Contrast Ultrasound Imaging and its Veterinary Clinical Applications

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Abstract

The concept of contrast enhancement has significantly extended the usefulness of ultrasound imaging in human medicine and medical research and the persistence and efficacy of ultrasound contrast agents has been improved and specific imaging sequences have been developed. Contrast ultrasound provides Doppler and grey-scale enhancement. Doppler examinations are improved when studying deep or small vessels and vessels with low flow velocities. In the last few years, contrast ultrasound has also been introduced in veterinary medicine. Its usefulness has been shown in diseases of the liver, spleen, kidney, pancreas, lymph nodes and superficial tumours.

Keywords: Ultrasound, Contrast agents, Microbubbles.

Introduction

The concept of contrast imaging was introduced to ultrasound almost 30 years ago. It was first observed in echocardiography, rather incidentally, when small air bubbles were noted surrounding a catheter tip placed in the left ventricle during cardiac catheterization producing transient high reflections (Gramiak and Shah, 1968). An ultrasound contrast agent is an exogenous substance, consisting of air microbubbles encapsulated by a shell of different composition that can be administered intravenously or into a body cavity to enhance ultrasonic signals. They are much smaller than the wavelength of the ultrasound beam (approximately 0.5 mm in water at 3 MHz) and therefore, behave as scattering reflectors because gases have acoustic impedance very different from blood and tissue, microbubble contrast agents have a good scattering yield (Dallapalma, 1999). Vascular enhancement usually lasts a few minutes. Most ultrasound contrast agents do not diffuse across the endothelium and thus are blood pool agents. Typically, the gas content of the contrast agent is eliminated via the lungs, while the shell components are filtered by the kidney and eliminated by the liver (Quaia, 2005a).

Principles of action

Microbubble under ultrasound beam is governed by many parameters such as resonance frequency, pulse repetition frequency, number and location of focal zones, acoustic power, the filling gas, damping coefficients and shell properties, but the local acoustic power is the principal parameter affecting microbubble behaviour (Quaia, 2005b). The local acoustic power depends on the output power of the ultrasound system, the transmit frequency and the attenuation of the ultrasound beam with depth (Correas *et al.,* 2001). The output power is reflected by the mechanical index (MI) which originally measures the potential for mechanical damage to tissues exposed to intense ultrasound pulses.

Linear and non linear behaviour of microbubbles: When acoustic power is low ($MI < 0.1$), the microbubble radius does not change with time and the bubble remains as a static object. The scattering intensity increases with the intensity and the frequency of the incident ultrasound beam, and the number and radius of the microbubbles (Bertolotto, 1999). This is linear behaviour of microbubbles. But when the acoustic power of the ultrasound beam at the resonance frequency increases (intermediate MI: $0.1< MI > 0.5$), the microbubbles will show a longer expansion than contraction phase and begin nonlinear (non-sigmoidal shaped) oscillation (Correas *et al*., 2001). This is known as nonlinear behaviour of microbubbles.

Imaging techniques

Fundamental and Harmonic imaging techniques: Imaging of contrast agents is more complex than mere addition of contrast media to conventional grey-scale and Doppler sequences. Bubble contrast agents are sensitive to the local deposition of sound energy, so sufficient energy (sound amplitude) must be provided to generate an adequate signal-to-noise ratio for agent

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detection, but not so high that bubble destruction occurs, preventing real-time display of perfusion. Ultrasound contrast agents can be used with conventional B-mode and Doppler sonography. Contrast agents cause significant enhancement of Doppler signals and are used for vascular studies. Fundamental Doppler modes commonly use the stimulated acoustic emission modality with high MI settings. The contrast agent increases the Doppler signal, thereby increasing the sensitivity for low flow situations and detection of small vessels (Dallapalma and Bertolotto, 1999).Harmonic imaging commonly employs the powerful emission of second-order harmonics for detection of contrast agents. The advantage of this technology is that only a single pulse is transmitted for each line of image formed, so there will be minimum bubble destruction.

Safety considerations: Ultrasound contrast agents are extremely safe and well tolerated. Hypersensitivity or allergic events occur rarely. However, there is the possibility of bioeffects such as microvascular rupture with the insonation of microbubbles. Further, premature ventricular contractions may occur when high mechanical index end systolic triggering is used in echocardiography. So far, no side effects have been reported with the use of Definity, Imagent, Sonovue and Levovist (contrast agents) in dogs and cats . Severe but self-limited hypotension was observed by using optison (contrast agent). So optison is contraindicated for clinical use in veterinary patients.

Veterinary clinical applications

The major clinical indications of contrast-enhanced in echocardiography are improved edge detection for M-mode imaging and myocardial perfusion. Perfusion assessment is especially important for the diagnosis of cardiac infarction. Perfusion assessment of the left ventricular free wall and septum can be performed in dogs and cats with the same technology and transducers used for abdominal imaging. In veterinary medicine the liver is a very common site of metastasis of intra-abdominal primary neoplasia, especially haemangiosarcoma, and benign nodules are prevalent in older dogs. The perfusion of liver in normal dogs has been described (Nyman *et al.,* 2005). A recent study indicated that contrast ultrasound is highly accurate for prediction of benign or malignant based on perfusion patterns (O'Brien *et al.,* 2004). Little has been published on contrast ultrasound of splenic lesions. Infarctions in the spleen, similar to other organs, are easily identified (De Morais and O'Brien, 2005). Contrast-enhanced colour and power Doppler ultrasonography has shown to be a promising tool to assess feline pancreatic disease (Rademacher *et al.,* 2005). In comparison to normal cats, vascularity and perfusion is significantly increased in cats with pancreatic diseases. Lesions of kidney that have been detected include infarction associated with thromboembolic disease,detection of otherwise isoechoic lesions, and characterization of masses (Nilsson, 2004). Contrast ultrasound perfusion imaging has been shown to be on a par with Technetium 99m diethylenetriamine pentaacetic acid (^{99m}Tc-DTPA) scans for assessment of renal perfusion (Kim *et al.,* 2005). In general contrast-enhanced ultrasound imaging verifies perfusion of an organ or lesion. This can be of assistance for categorization of lesions and when determining sites for biopsy procedures. Interesting, there are no clinical reports of contrast-enhanced ultrasound for the characterization of mass lesion in the lung. Finally, ultrasound contrast agents have therapeutic applications (Unger *et al.,* 2002). Targeting ligands,genes and drugs can be incorporated into microbubbles for specific diagnostic and therapeutic functions. As the agents are encapsulated in bubbles, toxic systemic effects are minimized and localized benefits maximized. Localized energy deposition associated with bubble destruction can also be used therapeutically for clot dissolution.

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