Clinical Applications of Color Doppler Ultrasound in Chest Medicine

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The wide application of recent advances in chest ultrasound has enabled color Doppler ultrasound (CDUS) to be used in evaluating thoracic lesions. Clinically, CDUS is helpful in assessing vessel signals within the thoracic lesions, differentiating lung cancers from benign lesions, assessing the neovascularity of lung cancers, diagnosing congenital vascular abnormalities (pulmonary sequestration and arteriovenous malformation), and avoiding the complication of US-guided needle biopsy injury to the great vessels. The CDUS "fluid color sign" can be used to detect minimal pleural effusion in thoracocentesis, and the CDUS "pulmonary artery vessel signal" is useful in predicting pulmonary benign lesions. Though CDUS still has some limitations in its capability to image vessel signals, the development of power Doppler US (US angiography) has improved images of vessel signals without angle limitation, and the newly developed dynamic flow US produces superior imaging quality with less color noise and blooming effect. The broad application and potential extension of CDUS in thoracic diseases has made CDUS a powerful and necessary imaging modality in chest medicine, especially in guiding transthoracic percutaneous needle biopsy of thoracic lesions and aiding in the differentiation of anatomic tissue.

KEY WORDS — biopsy, Doppler, lung, vessel

Introduction

For peripheral pulmonary lesions, conventional examinations such as sputum analysis, bronchoscopy, and routine chest radiographs are often limited in disease diagnosis. Thus, image-guided percutaneous needle biopsy (using fluoroscopy, computed tomography, and ultrasound [US]) has been used to sample tissues and aid in diagnosis [1–8]. Of these modalities, chest US examination and US-guided needle biopsy provide the simplest and most rapid and convenient diagnostic tools for all lesions abutting the chest wall [5–12]. Chest US examinations have

a number of advantages: they can be performed at the bedside, in the patient's most comfortable and appropriate position (sitting, prone, or supine), and without exposure to irradiation. In particular, improvements in US image resolution and the use of a well-suited puncture-guiding device have made US-guided needle biopsy increasingly real-time, safe, and convenient [5,7,11]. In the literature, chest US examinations and US-guided needle biopsy have been shown to be valuable in diagnosing lung cancers, mediastinal tumors, pleural lesions, chest wall lesions, and some peripheral pulmonary infections, with excellent results and minimal complications

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[5–12]. However, conventional grayscale chest US alone is somewhat limited in the assessment of vessel signals in thoracic lesions.

Color Doppler US (CDUS) is used for the evaluation of vessel signals in normal tissues and organs and in pathologic lesions; it has been widely used in the cardiovascular system, abdominal lesions, obstetric and gynecologic lesions, breast lesions, and carotid and intracranial vessels [13–20]. Recently, CDUS has also been applied in chest medicine. As reported in the literature and from our own experience, CDUS not only clearly demonstrates the vessel signals in thoracic lesions, but also enables assessment of hemodynamic changes, tumor neovascularity, congenital vascular anomalies, and anatomic tissue differentiation [21–27]. In particular, CDUS and its color-based puncture-guiding device readily disclose the prominent vessels and, therefore, significantly increase the safety and clinical extension of US-guided percutaneous needle biopsy [28,29]. The development of power Doppler US (PDUS) has further improved images of vessel signals without angle limitation, and the newly developed dynamic flow US (DFUS) discloses vessel signals with less color noise and blooming effect [19,20,30,31].

In the present report, we review the published literature and describe our experience with the clinical applications of CDUS in chest medicine.

Indications and Technique for Chest US and CDUS Examinations

Indications

Chest US is used initially to assess pleural effusion and pleural opacity [32,33]. However, any pulmonary lesions and mediastinal tumors abutting the chest wall, pleural lesions, and chest wall lesions are all suitable for chest US examination [5–12].

In usual clinical practice, a grayscale US examination is performed initially, after which CDUS examination can be added to assess vessel signals within the lesion. In the assessment of pulmonary consolidations and mediastinal tumors, CDUS readily demonstrates and evaluates the vessel signals and

can thus help prevent injury to prominent vessels when performing transthoracic US-guided needle biopsy [28,29].

In our experience, only a number of special conditions are contraindicated for chest US examination and US-guided needle biopsy: (1) when the patient is not cooperative in holding his/her breath while performing transthoracic US-guided needle biopsy for peripheral pulmonary lesions; (2) a bleeding tendency with platelets $< 20,000/mm^3$; if necessary, the US-guided needle biopsy can be performed within 12–24 hours after platelet transfusion; (3) recent myocardial infarction and/or unstable angina; and (4) lesions poorly demonstrated by US.

