Characteristics of ultrasound contrast agents

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Current contrast agents used for medical diagnosis consist of free or encapsulated gas bubbles. The presence of these bubbles in a fluid changes the acoustic properties of the mixture like: the resonant frequency, acoustic velocity, linear scattering, harmonic scattering, transient scattering. For scattering the linear mode is dominant for acoustic pressure below 50 kPascal. The non-linear (stationary) vibration of the (encapsulated) bubbles in the contrast agent contributes for acoustic pressures up to 100 to 200 Pascal. In this mode the vibration is reproducible. The scattered signal contains both fundamental frequencies and higher harmonics. For acoustic pressures up to 2 MPascal non-linear (transient) scattering occurs. The scattering of the (encapsulated) bubbles increases dramatically and even the scattering of individual bubbles can be observed. These properties are transient and last only for a few milliseconds. The spectrum of the scattered signal is broad, containing the fundamental frequency as well as second and third harmonics. This transient scattering opens new perspectives for imaging of contrast agents.

With the current imaging techniques, contrast agent disruption (gas release) and imaging are achieved during the early part and late part of a relatively long (several cycles) burst, respectively. However, it has been reported that the process of releasing gas bubbles is more efficient at lower frequencies, for a given number of cycles per burst and a fixed amplitude. It also improves with longer acoustic pulses of fixed amplitude and frequency, while imaging resolution improves at high frequencies and short pulses. A new method that resolves this situation by separating the "release" and "imaging" processes is presented. As a result, high resolution imaging can be achieved with optimum utilization of the contrast agent.

THE MULTI-PULSE DECORRELATION APPROACH

We propose a new contrast imaging approach based on the combination of a) a multi-pulse strategy and b) temporal decorrelation based detection. Multiple "imaging" pulses are used to survey the target before and after the disruption of contrast agent by a high power "release" burst (Figure 1). The change in echo signal arising from areas occupied by contrast agent is detected by temporal decorrelation analysis. The power required to disrupt the agent and release free gas bubbles is agent-dependent and within the capabilities of commercial ultrasound imaging systems. Other multi-pulse schemes can be designed for specific purposes.

FIGURE 1, A typical multi-pulse sequence consisting of two low amplitude, single cycle, 5 MHz "imaging" pulses and one high amplitude, four cycles, 2 MHz "release" burst.
Local decorrelation analysis is performed on small (one wavelength) sliding radiofrequency signal windows to obtain decorrelation profiles along the beam direction. Decorrelation detection performs well at high bandwidths, contrary to Doppler detection. Only areas where released gas is present will show significant decorrelation. A decorrelation threshold of 80% was defined empirically in order to differentiate tissue from contrast agent rich areas. An example is shown in Figure 2, where the measured correlation falls below the threshold level only within a region occupied by released gas. High decorrelation regions are displayed by superimposing a color-coded map on the original B-mode image, analogous to duplex imaging combining color Doppler and B-mode. Experiments on a test object consisting of fibers of 200 μm filled with Quantison™ (Andaris Ltd., Nottingham, UK) proved the feasibility of this approach.

![Decorrelation profile](image)

**FIGURE 2.** Decorrelation profile obtained from a single multi-pulse sequence. Thresholding the data, for example using a 80% correlation level, allows the detection of the area of bubble release.

**DISCUSSION AND CONCLUSION**

Separation of the bubble rupture and imaging processes, and decorrelation-based detection yields a powerful combination of resources that results in simultaneous high resolution imaging and optimal use of the contrast agent. Note that, in the reported experiment, high resolution detection could not have been achieved with a long, low frequency pulse and that bubble release could not have been easily achieved with a short, high frequency pulse. Thus, the synergy of the combination approach is responsible for the successful outcome.

The power and duration of the release burst can be designed to optimize the amount, and perhaps the type, of free gas bubbles released. This, in turn, translates into a longer period of imaging per unit amount of contrast agent, or alternatively in a lower dose of contrast agent required for imaging. Additionally, optimized agent usage can reduce attenuation caused by the contrast agent itself and thus improve imaging penetration. Due to the sensitivity of the decorrelation approach, as few as two signals can be used to detect the released gas (as demonstrated in the example herein). However, more than two signals can be used to obtain improved decorrelation estimates.

Due to the independence of bubble release and imaging processes, the multi-pulse decorrelation method has the potential to achieve high resolution, sensitivity and efficient contrast agent imaging heretofore unavailable.