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Parametric Mapping of Contrasted Ovarian Transvaginal Sonography

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Abstract

The purpose of this study was to assess the accuracy of parametric analysis of transvaginal contrast-enhanced ultrasound (TV-CEUS) for distinguishing benign versus malignant ovarian masses. A total of 48 ovarian masses (37 benign and 11 borderline/malignant) were examined with TV-CEUS (Definity, Lantheus, North Bilreca, MA; Philips iU22, Bothell, WA). Parametric images were created offline with a quantification software (Bracco Suisse SA, Geneva, Switzerland) with map color scales adjusted such that abnormal hemodynamics were represented by the color red and the presence of any red color could be used to differentiate benign and malignant tumors. Using these map color scales, low values of the perfusion parameter were coded in blue, and intermediate values of the perfusion parameter were coded in yellow. Additionally, for each individual color (red, blue, or yellow), a darker shade of that color indicated a higher intensity value. Our study found that the parametric mapping method was considerably more sensitive than standard ROI analysis for the detection of malignant tumors but was also less specific than standard ROI analysis. Parametric mapping allows for stricter cut-off criteria, as hemodynamics are visualized on a finer scale than ROI analyses, and as such, parametric maps are a useful addition to TV-CEUS analysis by allowing ROIs to be limited to areas of highest malignant potential.

Keywords

ovarian cancer; contrast enhanced transvaginal sonography; multiparameter mapping

Introduction

It is estimated that 24,000 women in the United States will be diagnosed with ovarian cancer this year, leading to approximately 14,000 deaths nationwide due to the disease. Even more

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staggering are the statistics for ovarian cancer worldwide—an estimated 204,449 patients will be diagnosed with the disease, and approximately 124,860 women across the globe will die of the disease.[1] Unfortunately, out of all the gynecological cancers, ovarian cancer is associated with the highest mortality and remains a disease with a poor prognosis.[2] Additionally, while the incidence of ovarian cancer has been steadily increasing over the past 10 years with the overall lifetime risk of the disease now at 1.8%, survival rates for the disease have remained relatively stagnant over the past 40 years despite innovations in both surgical technique and chemotherapeutic drugs, neither of which have managed to impact the overall mortality rate.[1,3] This is in part due to difficulties in early detection of the disease. While women diagnosed with stage I disease—disease which is confined to the ovary—often require less invasive or extensive treatments and carry a 5-year survival of approximately 90%, women with stage III or stage IV disease have a 5-year survival rate of only 27% and 16%, respectively.[4] It is the hope that through earlier detection and more accurate diagnosis of early-stage cancers, the prognosis and overall disease-related mortality for this disease can be impacted in a positive manner.

A variety of imaging studies are used in the pre-operative evaluation of ovarian masses including: transabdominal or transvaginal sonography, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET). However, many of these modalities are limited in their accurate assessment of adnexal masses. For example, while both CT and MRI can detect large pelvic masses, their ability to accurately characterize smaller ovarian masses is limited. As a result, many patients end up undergoing surgical procedures for both the diagnosis and as well as the possible treatment of benign and malignant ovarian disease.[5]

Ultrasonography is an established method for the evaluation of adnexal masses, and the advantages to using transvaginal sonography (TVS) include the ability to offer high-resolution imaging combined with a modality that uses no ionizing radiation and that is widely available. Previously, the evaluation of ovarian masses using conventional TVS suffered from somewhat limited sensitivity and specificity with regards to the definitive diagnosis of ovarian cancer due to certain overlapping characteristics shared by both benign and malignant tumors.[5] However, significant technological improvements in the sonographic imaging of ovarian cancer have resulted in advances in the detection of benign versus malignant disease, and a recent European multicenter study which established a set of “simple rules” for the distinction of benign and malignant ovarian masses yielded a sensitivity of 93% and a specificity of 90%.[6] With the advent of three-dimensional transvaginal sonography, the ability to demonstrate the morphological characteristics of ovarian masses surpassed the capability of traditional TVS, and the use of color Doppler assists in the identification of neovascularity in malignant tumors.[7] However, transvaginal color Doppler sonography (TV-CDS) is only able to demonstrate the network of macrovessels between 100 and 200 microns in diameter, and unfortunately, it has not aided in the diagnosis of malignant ovarian tumors in general populations.[8–10] Although TV-CDS is unable to visualize the microvessel capillary network of tumors, the use of contrast-enhanced transvaginal sonography (CE-TVS) using intravascular microbubble contrast permits the depiction of vessels less than 40 microns in diameter.[11]

Traditionally, the CE-TVS time-intensity curve has been averaged over a region of interest (ROI) covering solid components of masses with the highest malignant potential (irregular solid area, papillary excresences, and septa). However, parametric mapping of the time-intensity curve allows for the global visualization of tumor hemodynamics on a pixel-by-pixel basis. While parametric imaging has been used to differentiate malignant focal liver and breast masses, it has not been widely applied to the evaluation of ovarian masses and has remained limited to selecting the pixel with the greatest peak enhancement (PE) and using that pixel's time-intensity curve for analysis.[11–13] The aim of this study was to assess the accuracy of parametric analysis of TV-CEUS for distinguishing benign versus malignant ovarian masses using histology as a reference standard.