Techniques for CDUS examination

In performing a CDUS examination, we still use grayscale US first to localize the lesions before adding CDUS. Before the start of the CDUS examination, the Doppler filter is usually set at 50–100 Hz to eliminate low-frequency signals from vessel wall motion and avoid interference from respiratory and cardiac movement [13,21,24,34,35]. Color Doppler gain is also adjusted until only a few noise specks are visible in the background [14,24]. When the CDUS signal is detected, the sample volume is re-adjusted to approximate the size of the detected blood vessels, and the angle is repositioned to parallel the direction of blood flow (the Doppler angle θ between the ultrasound beam and flow signal is adjusted to obtain the largest frequency shift or velocity, while remaining below 60° if possible) [14,35]. The pulse repetitive frequency is also adjusted, depending on the blood flow velocity under investigation. Pulse-wave CDUS is used to detect flow signals within the lesions; all Doppler signal waveforms are recorded on color-printed sonopaper and/or on laser disc, thus enabling all data regarding the CDUS signals and spectral waveforms of the thoracic lesions to be reviewed and analyzed. In general, spectral waveforms that are reproducibly similar over three consecutive cardiac cycles are recorded as satisfactory [24,36].

CDUS is then used to assess vessel signals within the lesions, hemodynamic changes (resistive index [RI] and pulsatility index [PI]), tumor neovascularity,
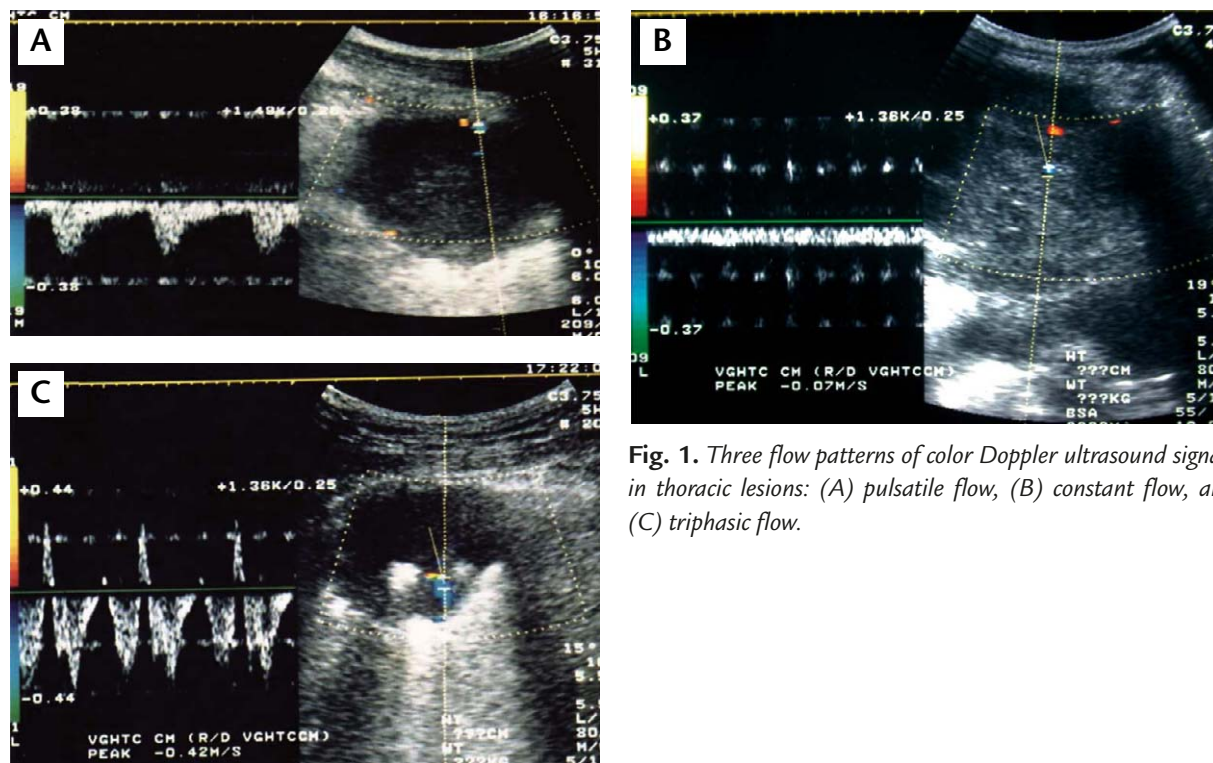
Fig. 1. *Three flow patterns of color Doppler ultrasound signals in thoracic lesions: (A) pulsatile flow, (B) constant flow, and (C) triphasic flow.*

any special vascular anomalies, and other tissue differentiation and clinical applications.

Applications of CDUS in Chest Medicine

CDUS has been used for thoracic diseases to evaluate vessel signals within lesions; however, from our perspective, the clinical applications of CDUS in chest medicine remain underutilized. The main applications of CDUS in the published literature and clinical practice are summarized below.

