Contrast-enhanced ultrasonography for characterising superficial lymphadenopathy and the quantitative evaluation under different reference conditions

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Authors: Y. Jin, L. Y. Peng, B. Ma, S. S. Parajuly, N. H. Zhao, S. Y. He; Chengdu/CN
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Aims and objectives

To explore the characteristic CEUS types of different lymphadenopathy and to select the appropriate reference conditions (surrounding tissues or arteries) in the differential diagnosis of lymph nodes by comparing the quantitative indexes.
Methods and materials

Prospectively, 76 patients (13 men, 63 women; mean age of 50 years, range: 22-81 years) were examined by US (gray scale, Doppler, and CEUS) and total number of 78 superficial lymph nodes. Quantitative evaluation was conducted in 55 lymph nodes in contrast to both adjacent arteries and soft tissues. The diagnoses were confirmed by US guided biopsy or by surgical removal of the lymph node and subsequent histological examination. The local Ethics Committee approved the study, and all participants gave their written informed consent prior to the investigation.

*Gray scale and color Doppler US examination*

All the patients were examined with a iU22 ultrasound machine with a high-frequency linear probe (5-12MHz). In Doppler US three patterns of nodal vascularization were defined: 1) hilar pattern with flow signals in the nodal hilum, 2) peripheral pattern with flow signals mainly in peripheral nodal parts, and 3) mixed pattern with both hilar and peripheral pattern.

*CEUS examination*

For CEUS examination (3-9MHz linear probe, mechanical index 0.08) a bolus of 2.4 ml of contrast agent (SonoVue, Bracco Imaging SpA, Milan, Italy) was administered intravenously, followed by the flushing of 10 ml saline solution. All CEUS examinations were digitally recorded. Six nodal enhancement patterns were defined: 1) intense homogeneous enhancement, 2) homogeneous hypoenhancement, 3) inhomogeneous enhancement with perfusion defects, 4) inhomogeneous hypoenhancement, 5) circle enhancement, 6) isoenhancement.

*QLAB analysis*

The lesions, adjacent arteries and surrounding tissues (connective tissues or muscles) were selected as region of interest (ROI) at the same time. Using Philips QLAB software for perfusion quantification the mean value (dB), rise time, time to peak (TTP- seconds), peak intensity and area under the curve (AUC - cm$^2$) were measured.

After the histological examination of the biopsy material or of the surgical removed node, the examined lymph nodes were divided into two groups: benign and malignant nodes and the US findings were compared with histological diagnosis.
Results

Pathologic results

Pathologic results showed that 56 of the 78 enlarged lymph nodes were benign, including 52 reactive lymph nodes (66.7%), 4 tuberculosis (5.1%); 17 were metastases (21.8%) and 5 were lymphomas (6.4%).

Contrast-Enhanced Ultrasonography

According to the qualitative analysis, there were 32 lymph nodes in category 1 (24 reactives, 5 metastases and 4 lymphomas), 12 in category 2 (12 reactives), 12 in category 3 (7 metastases, 3 reactives, 1 lymphoma and 1 tuberculosis), 5 in category 4 (2 reactives, 2 metastases and 1 tuberculosis), 11 in category 5 (5 reactives, 3 metastases, 1 lymphoma and 2 tuberculosis) and 6 in category 6 (6 reactives). Contrast-enhanced ultrasonographic examples of these categories are shown in Figure 1-6. The main perfusion pattern for metastatic lymph nodes was inhomogeneous hyperenhancement (7/17, 41.2%), lymphoma was homogeneous hyperenhancement (2/4, 50%), reactive lymph nodes were homogeneous hyperenhancement (24/52, 46.2%) and isoenhancement (6/52, 11.5%) and tuberculosis was circle enhancement (2/4, 50%). When lymph nodes in categories 1, 2 and 6 were diagnosed as benign and lymph nodes in categories 3, 4 and 5 were diagnosed as malignant, the sensitivity, specificity, and accuracy of CEUS were 71%, 74%, and 73%. The AUROC was 0.722 (Fig. 7).

Analysis of the QLAB Gamma Variate

Comparisons was shown in Fig. 8. There were no significant differences in the mean value, rise time, TTP, peak intensity and area under the curve between benign and malignant lymph nodes (P > .05). The mean value and peak intensity of adjacent arteries were greater than those of benign and malignant lymph nodes (P < .05), and the mean value and peak intensity of surrounding tissues were less than those of malignant lymph nodes (P < .05), but equal to those of benign lymph nodes (P > .05). There were no significant differences in the rise time between lymph nodes lesions and adjacent arteries and tissues (P > .05). Time to peak (TTP) of the surrounding tissues is longer than that of malignant lymph nodes (P < .05). The area under the curve of benign and malignant lymph nodes is less than that of adjacent arteries (P < .05) but same to that of surrounding tissues (P > .05).
**Fig. 1:** Homogeneous hyperenhancement (Lymphoma). Left figure: the CEUS mode, the red circle: lymph node; Right figure: the comparative gray-scale ultrasonography.

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Fig. 2: Homogeneous hypoenhancement (Reactive lymphadenopathy). Left figure: the CEUS mode, the red circle: lymph node; Right figure: the comparative gray-scale ultrasonography.

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**Fig. 3:** Inhomogeneous hyperenhancement (Metastasis). Left figure: the CEUS mode, the red circle: lymph node; Right figure: the comparative gray-scale ultrasonography.

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Fig. 4: Inhomogeneous hypoenhancement (Metastasis). Left figure: the CEUS mode, the red circle: lymph node, the yellow circle: surrounding tissue, the blue circle: artery; Right figure: the comparative gray-scale ultrasonography.

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**Fig. 5:** Circle enhancement (Tuberculosis). Left figure: the CEUS mode, the red circle: lymph node, the yellow circle: surrounding tissue, the blue circle: artery; Right figure: the comparative gray-scale ultrasonography.

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Fig. 6: Isoenhancement (Reactive lymphadenopathy). Left figure: the CEUS mode, the red circle: lymph node; Right figure: the comparative gray-scale ultrasonography.

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**Fig. 7:** ROC analysis for CEUS.

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**Fig. 8:** The analysis of Time-intensity Curve.

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Conclusion

There are characteristic CEUS perfusion patterns of different types of lymph node lesions and CEUS is of great value in the differential diagnosis. In addition, the surrounding tissues as the reference condition, analyzing the time-intensity curve is also of great value in the differential diagnosis of superficial lymphadenopathy.
References


