as a non-invasive method to assess changes in blood flow in the pelvic organs [26].

Because it is more sensitive, less angle-dependent, and not susceptible to aliasing [29], power Doppler Sonography has the potential to detect fluctuations in blood flow [28], with results superior to those of frequency-based color Doppler sonography, particularly in situations of low-velocity blood flow [27]. Our results indicate that 3-D ultrasound scanning may reduce the number of false positives by detailed investigation. This technique is also useful for the evaluation of complex ovarian lesions, such as ovarian dermoids, endometriomas, and fibromas, which could produce erroneous indications of malignancy when diagnosed using conventional transvaginal sonography and color Doppler ultrasound [30]. Few previous studies regarding the use of 3D power Doppler ultrasonography for uterine diagnostics have been conducted, and most of these have focused on malignant uterine tumors [31]. This study appears to be the first report of 3D power Doppler ultrasonography used to differentiate between uterine adenomyosis and leiomyoma. The newly developed power or energy modes of color Doppler imaging permit the depiction of ever smaller vessels; however, paradoxically, small intraparenchymal arterioles in benign and normal tissue may show low impedance and low-velocity blood flow patterns, giving rise to false-positive results [32]. Presenting images in three dimensions allows physicians to visualize many overlapping vessels quickly and easily and provides the ability to assess their relationship to disease. This enables physicians to view structures in 3D interactively, rather than having to assemble sectional images in his/her mind. The interactive rotation provided by power Doppler imaging provides improved visualization of tissue vasculature to differentiate between uterine adenomyosis and leiomyoma prior to surgery.

Adenomyosis and leiomyoma are common gynecologic diseases; however, they appear without specific symptoms. 3D power Doppler ultrasonography can be applied to differentiate between uterine adenomyosis and leiomyoma more effectively than prior methods, and shows considerable potential for a wide range of research purposes and clinical applications.

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## References

[1] M. Popovic, S. Puchner, D. Berzaczy, J. Lammer, R.A. Bucek, J Vasc Interv Radiol. **22**, 901 (2011).
[2] A. Tahlan, A. Nanda, Mohan H. Int J Gynecol Pathol. **25**, 361 (2006).
[3] A. Malvasi, A. Tinelli, S. Rahimi, G. D'Agnese, C. Rotoni, D. Dell'Edera, D.A. Tsin, C. Cavallotti. Biomed Pharmacother. **25**, 359 (2011).
[4] C. Farquhar, I. Brosens. Best Pract Res Clin Obstet Gynaecol. **20**, 603. (2006)
[5] W.H. Parker, J. Einarsson, O. Istre, J.B. Dubuisson. J Minim Invasive Gynecol. **17**, 551. (2010).
[6] A.C. Testa, S. Ajossa, G. Ferrandina, E. Fruscella, M. Ludovisi, M. Malaggese, G. Scambia, G.B. Melis, S. Guerriero. Ultrasound Obstet Gynecol. **26**, 67. (2005).
[7] S.F. Matin, I.S. Gill. J Endourol. **15**, 87. (2001).
[8] K.D. Kalache, R. Chaoui, J. Hartung, K.D. Wernecke, R. Bollmann. Ultrasound Obstet Gynecol. **12**, 27. (1998).
[9] Z. Merhemic, M. Breitenseher, S. Trattnig, B. Happel, C. Kukla, T. Rand, H. Imhof. Radiologe. **39**, 41. (1999).
[10] H. Liu, J.H. Lang. Med Sci Monit. **17**, 92. (2011).
[11] A. Tahlan, A. Nanda, H. Mohan. Int J Gynecol Pathol. **25**, 361. (2006).
[12] F.A. Taran, G.K. Hesley, K.R. Gorny, E.A. Stewart. Fertil Steril. **94**, 331. (2010).
[13] Q. Yang, L.H. Zhang, J. Su, J. Liu. Eur J Radiol. **79,** 47. (2011).
[14] P. Mabeta, M.S. Pepper. Int J Dev Biol. **55**, 431. (2011).
[15] M. Potente, H. Gerhardt, P.Carmeliet. Cell. **146**, 873. (2011).
[16] L.L. Arnold, S.M. Ascher, J.J. Schruefer, J.A. Simon. Obstet Gynecol. **86**, 461. (1995).
[17] G.F. Grimbizis, D. Tsolakidis, T. Mikos, E. Anagnostou, E. Asimakopoulos, P. Stamatopoulos, B.C. Tarlatzis. Fertil Steril. **94**, 2720. (2010).
[18] R.T. Huang, C.Y. Chou, C.H. Chang, C.H. Yu, S.C. Huang, B.L. Yao. Ultrasound Obstet Gynecol. **5**, 47. (1995).
[19] S.M. Ascher, L.L. Arnold, R.H. Patt, J.J. Schruefer, A.S. Bagley, R.C. Semelka, R.K. Zeman, J.A. Simon. Radiology. **190**, 803. (1994).
[20] C. Reinhold, S. McCarthy, P.M. Bret, A. Mehio, M. Atri, R. Zakarian, Y. Glaude, L. Liang, R.J. Seymour. Radiology. **199**, 151. (1996).
[21] A.C. Fleischer. Ultrasound Q. **19**, 179. (2003).
[22] A.C. Fleischer, D.M. Kepple, J. Vasquez. Current clinical applications. Radiol Clin North Am. **30**, 693. (1992).
[23] M. Hirai, K. Shibata, H. Sagai, S. Sekiya, B.B. Goldberg. J Ultrasound Med. **14**, 529. (1995).
[24] C.H. Chiang, M.Y. Chang, J.J. Hsu, T.H. Chiu, K.F. Lee, T.T. Hsieh, Y.K. Soong. J Assist Reprod Genet. **16**, 268. (1999).
[25] D. Botsis, D. Kassanos, G. Antoniou, E. Pyrgiotis, P. Karakitsos, D. Kalogirou. J Clin Ultrasound. **26**, 21. (1998).
[26] S. Guerriero, S. Ajossa, S. Piras, M. Gerada, S. Floris, N. Garau, L. Minerba, A.M. Paoletti, G.B. Melis. J Ultrasound Med. **26**, 1271. (2007).
[27] J.M. Rubin, R.O. Bude, P.L. Carson, R.L. Bree, R.S. Adler. Radiology. **190**, 853. (1994).
[28] J.M. Rubin, R.S. Adler, J.B. Fowlkes, S. Spratt, J.E. Pallister, J.F. Chen, P.L. Carson. Radiology. **190**, 183. (1995).
[29] C.B. Meyerowitz, A.C. Fleischer, D.R. Pickens, G.B. Thurman, A.D. Borowsky, G. Thirsk, C.G. Hellerqvist. J Ultrasound Med. **15**, 827. (1996).
[30] W. Henrich , C. Fotopoulou , I. Fuchs, C. Wolf, A. Schmider, C. Denkert, W. Lichtenegger, J. Sehouli. Anticancer Res. **27**, 4289. (2007).
[31] C.C. Chia, S.C. Huang, S.S. Chen, J.Y. Kang, J.C. Lin, Y.S. Lin, K.F. Huang, H.J. Lee, C.C. Zheng. Taiwan J Obstet Gynecol. **45**, 124. (2006).
[32] A.R. Chimpiri, N. Balasubramani. Semin Intervent Radiol. **26**, 253. (2009).