Correlation of CDUS signals with resected histologic specimens

CDUS has been reported as a valuable tool in assessing the vessel signals of thoracic lesions. Hsu et al reported their findings on the correlation of CDUS vessel signals with resected histologic specimens [21]. In their report, they found three vessel signal flow patterns in lung cancers: pulsatile flow (artery), triphasic flow (vein), and constant flow (Fig. 1); only two flow patterns were present in benign

lesions: pulsatile flow and triphasic flow. In correlating CDUS vessel signals with resected histologic specimens, constant flow was representative of the true neovascularity of lung cancers and was valuable in differentiating lung cancers from benign lesions ($p < 0.001$). The correlation between CDUS vessel signals and resected histologic specimens was also excellent. Nevertheless, thoracic lesions without CDUS vessel signals may be completely lacking in blood vessels or have blood vessels that cannot be detected by present-day CDUS equipment.

With increasing experience in using CDUS examinations in thoracic lesions, we recently found some pulmonary veins (often in the collapsed lung and distal to a central endobronchial tumor) that could present with constant flows. Thus, we should be careful in the interpretation of CDUS constant flow vessel signals within collapsed lungs and in some benign lesions.

CDUS pulsatile flow in the assessment of lung cancers and benign lesions

CDUS pulsatile flows have been used to assess and differentiate malignancies from benign tumors, including breast, ovary, kidney, and other organ

tumors [13–16,34–36]. In the assessment of pulsatile flows, two parameters are often used: RI (calculated as peak systolic velocity – end diastolic velocity/peak systolic velocity), and PI (calculated as peak systolic velocity – end diastolic velocity/mean velocity). Because malignancies often have sinusoid-like or large capillary-like tumor vessels and even arteriovenous shunts, malignancies are reported to have statistically significantly lower RI and PI values than benign lesions [13,14,16,34–36].

Yuan et al first reported the application of CDUS pulsatile flows in the assessment of thoracic lesions. In their report, RI and PI values were significant in differentiating lung cancers from benign lesions (both $p < 0.01$) [24]. However, in our experience, overlapping RI and PI values between lung cancers and benign lesions are common, thereby limiting the application of RI and PI values in differentiating lung cancers from benign lesions [27,37]. An interesting finding in our series was the lower RI and PI values in small cell lung cancers when compared with those in non-small cell lung cancers (adenocarcinoma and squamous cell carcinoma). The lower RI and PI values in small cell lung cancers may imply an increasing and intense downstream angiogenesis; conversely, the relatively high RI and PI values in non-small cell lung cancers probably indicate sparse angiogenesis. Thus, compared with the clinical presentations and biologic behavior of lung cancers, small cell lung cancer with intense angiogenesis has a greater range of clinical presentations than non-small cell lung cancer; these presentations include rapid tumor growth, early metastasis, and sensitivity to chemotherapy. Further study is warranted to determine whether CDUS pulsatile flow is helpful in differentiating lung cancers from benign lesions.

CDUS "Pulmonary Artery Vessel Signal": A Sign for Predicting Benign Lesions

Lung cancers are always supplied by the bronchial artery system; thus, pulmonary and bronchial angiograms were previously used to diagnose and differentiate lung cancers from benign lesions. If vessel signals within pulmonary lesions can be confirmed to be those of the pulmonary artery, CDUS should be able to predict and differentiate benign lesions from lung cancers (Fig. 2).

We previously arbitrarily defined a CDUS "pulmonary artery vessel signal" as a pulsatile flow with a vessel signal length of ≥ 1 cm that is demonstrated smoothly by CDUS [38]. Using this CDUS vessel signal, thoracic lesions with at least a detectable CDUS "pulmonary artery vessel signal" were considered to be benign. In a study lasting more than 6 years, we screened and analyzed 264 thoracic lesions (125 lung cancers and 139 benign lesions) and found that the CDUS "pulmonary artery vessel signal" was reliable in predicting and differentiating benign lesions from lung cancers ($p < 0.0001$; sensitivity, 0.53 [74/139]; specificity, 0.98 [123/125]; positive likelihood ratio, 26.5) (Figs. 3 and 4). Only two specific alveolar cell carcinomas with lobar consolidation presented with a CDUS "pulmonary artery vessel signal"; these were the only exceptions among the lung cancers. Our results suggest that the CDUS "pulmonary artery vessel signal" deserves a wide clinical application in predicting benign pulmonary lesions [38].

CDUS "Fluid Color Sign" to Assess the Thoracocentesis of Minimal Pleural Effusion

Chest US can be used to assess minimal pleural effusion and guide thoracocentesis. However, CDUS can be more useful than grayscale US in predicting the success of thoracocentesis of minimal pleural effusion. Respiratory movement will cause the minimal pleural effusion to move and create a color signal under CDUS. Wu et al reported this finding as a CDUS "fluid color sign" and proved it to be more sensitive than grayscale US in predicting the success of thoracocentesis (Fig. 5) [23,25].