Materials and Methods

48 patients ages 24–73 years (average +/− SD, 48.3 +/− 2.1 years) with morphologically abnormal ovarian masses smaller than 10 cm who had been referred for surgical treatment were examined with TV-CEUS. A morphologically abnormal mass was defined as: solid or cystic with papillary excrescences, focally thickened walls, or irregular solid areas. Retrospective analysis included data obtained from our previously reported published series as well as the data from 19 additional patients.[14,15] All patients with known right-to-left, bidirectional, or transient right-to-left cardiac shunts as well as a hypersensitivity reaction to the contrast agent or its components were excluded from the study. After thorough evaluation and screening by gynecologic oncologists and radiologists, all patients were scheduled for surgical treatment. The study was approved by the Institutional Review Board, and written informed consent was obtained from each patient. All women in the study were treated by oophorectomy using surgical laparoscopy or laparotomy within 3 days of the sonographic examination. Final histologic diagnoses were obtained for all lesions included in the study and were used as reference standards.

As the first part of the examination, transvaginal gray scale sonography was performed with an iU22 scanner (Phillips Medical Systems, Bothell, WA) and an 8-5 convex transvaginal probe to identify the ovarian mass. An experienced sonographer performed all the scans, after which color Doppler sonography was used to identify the area of the tumor with the most prominent vascularity. Once this region of interest (ROI) was assigned based on the gray scale and color Doppler sonographic findings, a contrast-enhanced study of the area was conducted to optimize the visualization of the mass.

A 3 μL/kg dose of perflutren microbubble contrast agent (Definity; Lantheus, North Billerica, MA) was injected into an antecubital vein over 2 seconds. This was subsequently followed by a bolus of 10 mL of normal saline. Per the manufacturer's recommendation for Definity, the patient's blood pressure, respiration, heart rate, and oxygen saturation were monitored both during the procedure as well as for 15 to 20 minutes after the procedure. A 3-minute cine loop recording was started at the time of the intravenous injection, and the sonographer was instructed not to move the transducer during the 3-minute recording. The acquired 3-minute cine loops were stored on the scanner's internal hard drive and exported to a computer workstation for later analysis. Following this, the injection was repeated (up to 2 injections of the contrast agent per tumor examined). Both cine loops were analyzed,

and the recording that showed the most prominent enhancement for each tumor was chosen for further study and evaluation. Each 3-minute video clip was then analyzed offline.

Image analysis was performed offline using quantification software prototype (Bracco Suisse SA, Geneva, Switzerland). Using the intravenous contrast signals, the software creates color-coded parametric maps of each perfusion parameter on a pixel-by-pixel basis for the previously defined region of interest in each mass.

First, a conventional ROI average analysis was performed. A region of interest (ROI) for each mass was manually placed to include all solid components and papillary projections while excluding any cystic areas or septations. Multiple parameters that have been previously described as having some potential diagnostic accuracy in CEUS cancer diagnosis were evaluated. The following contrast kinetic parameters were examined: time to peak (T_p; the time from injection of the contrast agent to peak signal intensity, measured in seconds), peak enhancement (PE; peak signal intensity during the contrast transit, measured in dB), wash-in AUC (WiAUC; the integral of the contrast wash-in curve, measured in arbitrary units, a.u), wash-out AUC (WoAUC; the integral of the contrast wash-out curve, measured in a.u), wash-in-wash-out AUC (WiWoAUC; the integral of the contrast wash-in and wash-out curve, measured in a.u), and wash-out rate (WoR; rate of wash-out of the contrast agent, measured in a.u).

For each examined contrast kinetic parameter, the values within the ROI were averaged. Then, receiver operating characteristic (ROC) curves were created to determine cut-off criterion with best diagnostic accuracy for ovarian cancer. These values were based on receiver operator curves obtained from the authors' original data optimizing sensitivity and specificity.[15] These cut-offs were used as a threshold values to create parametric maps of the ovarian lesions. For all diagnostic criteria, the cut-off with maximal diagnostic accuracy was chosen based on the ROC analysis.

For each perfusion parameter, map color scales were adjusted such that abnormal hemodynamics were represented by the color red, and the presence of any red color was used to differentiate benign and malignant tumors. Using these map color scales, low values of the perfusion parameter were coded in blue, and intermediate values of the perfusion parameter were coded in yellow. Additionally, for each individual color (red, blue, or yellow), a darker shade of that color indicated a higher intensity value. These abnormal hemodynamics were represented on the map color scales by the color red for: PE > 24 a.u, T_p; < 11 seconds, wiAUC > 35 a.u, WoAUC > 38 a.u, WiWoAUC > 38 a.u, or WoR > 9 a.u.. Cutoffs were chosen based on optimum points on receiver operating curves.

In order to compare parametric mapping to traditional TV-CEUS analysis, ROI analysis was also performed using the same perfusion parameters (PE, T_p;, wiAUC, WoAUC, WiWoAUC, and WoR) as were used in the parametric mapping. A region of interest (ROI) for each mass was identified and defined by the operator analyzing the time-intensity curves. The ROI was manually selected and drawn to include all solid components and papillary projections while excluding any cystic areas or septations. The ROI was kept constant in size between subjects, and the operator was unaware of the histologic diagnosis of each

mass prior to or while performing this analysis. ROI analysis was performed by averaging the parameters from all pixels of the time-intensity curve corresponding to the selected region of interest, and receiver operating characteristic (ROC) curves were created to determine cut-off criterion with best diagnostic accuracy.

Statistical analysis was performed with means and 95% confidence intervals (CIs). The test sensitivity was defined as a true positive rate of ovarian cancer diagnosis. The analysis of variance test was used to compare the contrast parameters of enhancing benign versus malignant ovarian masses. The results were considered significant at $P < 0.05$.

Results

A total of 48 masses were studied. Of these, 37 were benign while 11 masses were malignant. The histologic types of the ovarian masses are listed in Table 1.

