Echoes of Change: Contrast-Enhanced Ultrasound and the Potential Applications for Non-Invasive Imaging

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The long-awaited approval of diagnostic ultrasound contrast agents by the United States Food & Drug Administration (FDA) has finally come to fruition. On October 1, 2015, the United States Centers for Medicare and Medicaid Services (CMS) approved sulfur hexafluoride lipid-type A microspheres (Lumason, Bracco Diagnostics) for use in abdominal (liver mass) imaging with an assigned Healthcare Common Procedure Coding System (HCPCS) code C9457 for pass-through reimbursement.

Contrast-enhanced ultrasound (CEUS) utilizes gas-containing microspheres to enhance the acoustic impedance of flowing blood, making the blood echogenic. The microspheres remain in the blood pool and do not enter the surrounding tissues. The microspheres have a mean diameter of 1.5 µm to 2.5 µm and circulate for approximately 2 minutes to 5 minutes of useful imaging after a blood peak of 0.5 minutes to 1 minute when administered as a bolus. Over time, the lipid layer breaks down and the gas is eliminated in the lungs with little to no biotransformation. No renal effects exist, and patients with renal insufficiency can undergo safe administration. Potential side effects include rare hypersensitivity and cardiopulmonary reactions, including fatalities. It is otherwise well tolerated. It is intended for intravenous administration only and has unproven but theoretical risks of vascular occlusion and subsequent ischemia if right-to-left shunts exist and the contrast agent bypasses lung filtration.

While CEUS has been used for years in cardiac imaging in the United States, this landmark change in indications opens the door for broader applications for diagnostic radiology and vascular imaging.

ENDOVASCULAR ANEURYSM REPAIR

One of the greatest potentials for use of CEUS is follow-up imaging of the abdominal aorta after endovascular aneurysm repair (EVAR) (Figure 1). While practice patterns vary, postoperative patients from EVAR are followed at 1, 6, and 12 months and yearly thereafter with contrast-enhanced computed tomographic angiography (CTA) or magnetic resonance angiography (MRA). Due to associated comorbidities, many of these patients have renal insufficiency, which limits the ability to administer iodinated or gadolinium-containing agents because of the risk of worsening renal insufficiency or inciting nephrogenic systemic sclerosis, respectively.

Figure 1. Enlarging aneurysm sac noted on computed tomography (CT). Patient underwent previous repair of an abdominal aortic aneurysm with a bifurcating endograft. Non-contrast CT (not shown) demonstrates enlargement of the aneurysm sac. Duplex ultrasound image (A) shows flow within the aneurysm sac outside of the endograft (arrows). CEUS (B-D) shows flow within the limb of the endograft (open arrows) as well as accumulation within the aneurysm sac (arrows). This is seen arising from the inferior mesenteric artery (arrowheads) consistent with a type II endoleak. Images courtesy Dr Richard Barr and Dr Andrej Lyshchik.
Moreover, the concerns of repeatedly exposing patients to ionizing radiation with CTA and subsequent risks of stochastic and threshold carcinogenic effects make the use of ultrasound more appealing. In comparison with MRA, substantial cost savings and patient throughput are achieved when CEUS is employed.

The use of CEUS to detect endoleaks has been studied. Not only are there benefits to radiation dose reduction and elimination of the potential for renal complications, but several studies indicate improved sensitivity and specificity of CEUS for detecting endoleaks when compared with CTA and MRA. Furthermore, patients who have undergone coil embolization or administration of ethylene vinyl alcohol copolymer into an endoleak will have substantial beam-hardening (streak) artifact with CTA, reducing the sensitivity for detecting endoleak recurrence. However, CEUS is not susceptible to this limitation.

CAROTID ATHEROSCLEROTIC DISEASE

Identifying which patients are at risk of complications associated with atherosclerotic plaques in the carotid arteries continues to elude researchers and clinicians. Plaque instability or vulnerability has been regarded as a surrogate marker for risk of future events. Studies have suggested that vascular flow in the vasa vasorum and subsequent intraplaque neovascularity are indicators of plaque vulnerability. CEUS not only allows better visualization of the lumen of the carotid artery but also qualifies the degree of intraplaque flow and neovascularity.

IMAGING OF VASCULITIS

With the above principles of carotid imaging, large-vessel vasculitis can be evaluated with CEUS. In particular, Takayasu’s arteritis and giant cell arteritis have been studied. Increased vascularity and enhancement in the walls of the vessel correlate with increasing 18F-FDG activity; this indicates active inflammation within the vessel wall. Furthermore, changes in vessel wall enhancement may potentially indicate response to anti-inflammatory therapy.

APPLICATIONS IN INTERVENTIONAL ONCOLOGY

Embolization. Treatment of solid organ tumors with bland embolization, chemoembolization, and radioembolization results in loss of tumor vascularity and overall decrease in associated arterial flow. Hypervascular tumors, including hepatocellular carcinoma (HCC), have distinct enhancement patterns on CEUS prior to treatment. In the case of HCC, tumors typically demonstrate arterial-phase enhancement with early washout when compared with the background hepatic parenchyma. Following embolization, adequate treatment response should result in a loss of enhancement on CEUS. Residual enhancement may indicate an incomplete response and may prompt the need for additional therapy. Unlike enhancement on CT, which may be obscured by high-density embolization material, CEUS can be employed in the immediate post-treatment period to assess for enhancement.

Biopsy and Ablation. In lesions that are particularly difficult to visualize and target on ultrasound, CEUS can be utilized to enhance discrimination between the mass and surrounding tissues. This is particularly important for hepatic and renal tumors. Once malignancy is confirmed, CEUS to assess response after treatment – with techniques including percutaneous ablation – can be employed as outlined above for embolization. A similar decrease in tumor vascularity is expected following percutaneous ablation.

CONCLUSION

The approval of ultrasound contrast has provided an avenue for development of novel methods of vascular assessment. The full application in non-invasive imaging has yet to be elucidated for development of novel methods of vascular assessment. The full application in non-invasive imaging has yet to be elucidated and new innovative techniques in CEUS will pave the way for better patient care.

REFERENCES