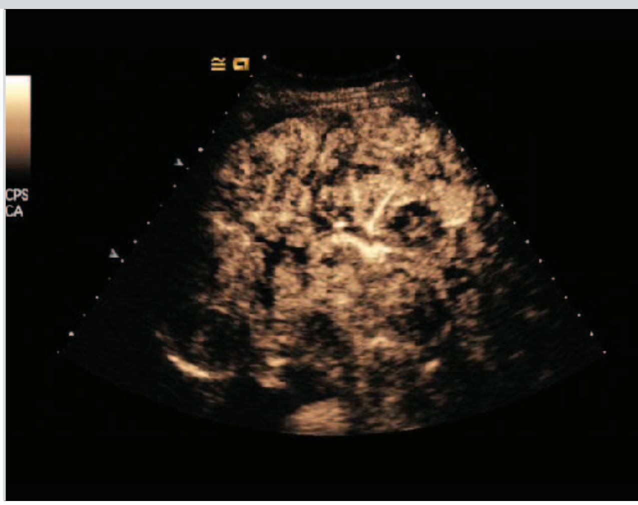
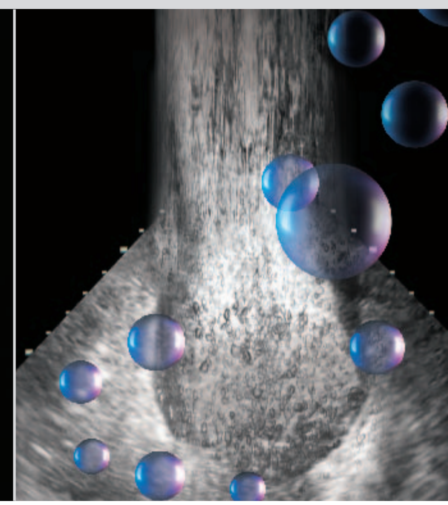
Whitepaper





Cadence Contrast Agent Imaging Technology*
on the ACUSON Sequoia Ultrasound Platform

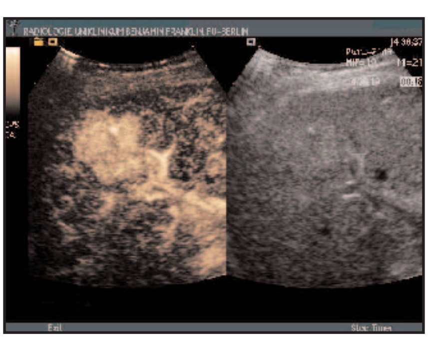
Dennis Paul, RDMS, RDCS; Patrick J. Phillips, Ph.D.
Siemens Medical Solutions USA, Inc., Ultrasound Division,
Mountain View, California

SIEMENS
medical

Cadence Contrast Agent Imaging Technology*
on the ACUSON Sequoia Ultrasound Platform

Introduction

Ultrasound contrast imaging is becoming increasingly important in clinical investigations. Traditional contrast agent ultrasound imaging technologies, such as second harmonic inversion imaging, have focused on the second harmonic properties of the contrast agents and tissue. While these techniques have proven helpful, it has been recognized that the second harmonic signals provide limited performance relative to contrast agent signal strength. In addition, these older harmonic technologies inherently combined the acoustic signals returning from tissue (tissue harmonics) with those returning from the contrast agents, thereby limiting the specificity or uniqueness of the contrast agent response.



Unique Live Dual display allows for simultaneous real-time viewing of CPS contrast image and derived B-mode image.