The results of the parametric analysis are shown in Table 2, while representative images of parametric maps can be seen in Figures 1, 2, 3, 4, and 5. Our results show the greatest diagnostic sensitivity for maps of wash-out related variables such as WoAUC (sensitivity 100%), WiWoAUC (sensitivity 100%), and WoR (sensitivity 90.9%); however, these parameters suffered from somewhat lower specificity, with specificity values ranging from 48.6% (WoAUC and WiWoAUC) to 64.9% (WoR). Similarly, while both the PE and T_p were highly sensitive (100%), these parameters were the least specific on parametric maps, with the specificity of PE being 32.4% and that of T_p being 8.1%. The WiAUC remained a somewhat moderately sensitive (63.6%) and highly specific (89.2%) parameter during parametric analysis.

The results of the standard ROI analysis are shown in Table 3. The mean values for PE (p=0.0004), WiAUC (p=0.0070), WoAUC (p=0.0015), WiWoAUC (p=0.0031), and WoR (p=0.006) were all significantly different between benign and borderline/malignant tumors, while the mean values for T_p were not significant in benign versus borderline/malignant tumors.

A comparison of parametric analysis versus ROI analysis can be found in Table 4. While parametric analysis was consistently of equal (as for WiAUC) or higher sensitivity (as for PE, T_p, WoAUC, WiWoAUC, and WoR) than standard ROI analysis for all parameters analyzed, the specificity of parametric maps was reduced significantly when compared to specificity values for standard ROI analysis. Only the WiAUC parametric mapping achieved greater specificity than standard ROI analysis, and this was only by a margin of 0.1%.

Discussion

Contrast-enhanced TVS can significantly augment the diagnostic capacity of transvaginal sonography in identifying tumor neovascuarlization on a microvessel scale.[11, 14, 16–17] This is a substantial improvement in the potential diagnostic ability of sonography when compared to previous technology such as color Doppler imaging, which is limited demonstrating macrovessels within malignant tumors.[8] Given the poor prognosis of ovarian cancer when it is detected at a later stage, the identification of early microvascular changes

associated with early-stage ovarian cancer development is critical in reducing mortality associated with the disease, which has unfortunately remained relatively stagnant over the past 40 years.[1]

Several prior studies have demonstrated the use of contrast-enhanced TVS in the differentiation between benign and malignant ovarian tumors due to the greater peak enhancement and more prolonged contrast washout time in malignant tumors as compared to benign tumors.[18] However, simple documentation of tumor enhancement is not necessarily sufficient because some benign tumors show detectable contrast enhancement. To address this limitation, a few studies using enhancement kinetic parameters of the contrast agent to compare benign versus malignant tumors in the power Doppler mode have been performed. Using color Doppler sonography, Orden et al (2003) demonstrated that malignant and benign adnexal masses behaved differently with regards to degree, onset, and duration of Doppler US enhancement after injection with microbubble contrast, and according to the study from Marret et al (2004), the wash-out times and AUC were significantly greater in malignant ovarian tumors than in other benign ovarian masses.[16, 19]

Our preliminary clinical studies evaluated enhancement parameters in benign and malignant adnexal masses using pulse inversion nonlinear imaging, a new method of CE-TVS which provides more consistent and reliable estimates of tumor vascularity and perfusion compared to traditional Doppler-based CE-TVS. Our data indicated that the peak enhancement and wash-out parameters had the best sensitivity and specificity for the diagnosis of malignant ovarian tumors while the wash-in and time to peak parameters were less accurately predictive of malignant status, possibly related to its variability with regards to contrast injection and circulation times.[15] As such, during the next phase of our study, we analyzed the use of enhancement variables with parametric mapping, a technique which had previously been used in determination of focal liver and breast masses.[12,13] To our knowledge, only the study by Testa et al (2009) has explored the use of parametric mapping in ovarian cancer detection. Although the study by Testa et al (2009) used parametric mapping, its application remained limited to selecting the pixel with the greatest peak enhancement and using that pixel's time-intensity curve for analysis rather than using the map strictly for differentiation of benign versus malignant masses.[11]

Parametric mapping allows the finer scale visualization of tumor neovascularity on a pixel-by-pixel basis, and ideally, in identifying early microvessel changes that might be associated with malignancy, parametric maps could be used to detect ovarian cancer in earlier stages, as late diagnosis of advanced disease carries a poor prognosis.[4] While our study demonstrated that parametric maps were more sensitive than standard ROI analysis, they were considerably less specific than standard ROI analysis. Our methods were designed to give a high sensitivity, as is needed for any screening test, and therefore the specificity was somewhat reduced. We selected cut-off values with a high sensitivity (and therefore somewhat lower specificity) to detect lesions requiring further evaluation with other confirmatory tests such as MRI. Although a higher sensitivity is ideal for a screening test, as it is indicative of a test's ability to identify true positive results, a good diagnostic test requires both high sensitivity as well as high specificity. Otherwise, it will fail to identify patients who are truly negative for the disease and risks exposing patients to both further

medical testing as well as potentially unnecessary procedures and interventions. Thus, despite its reduced sensitivity compared to parametric maps in our study, standard ROI analysis with its consistently higher specificity values is more accurate than parametric maps in differentiating benign from malignant ovarian masses. However, despite this, we do believe that parametric mapping serves a useful purpose when applied as part of screening measures rather than the sole diagnostic test.