Loculated pleural effusion, however, will not present with a CDUS "fluid color sign," even if it can be aspirated smoothly. Therefore, the CDUS "fluid color sign" is not present and cannot be applied to localized and loculated pleural effusions.

Diagnosis of Specific Vascular Anomalies and Utility for Tissue Differentiation

Pulmonary sequestration is a congenital malformation with non-functioning lung tissue that is
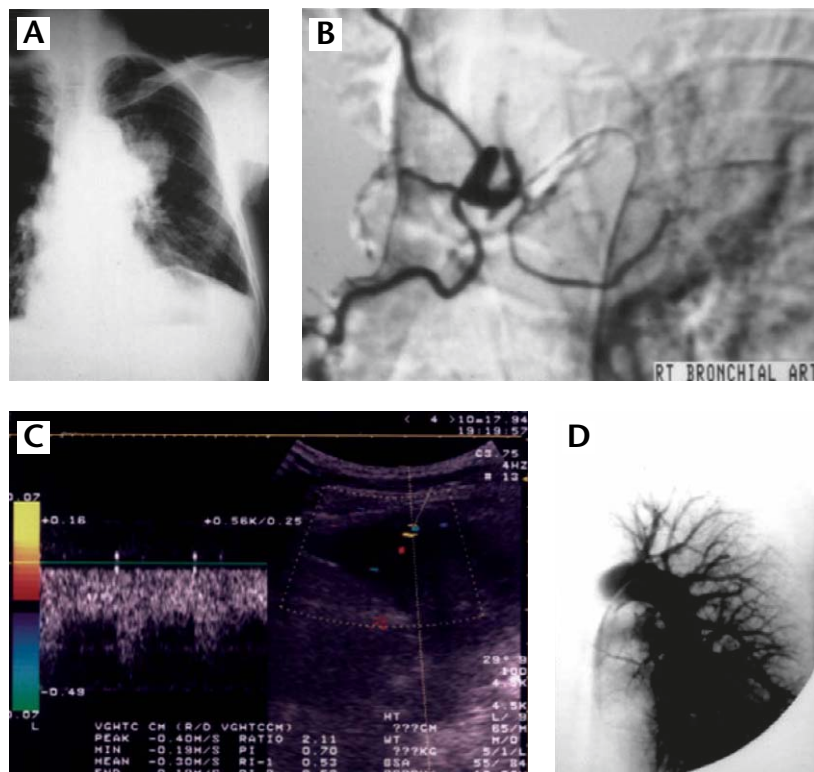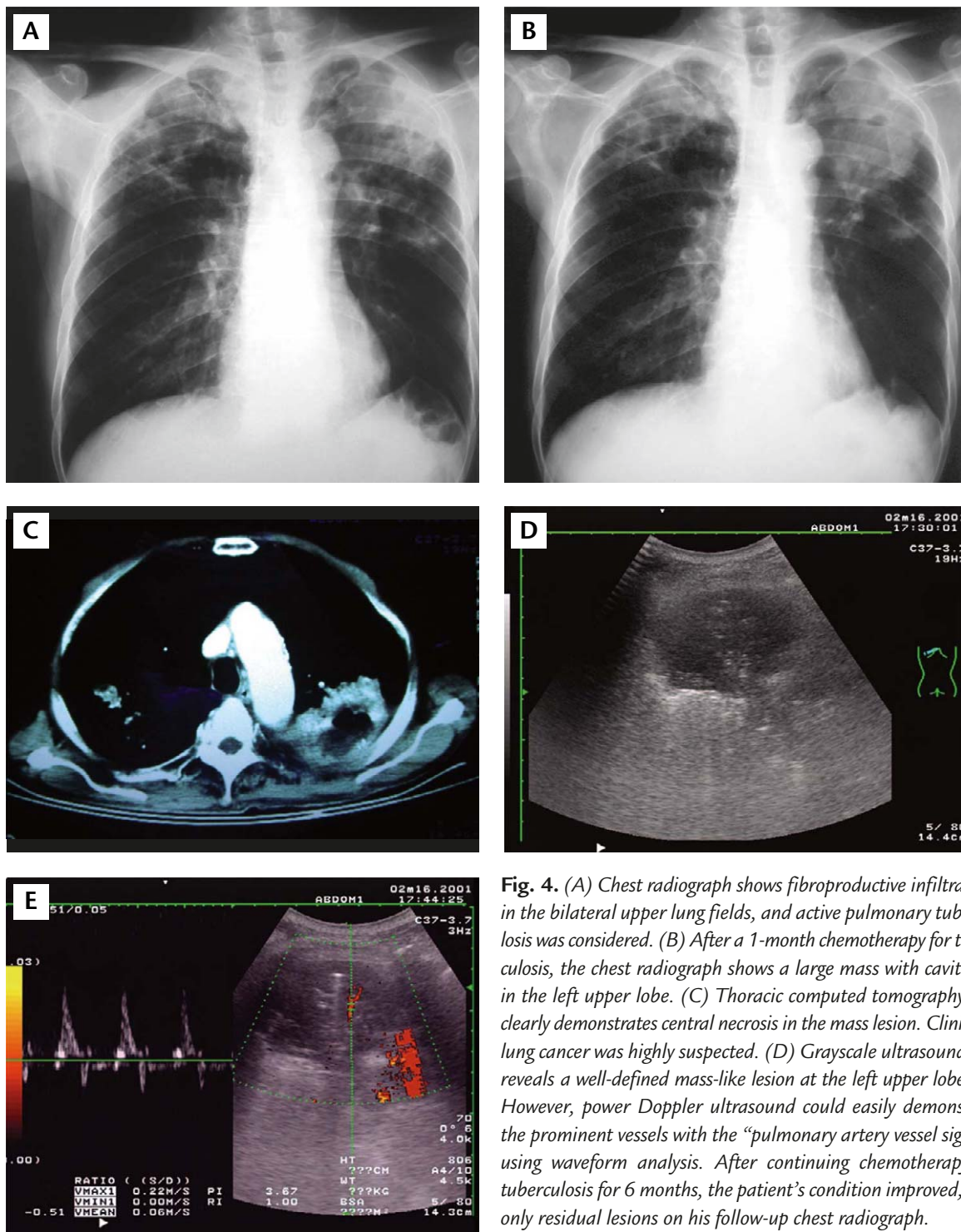
Fig. 2. *(A) Chest radiograph shows a mass in the left upper lobe. Squamous cell carcinoma was diagnosed by ultrasound-guided fine-needle aspiration. (B) Bronchial arteriogram shows that the tumor was supplied