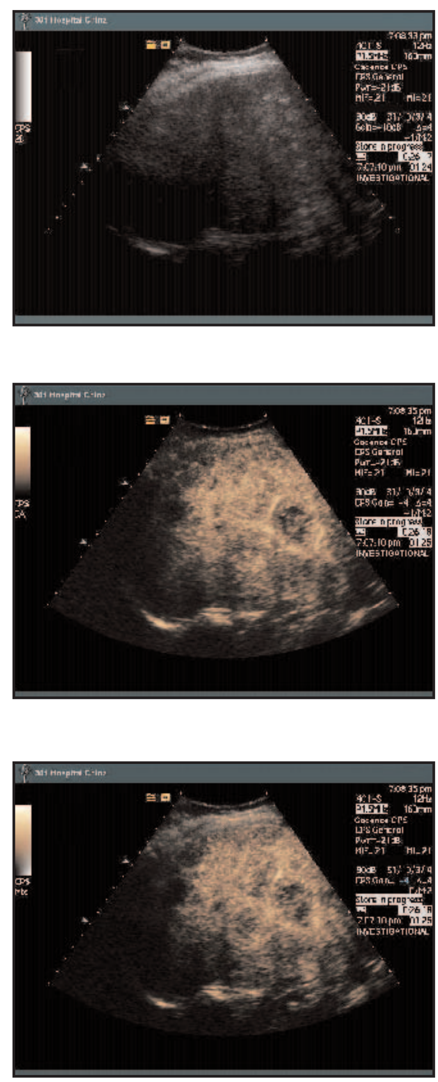
Although the contrast agent signal can add important information to the ultrasound image, improved clinical scanning is accomplished when the conventional tissue signals can be directly and independently compared to the contrast agent signals. Both signal types hold valuable information.

An ideal process would be one that simultaneously detects signatures that are unique to contrast agents and unique to tissue. Such a method would thereby allow the clinician to view the contrast agent signals separately from the tissue signals, regardless of the contrast agent selected or whether a high-MI (mechanical index) or low-MI technique is utilized.

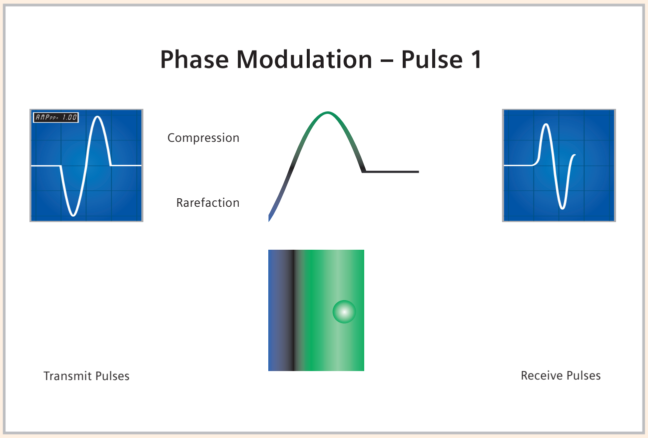
The ACUSON Sequoia™ ultrasound platform offers unique Cadence™ contrast agent imaging technologies for high-MI and low-MI imaging with unique agent-to-tissue specificity and display options.

Understanding Cadence Contrast Pulse Sequencing

Low MI imaging that provides "tissue only, contrast only, or both"



Cadence CPS technology display selection of tissue-only image, contrast agent-only perfusion image, or both together.



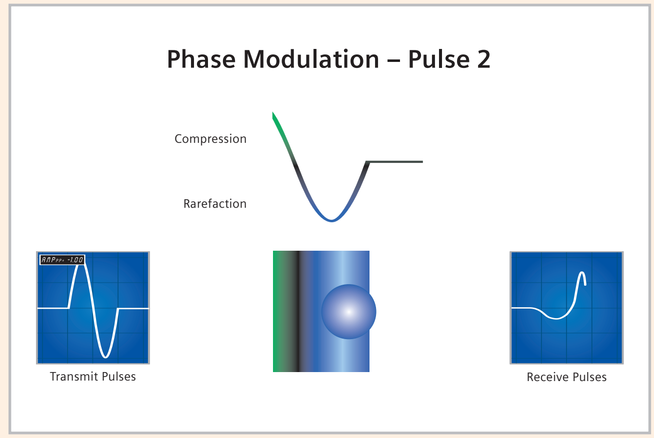


Figure 1: In the simple case of a pulse with a leading edge that expands the contrast agent bubble, a typical response may look like this.