Although parametric mapping might not provide the best diagnostic accuracy for ovarian cancer, its use has significant potential benefit in TV-CEUS. Parametric mapping allows for stricter cut-off criteria since hemodynamics are visualized on a finer scale than in ROI analyses based on mean time-intensity curves for heterogeneous regions chosen on morphology alone. Because potentially small areas of neovascularity can be overlooked in standard ROI analysis as these pockets are averaged over larger areas, parametric mapping are a useful addition to TV-CEUS analysis by allowing ROIs to be limited to areas of highest malignant potential.

There are several limitations of this study. Since this is a pilot study, no inter- and intra-observer ROI selection variability analysis was performed. Another potential limitation of our study includes the sample size of masses evaluated. Although we analyzed 48 adnexal masses, only 11 of these were borderline or malignant ovarian tumors while 37 of these were benign masses. Additionally, although parametric mapping detects small areas of neovascularity that might not be detected with traditional ROI analysis, it is possible that certain benign or inflammatory processes might also demonstrate changes in vascularity detected by parametric mapping, and this might contribute towards the somewhat reduced specificity in our study. Similarly, it is possible that different histological subtypes of borderline or malignant ovarian tumors might demonstrate vastly different enhancement patterns and that certain subtypes might be more amenable to accurate diagnosis with parametric mapping. Even though our study analyzed a wide range of different subgroups of borderline/malignant tumors, some of these subtypes only contained a sample size of n=1 or n=2. As a result, future larger-scale studies with more borderline or malignant tumors evaluated would be helpful in further evaluation of the use of parametric mapping analysis. Additionally, in this study, only qualitative analysis of the parametric naps was performed, and only one criterion cut-off was analyzed for each parameter. More advanced quantitative methods of parametric map analysis, including testing multiple other cut-off values, should be performed to improve diagnostic accuracy of this method and improve test sensitivity and specificity.

In summary, parametric mapping remains an area of significant potential benefit in the diagnosis of ovarian cancer, with particular emphasis on the earlier diagnosis of this dreaded disease. The advantages of parametric analysis include the ability to visualize abnormal tumor hemodynamics on a pixel-by-pixel level with the added of benefit of potentially demonstrating small areas of neovascularization indicative of early malignant changes that might be missed using standard ROI analyisis. While our results demonstrated that parametric mapping can be a highly sensitive method for determining if an ovarian mass is benign versus malignant, parametric maps alone were considerably less specific than standard ROI analysis in making this distinction. We found the enhancement parameters of

wash-out AUC, wash-in-wash-out AUC, and wash-out rate to be the most diagnostically accurate out of all the parameters included in our study, and the peak enhancement and time to peak variables were less helpful. Overall, parametric maps are a useful addition to traditional TV-CEUS analysis by allowing for ROIs to be limited strictly to the areas of the most malignant potential, and, as such, parametric mapping remains a significant area of potential exploration and development in the field of ovarian cancer diagnosis.

References

1. Jinawath, N.; Shih, I. Biology and pathology of ovarian cancer. In: Briston, R.; Armstrong, D., editors. Early Diagnosis and Treatment of Cancer. Ovarian Cancer. Philadelphia, Pa, USA: Saunders; 2011. p. 17-32.
2. Jemal A, Thomas A, Murray T, et al. Cancer statistics, 2002. CA Cancer J Clin. 2002; 52(1):2347.
3. Berrino F, De Angelis R, Sant M, et al. Survival for eight major cancers and all cancers combined for European adults diagnosed in 1995–99: results of the EUROCARE-4 study. Lancet Oncol. 2007; 8(9):773–783. [PubMed: 17714991]
4. Engel J, Eckel R, Schubert-Fritschle G, et al. Moderate progress for ovarian cancer in the last 20 years: prolongation of survival, but no improvement in the cure rate. Eur J Cancer. 2002; 38(18): 2435–2445. [PubMed: 12460789]
5. Fleischer AC, Lyshchik A, Hirari M, et al. Early detection of ovarian cancer with conventional and contrast-enhanced transvaginal sonography: recent advances and potential improvements. J Oncol. 2012:302–858.
6. Timmerman D, Testa AC, Bourne T, et al. Simple ultrasound-based rules for the Diagnosis of ovarian cancer. Ultrasound Obstet Gynecol. 2008; 31(6):681–690. 2008. [PubMed: 18504770]
7. Testa AC, Ferrandina G, Fruscella E, et al. The use of contrasted transvaginal sonography in the diagnosis of gynecologic diseases: a preliminary study. J Ultrasound Med. 2005; 24(9):1267–1278. [PubMed: 16123187]
8. Fleischer AC, Lyshchik A, Andreotti RF, et al. Advances in sonographic detection of ovarian cancer: depiction of tumor neovascularity with microbubbles. Am J Roentgenol. 2010; 194(2):343–348. [PubMed: 20093594]
9. Valentin L. Pattern recognition of pelvic masses by gray-scale ultrasound imaging: the contribution of Doppler ultrasound. Ultrasound Obstet Gynecol. 1999; 14(5):338–347. [PubMed: 10623994]
10. Valentin L. Prospective cross-validation of Doppler ultrasound examination and gray-scale ultrasound imaging for discrimination of benign and malignant pelvic masses. Ultrasound Obstet Gynecol. 1999; 14(4):273–283. [PubMed: 10586480]
11. Testa AC, Timmerman D, Van Belle V, et al. Intravenous contrast ultrasound examination using contrast-tuned imaging (CnTI) and the contrast medium SonoVue for discrimination between benign and malignant adnexal masses with solid components. Ultrasound Obstet Gynecol. 2009; 34(6):699–710. [PubMed: 19924735]
12. Anaye A, Perrenoud G, Rognin N, et al. Differentiation of focal liver lesions: usefulness of parametric imaging with contrast-enhanced US. Radiology. 2011; 261(1):300–310. [PubMed: 21746815]
13. Eisenbrey JR, Dave JK, Merton DA, et al. Parametric imaging using subharmonic signals from ultrasound contrast agents in patients with breast lesions. J Ultrasound Med. 2011; 30(1):85–92. [PubMed: 21193708]
14. Fleischer AC, Lyshchik A, Jones HW, et al. Contrast-enhanced transvaginal sonography of benign versus malignant ovarian masses: preliminary findings. J Ultrasound Med. 2008; 27(7):1011–1018. [PubMed: 18577664]
15. Fleischer AC, Lyshchik A, Jones HW, et al. Diagnostic parameters to differentiate benign from malignant ovarian masses with contrast-enhanced transvaginal sonography. J Ultrasound Med. 2009; 28(10):1273–1280. [PubMed: 19778872]