by the bronchial arteries, originating from the same level as the right bronchial artery. However, the vessels within the tumor were torturous, small, and irregular (without predictable direction). (C) Color Doppler ultrasound demonstrated only a small short segment of pulsatile flows within the tumor. (D) Pulmonary angiogram shows the pulmonary arteries running smoothly and regularly.*
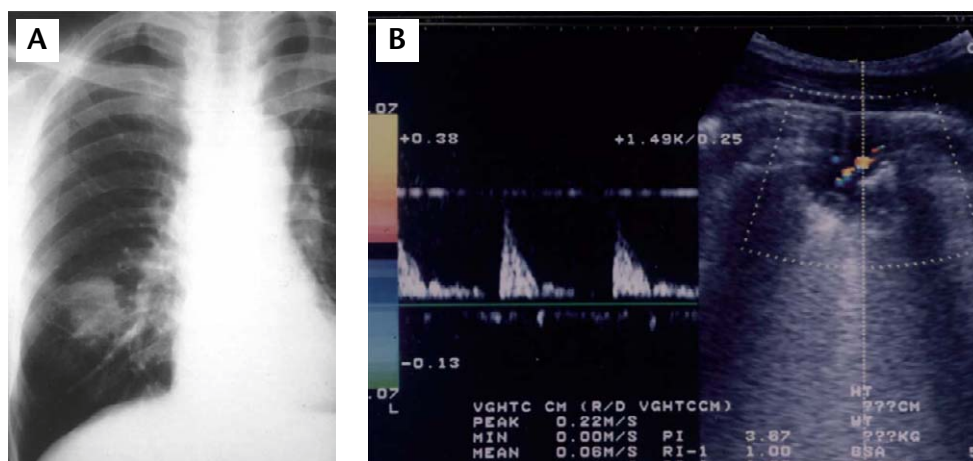
Fig. 3. *(A) Chest radiography shows a mass-like lesion in the right middle lung field. (B) Color Doppler ultrasound reveals pulsatile flow within the lesion with the "pulmonary artery vessel signal" present. The pulmonary lesion completely resolved after antibiotic treatment.*