Figure 2: In the simple case of an inverted pulse (a leading edge that compresses the contrast agent bubble), a typical response may look like this.

A new technology is now available on the Sequoia platform that recognizes and processes the unique nonlinear fundamental and higher order harmonic signals that are generated by ultrasound contrast agents. Recent introductions of novel ultrasound contrast agents that perform well at low MI include SonoVue®, Definity®, Optison, and Imagent®. By means of a proprietary new pulse sequence technology ideally designed for contrast agents, the agent-to-tissue specificity of contrast imaging is significantly increased thereby providing improved performance even at low MI power levels. By taking advantage of the extreme flexibility of the Sequoia system, Cadence contrast pulse sequencing technology (CPS) achieves this new level of performance by simultaneously processing received signals from multiple transmitted pulses of varying phase modulation and varying amplitude modulation.

It is now understood that by varying the phase and amplitude of multiple pulse interactions with a contrast agent, the agent response is unique and can be efficiently separated from the tissue signals. The precise control of pulse amplitude and phase allows the detection of strong *nonlinear fundamental* energy exclusively from the contrast agent. This unique response is termed nonlinear, as it arises as a result of the bubble's nonlinear expansion and contraction with the ultrasound pulse. This response is also termed fundamental, as the bubble's strongest returned response is at the same frequency as the transmitted pulse.

Phase Modulation – changing phase: A bubble's nonlinear expansion and contraction is sensitive to the initial phase as shown above (Figures 1 and 2). In these examples, the received pulses on the far right from two excitation pulses of opposite phase help identify the bubble from tissue. The recorded signals are not simply inverted copies of each other, unlike that of tissue. Amplitude Modulation – changing amplitude: In further describing the interaction of contrast agent bubbles with ultrasound, consider a pressure pulse and the positive, compressional section of the pulse. This particular pulse section compresses a bubble. When the bubble is compressed, a fixed amount of sound is scattered and reflected back to the transducer.

Next, consider a second pressure pulse that is twice as large as the first with twice the amplitude. During the compressional section of this pulse, the bubble is compressed more than during the same section of the smaller, first pulse. However, a bubble expands much more easily than it contracts; it has a nonlinear response. Therefore, the section of the second pulse does not necessarily return half as much energy; i.e. the volume and scattering properties did not just simply drop by a factor of two. If the result were simply a factor of two in the scattered energy, this energy would be termed "linear". In this example when the energy scattered is not a factor of two different, it is termed

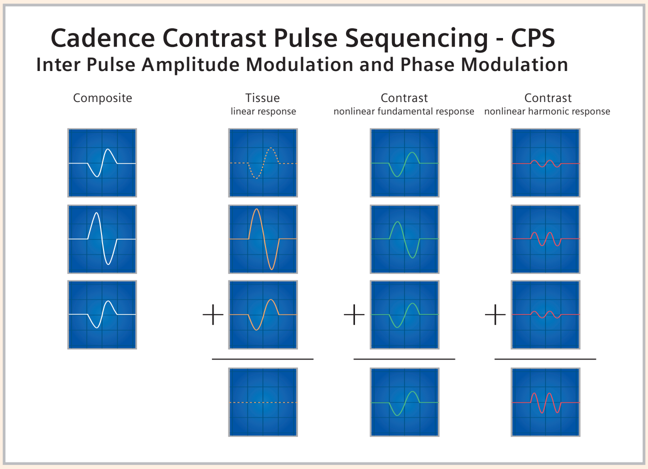


Figure 3: Cadence CPS removes the linear fundamental signal leaving the strong nonlinear fundamental and other harmonic signals

"nonlinear". With Cadence CPS technology, we transmit a fundamental frequency and then detect a returned fundamental frequency (the nonlinear fundamental) as well as higher order harmonics from the wobbling bubbles.