16. Marret H, Sauget S, Giraudeau B, et al. Contrast enhanced sonography helps in discrimination of benign from malignant adnexal masses. J Ultrasound Med. 2004; 23(12):1629–1639. [PubMed: 15557306]

17. Niermann KJ, Fleischer AC, Huamani J, et al. Measuring tumor perfusion in control and treated murine tumors: correlation of microbubble contrast-enhanced sonography to dynamic contrast-enhanced magnetic resonance imaging and fluorodeoxyglucose positron emission tomography. J Ultrasound Med. 2007; 26(6):749–756. [PubMed: 17526606]

18. Kupesic S, Kurjak A. Contrast-enhanced, three-dimensional power Doppler sonography for differentiation of adnexal masses. Obstet Gynecol. 2000; 96(3):452–458. [PubMed: 10960641]

19. Ordén MR, Jurvelin JS, Kirkinen PP. Kinetics of a US contrast agent in benign and malignant adnexal tumors. Radiology. 2003; 226(2):405–410. [PubMed: 12563133]

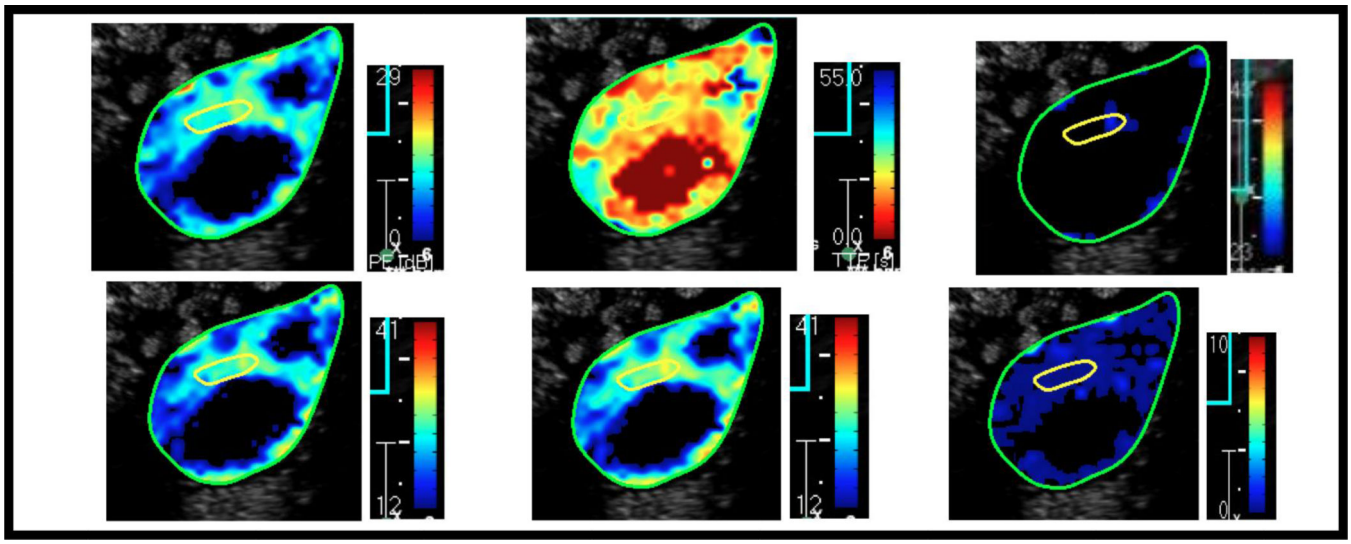

Figure 1.

Parametric map of a corpus luteum cyst during peak enhancement (a), time to peak (b), wiAUC (c), woAUC (d), wiwoAUC (e), and woR (f). Map color scales were constructed to show possible tumor neovascularity as shades of red. The majority of the region of interest is depicted in blue colors with the exception of time to peak, which was shown to be non-specific.