supplied by an aberrant systemic artery. Hernanz-Schulman et al reported that CDUS can demonstrate the aberrant systemic artery supplying the abnormal lung tissue, and then diagnose pulmonary sequestration smoothly [26]. In our limited experience, the aberrant systemic artery that supplies the pulmonary sequestration is sometimes easily found by CDUS, but this task generally proves difficult (Fig. 6).

Fig. 4. *(A) Chest radiograph shows fibroproductive infiltrations in the bilateral upper lung fields, and active pulmonary tuberculosis was considered. (B) After a 1-month chemotherapy for tuberculosis, the chest radiograph shows a large mass with cavitation in the left upper lobe. (C) Thoracic computed tomography also clearly demonstrates central necrosis in the mass lesion. Clinically, lung cancer was highly suspected. (D) Grayscale ultrasound also reveals a well-defined mass-like lesion at the left upper lobe. (E) However, power Doppler ultrasound could easily demonstrate the prominent vessels with the "pulmonary artery vessel signal," using waveform analysis. After continuing chemotherapy for tuberculosis for 6 months, the patient's condition improved, with only residual lesions on his follow-up chest radiograph.*

Pulmonary arteriovenous malformation is occasionally encountered by chest physicians. Chest radiograph, computed tomography, and pulmonary angiography are all valuable in this regard and provide the potential to detect vascular malformation.

However, CDUS provides a real-time, noninvasive and convenient imaging modality in rapidly diagnosing pulmonary arteriovenous malformation (Fig. 7) [22].

For specific vascular lesions, CDUS undoubtedly has a more powerful imaging function and greater

Fig. 5. *Color Doppler ultrasound "fluid color sign" is present in a patient with left pleural effusion, which indicates that thoracocentesis should be successful.*
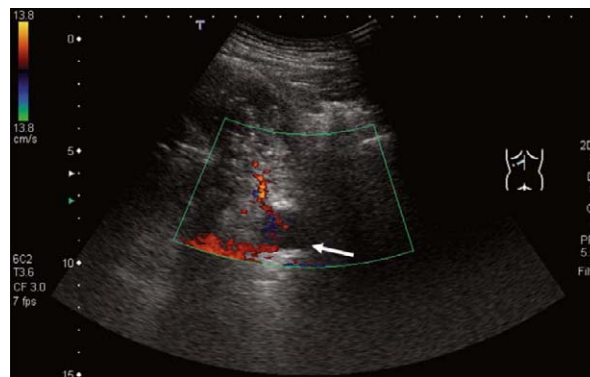
Fig. 6. *Color Doppler ultrasound shows the aberrant systemic artery originating from the aorta (arrow) and supplying the consolidated lung.*

Fig. 7. *(A) Grayscale ultrasound only shows a large anechoic lesion. (B) Color Doppler ultrasound reveals turbulent vessel signal within the lesion; a large pulmonary arteriovenous malformation was confirmed.*

potential than grayscale US in assessing and diagnosing vascular anomalies (Figs. 6 and 7). In some specific uncommon thoracic lesions, CDUS can diagnose the underlying diseases and differentiate the tissue characteristics solely on the basis of information from its imaging vessel signals (Fig. 8).

CDUS Equipped with a Color-based Puncture-guiding Device

Though CDUS can readily demonstrate vessel signals within lesions, CDUS equipped with a color-based puncture-guiding device is useful in guiding needle biopsy, especially in cases of pulmonary consolidation and mediastinal tumors (Fig. 9). Wang et al compared grayscale US-guided needle biopsy with CDUS-guided needle biopsy [28] and found that the diagnostic results and associated complications were similar; however, visualization of blood vessels was more common with CDUS than grayscale US ($p < 0.05$). Clinically, CDUS equipped with a color-based puncture-guiding device can easily demonstrate the prominent vessels and confidently guide transthoracic needle biopsy [28,29].

PDUS in the Detection of Vessel Signals

Conventional CDUS has a number of limitations in assessing vessel signals in thoracic lesions, including the insonating angle, flow velocity, US probe, anatomic narrowing interface, and the necessity of patient cooperation. Of these, the limitations in
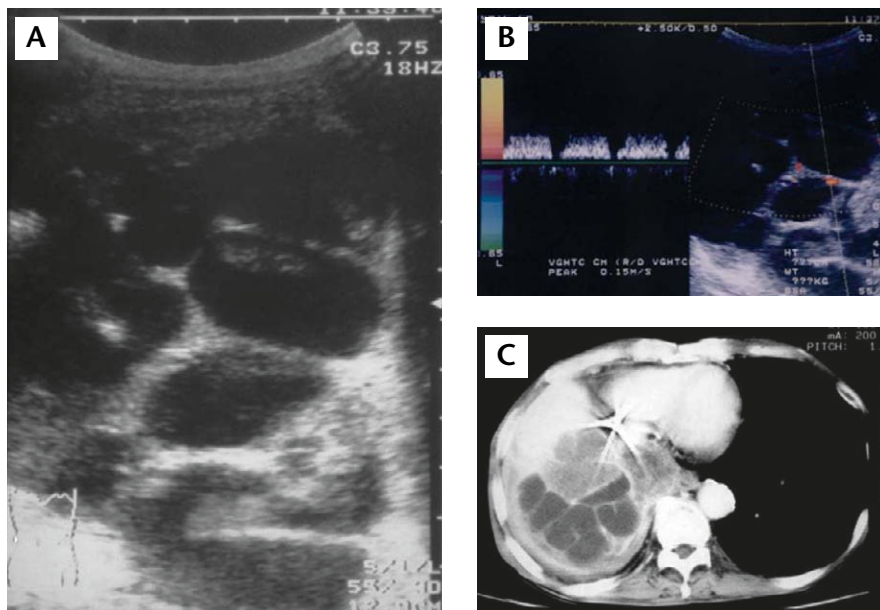
Fig. 8. *(A) Grayscale ultrasound only discloses a typical complex-septated pleural effusion. (B) Color Doppler ultrasound (CDUS) demonstrates venous flows within the septa; tumor with central necrosis was suspected. (C) Computed tomography confirmed the diagnosis to be the same as the CDUS findings.*
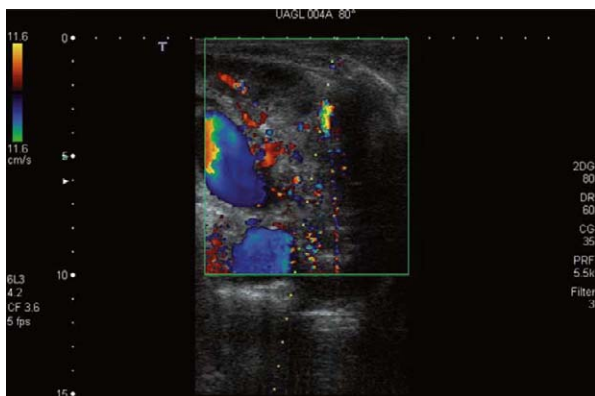
Fig. 9. *The color Doppler ultrasound puncture device has the advantages of adjusted angle selection for needle biopsy, and detects the prominent vessels easily, thereby preventing the possible complication of injury to the great vessels.*

detecting vessels with slow flow and the influence of the insonating angle are the main concerns in CDUS [17].

PDUS (or US angiography) has overcome some of the main limitations of CDUS, especially the influence of the insonating angle. In the literature, PDUS is reported to be angle-independent, more sensitive in detecting vessels with slow flow, and have less aliasing [19,20]. In our experience, PDUS is commonly more sensitive in the detection and

illustration of vessel signals than conventional CDUS (Fig. 10). Nevertheless, the clinical application of PDUS in chest medicine requires further study.

DFUS in the Illustration of Vessel Signals

CDUS and PDUS can readily produce blooming effects of vessels and color noise in demonstrating lesions that abut pulsatile organs [17,25]. The blooming effect of vessels renders the US assessment of vessel signals less real, and color noise lowers confidence in the US demonstration of vessel signals. For vessel signals in thoracic lesions, both CDUS and PDUS often produce more prominent blooming effects and color noises because of the respiratory movement of the lung, diaphragm, and pulsatile organs within the thorax. Therefore, the use of CDUS and PDUS in the assessment of vessel signals in thoracic lesions is always difficult.