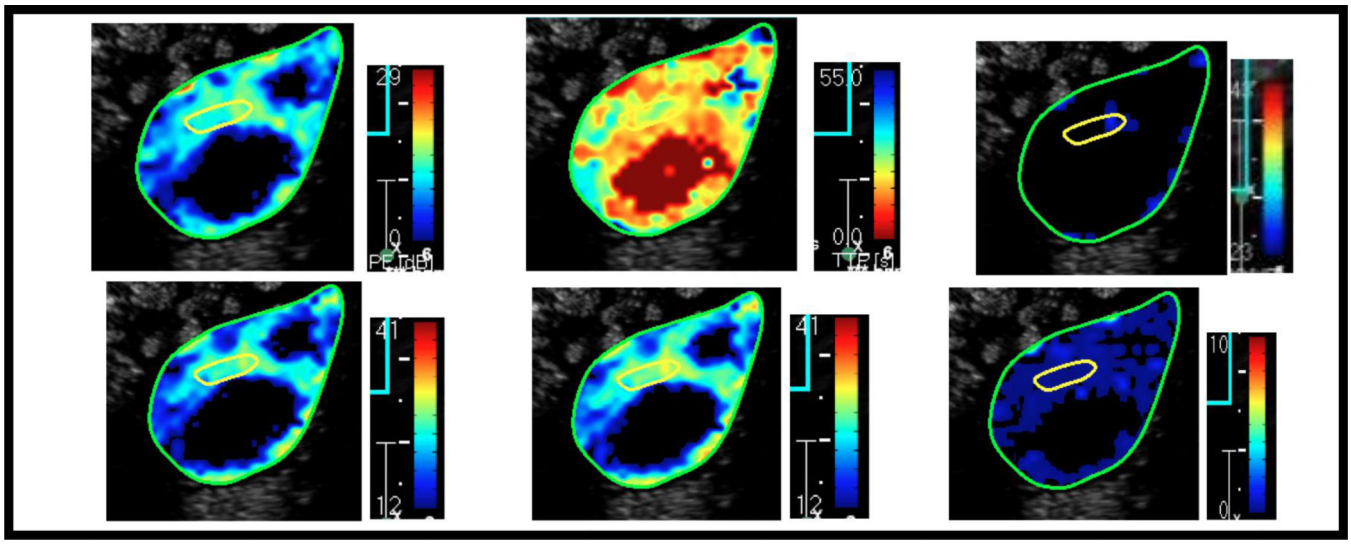

Figure 2.

Parametric map of a fibrothecoma during peak enhancement (a), time to peak (b), wiAUC (c), woAUC (d), wiwoAUC (e), and woR (f). Consistent with the rest of our analysis, the time to peak was the least specific for detecting malignancy out of all the variables analyzed, as dark red areas are supposed to correlate with abnormal hemodynamics.

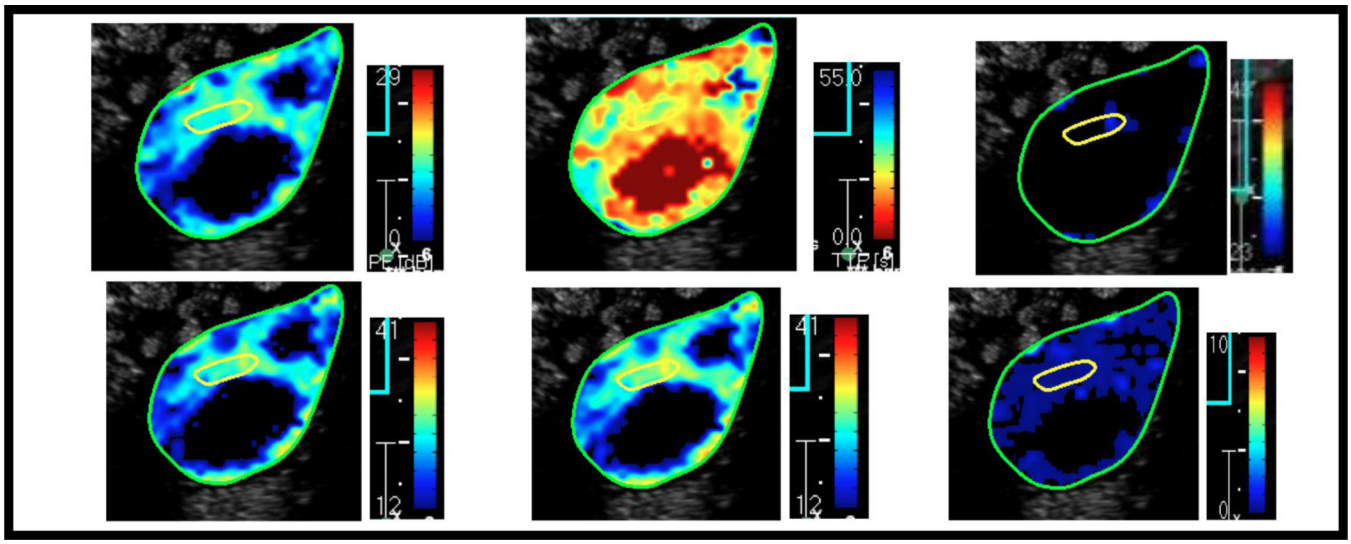

Figure 3.

Parametric map of a serous borderline tumor during peak enhancement (a), time to peak (b), wiAUC (c), woAUC (d), wiwoAUC (e), and woR (f). All six enhancement kinetic parameters studied revealed marked areas of dark red indicating malignancy, and this was later correlated with histopathology.