DFUS is a newly developed color Doppler imaging method reported to provide better B-mode imaging with fewer blooming effects and color noises, compared with those of conventional CDUS and PDUS [30,31,39,40]. Clinically, we have used DFUS, CDUS, and PDUS to evaluate the vessel signals in 34 thoracic lesions abutting pulsatile organs and
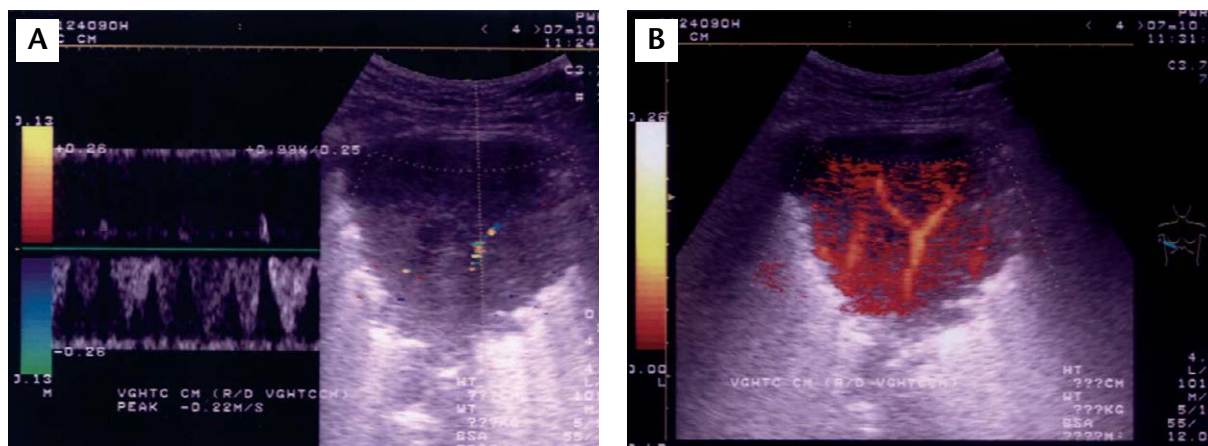
Fig. 10. *(A) Traditional color Doppler ultrasound only shows pulmonary venous flow within the lesion. (B) Power Doppler ultrasound demonstrates the vessels within the lesion more clearly.*
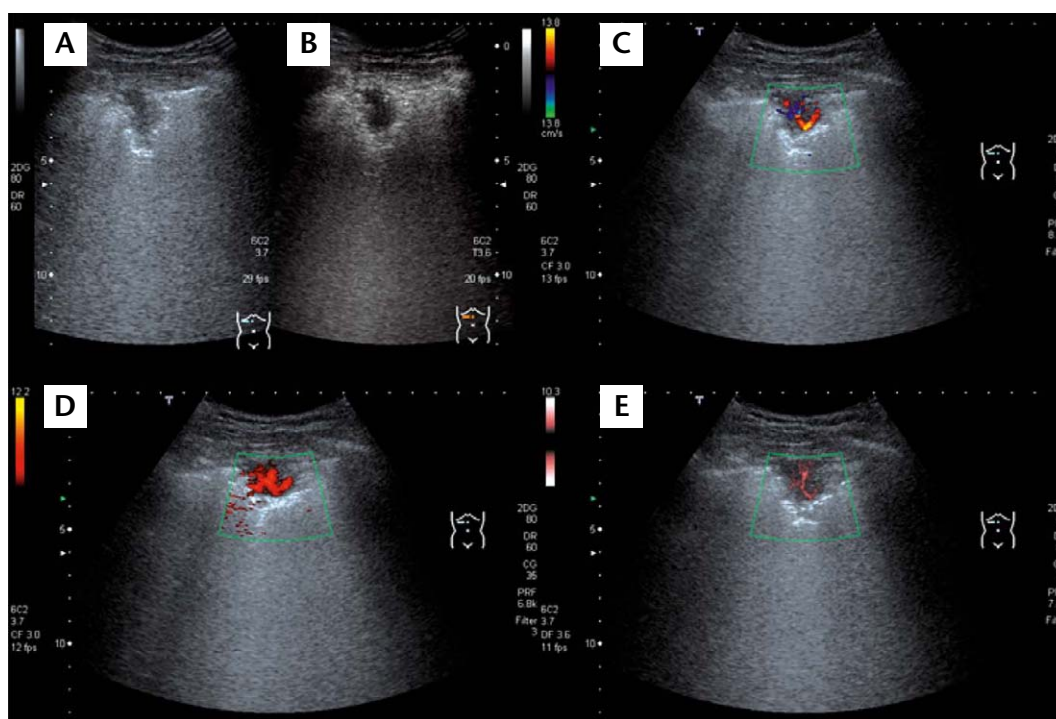
Fig. 11. *(A) Grayscale ultrasound (US) shows a hypoechoic lesion. (B) Tissue harmonic imaging also discloses a hypoechoic lesion. (C) Color Doppler ultrasound shows the vessel signals with a blooming effect apparent within the lesion. (D) Power Doppler US also detects the vessel signals with a prominent blooming effect. (E) Dynamic flow US illustrates the vessel signals without the blooming effect.*

compared the imaging quality of the vessel signals in different US modes. Our preliminary results showed that DFUS, CDUS, and PDUS could all demonstrate the vessel signals clearly (all $p > 0.05$). However, when focusing on the blooming effect and color noise, DFUS showed superior imaging quality to CDUS and PDUS (all $p \leq 0.001$) (Fig. 11). In the assessment of decision making for percutaneous needle biopsy in particular, DFUS had less influence than CDUS and PDUS (both $p < 0.01$) [41]. Therefore, DFUS clearly has a superior imaging quality to CDUS and PDUS in demonstrating the

vessel signals of thoracic lesions, with less blooming effect and color noise. Larger studies are necessary in the future to confirm our results.

Conclusion

Chest US examination and US-guided needle biopsy have become useful diagnostic tools in clinical practice. The application of CDUS further extends the potential function, clinical utility, and uses in research of US in chest medicine. CDUS renders the US examination safer and more confident and prevents possible injury to great vessels. The development of PDUS (US angiography) improves the illustration of vessel signals without angle limitation, and newly developed DFUS exhibits superior imaging quality with reduced color noise and blooming effect. The broad applications of CDUS in thoracic diseases have made CDUS a clinically powerful and necessary imaging modality, especially in guiding transthoracic percutaneous needle biopsy of thoracic lesions. We believe that CDUS will be widely applied in chest medicine in the future.

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