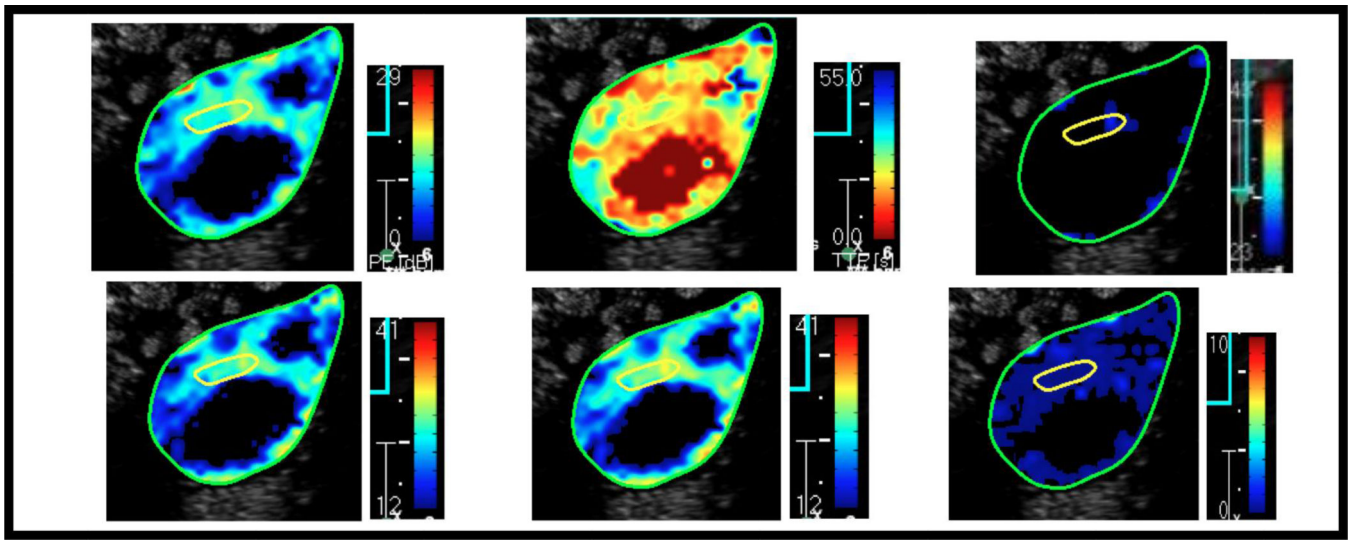

Figure 4.

Parametric map of a serous adenocarcinoma during peak enhancement (a), time to peak (b), wiAUC (c), woAUC (d), wiwoAUC (e), and woR (f). Areas of tumor neovascularity in red contrast sharply with the cystic portion of the tumor shown in blue.

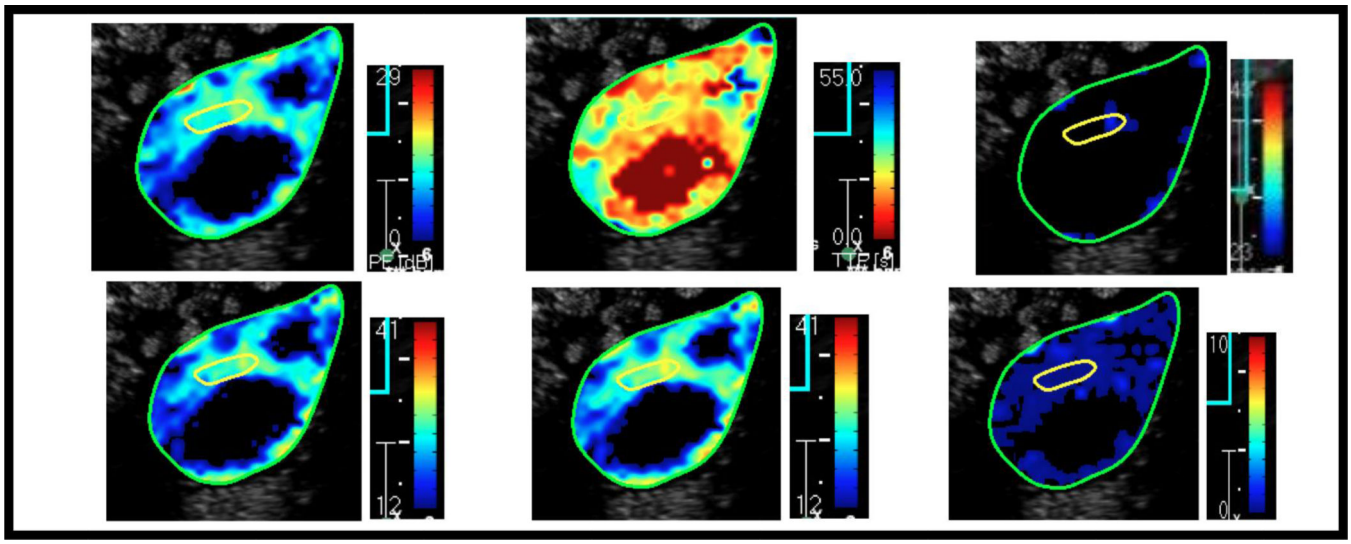

Figure 5.

Parametric map of metastatic breast cancer during peak enhancement (a), time to peak (b), wiAUC (c), woAUC (d), wiwoAUC (e), and woR (f). Multiple areas of tumor neovascularity, as shown as shades of red, are present.

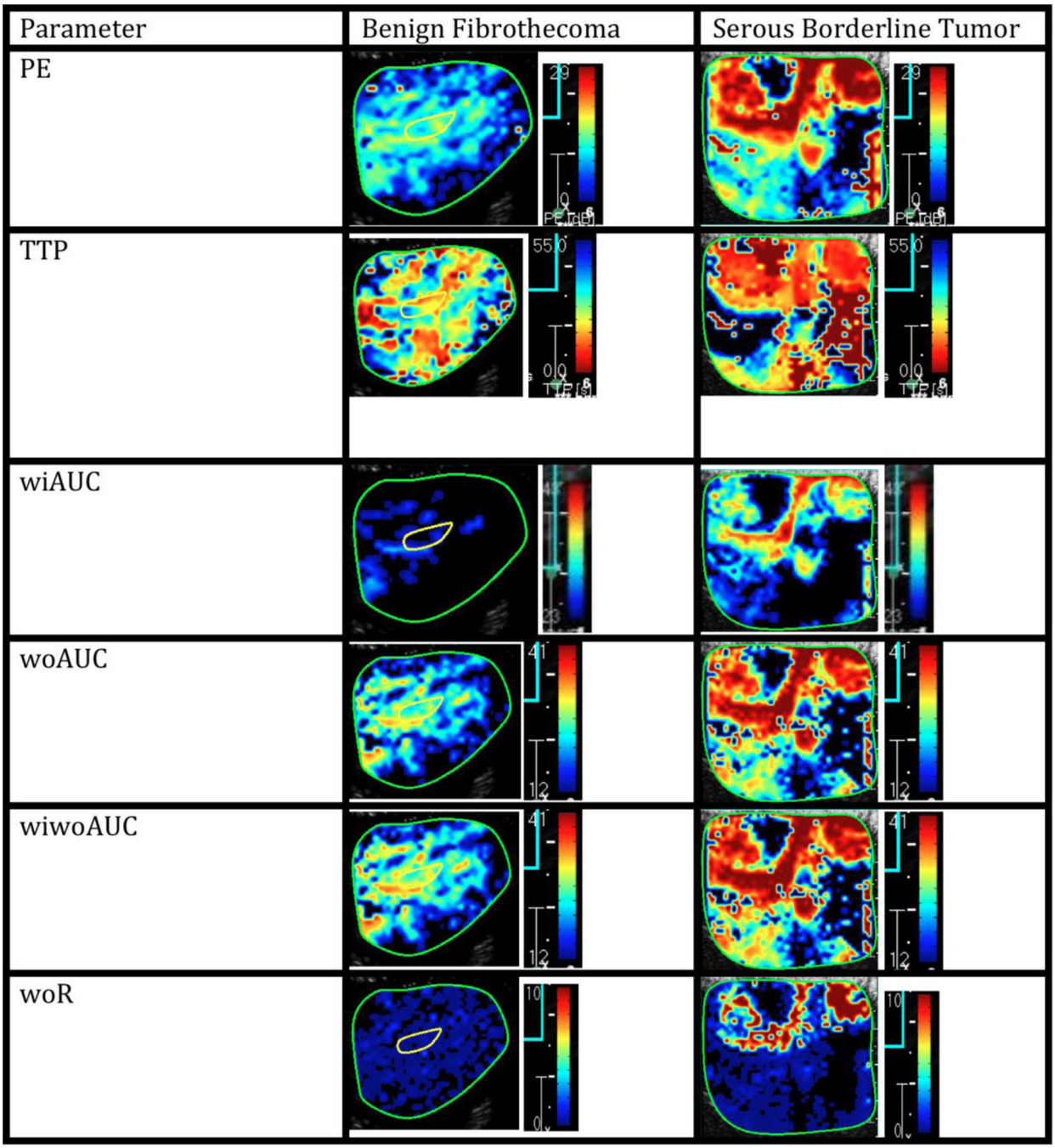

Figure 6.

a direct, side-by-side comparison of parametric maps of the above benign fibrothecoma (from Figure 2) and above borderline serous adenocarcinoma (from Figure 3).

Table 1

Histologic types of ovarian masses

Type	**N=**
Benign (n=37)	
Simple cyst	10
Endometrioma	6
Serous cystadenoma	7
Corpus luteum cyst	5
Teratoma	3
Mucinous cystadenoma	3
Fibroma	2
Paraovarian/paratubal cyst	1
Malignant (n=11)	
Serous adenocarcinoma	5
Endometriod adenocarcinoma	2
Borderline serous adenocarcinoma	2
Borderline mucinous cystadenocarcinoma	1
Breast cancer metastasis	1

Table 2

Diagnostic accuracies of parametric mapping

	PE	T_p	WiAUC	WoAUC	WiWoAUC	WoR
Sensitivity	100%	100%	63.6%	100%	100%	90.9%
Specificity	32.4%	8.1%	89.2%	48.6%	48.6%	64.9%

Table 3

Diagnostic accuracies of ROI analysis

	PE	T_p	WiAUC	WoAUC	WiWoAUC	WoR
Benign: Mean (SD)	28.9 (44.2)	19.2 (16.3)	197.0 (312.3)	529.1 (813.7)	1056.9 (2286.6)	2.81 (6.5)
Malignant: Mean (SD)	219.0 (350.9)	11.9 (5.4)	1050.2 (1395.0)	2374.5 (2916.6)	3424.8 (4303.5)	29.0 (49.7)
P-value	0.0004	0.10	0.0070	0.0015	0.0031	0.0006
Cutoff	>71.0 db	<15.7 sec	>369.4 a.u	>450.4 a.u	> 622.2 a.u	>2.5 a.u
Sensitivity	63.6%	90.9%	63.6%	81.8%	81.8%	72.7%
Specificity	91.9%	45.6%	89.1%	73.0%	70.3%	78.4%

Table 4

Comparison of diagnostic accuracies of parametric maps (left) versus ROI analysis (right)

	PE: Parametric (L) vs ROI (R)		**Tp Parametric (L) vs ROI (R)**		**WiAUC Parametric (L) vs ROI (R)**		**WoAUC Parametric (L) vs ROI (R)**		**WiWoAUC Parametric (L) vs ROI (R)**		**WoR Parametric (L) vs ROI (R)**	
Sensitivity	100%	63.6%	100%	90.9%	63.6%	63.6%	100%	81.8%	100%	81.8%	90.9%	72.7%
Specificity	32.4%	91.9%	8.1%	45.6%	89.2%	89.1%	48.6%	73.0%	48.6%	70.3%	64.9%	78.4%