Cadence CPS technology combines multiple received pulses to extract the strong nonlinear signals. Conventional filtering methods like those used with phase inversion technologies are insufficient for detecting nonlinear fundamental energy. Spectral filters that separate signals in the frequency domain are not effective for separating linearly scattered fundamental tissue signals from nonlinearly generated fundamental bubble signals, as both signal types are in the same fundamental frequency band. Instead, separation is achieved by proprietary combinations of multiple pulses with Cadence CPS technology. Proper amplitude and phase combinations support effective tissue signal rejection and bubble signal extraction all within the same fundamental frequency band.

Although Cadence CPS technology encompasses the design of many different pulse sequences for different imaging characteristics, we present one example of a Cadence CPS technology implementation (Figure 3), breaking down the components of this multipulse technology.

A half-amplitude, positive 0 degree pulse is transmitted. The processed received signal includes:

- linear fundamental tissue,
- nonlinear fundamental contrast agent, and - nonlinear harmonic contrast agent components.

As the transmit power is very low, the nonlinear tissue harmonic component of the received signal is very low and can be suppressed with processing inherent in the Sequoia system's Coherent Imageformer. The linear tissue response and the nonlinear fundamental response carry the same polarity as the transmitted pulse. The nonlinear harmonic response carries its own polarity.

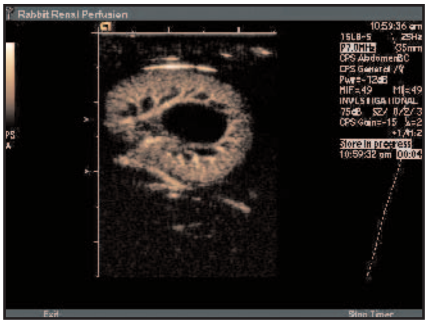
Next, a full-amplitude, negative polarity, 180 degree, pulse is transmitted. The processed received signal includes similar significant components as the first received signal (linear fundamental tissue, nonlinear fundamental contrast agent, and nonlinear harmonic contrast agent components). The linear tissue response and the nonlinear fundamental response, again, carry the same polarity of the transmitted pulse. However, due to the bubble's nonlinear behavior, the nonlinear fundamental contrast response from this pulse exhibits a higher amplitude than the nonlinear fundamental contrast response from the first half-amplitude pulse. In addition, the nonlinear harmonic response carries its own polarity.

Another half amplitude, positive 0 degree pulse is transmitted. The processed received signal includes similar significant components as the first two received signals. The linear tissue response and the nonlinear fundamental response carry the same polarity as the transmitted pulse. The amplitude of the nonlinear fundamental contrast response is similar to the first received pulse. The nonlinear harmonic response carries its own polarity.

When the received composite sequence of signals is summed, the tissue components from the half-amplitude, positive polarity pulses 1 and 3 equal the full amplitude, negative polarity pulse 2 and therefore cancel out. The contrast agent's nonlinear fundamental signals add to form a significant, strong signal. The nonlinear contrast agent harmonic signals also add and make a smaller contribution to the contrast agent signal. Cadence CPS technology has the unique ability to combine the nonlinear fundamental and higher order harmonic contrast signals to form a highly specific and sensitive contrast agent display. By utilizing this sequencing strategy, the Cadence CPS technology can effectively separate tissue signal from contrast agent signal, or can combine them together – at the discretion of the clinician.

The nonlinear fundamental component of the contrast agent signal is very attractive for a number of reasons:

- Given the nonlinear fundamental signals are the strongest signals from bubbles, sequences can be designed to operate in the most sensitive parts of the transducer. These sequences are not constrained to also include the full received bandwidth of all the second harmonic signals, unlike second harmonic-only imaging methods.
- The nonlinear fundamental signal is generated exclusively by the contrast agent. In comparison to the standard fundamental tissue signal, it is possible to specifically separate, or link, the contrast agent signal and the tissue signal. This allows the clinician to selectively view "tissue only, contrast agent only, or both together", even with low-MI imaging.
- There is no need for complicated subtraction or replay methods. The clinical images are generated and observed in real-time.
- Cadence CPS technology is an attractive technology for higher frequency imaging, where acquiring useful harmonic frequencies would be beyond the bandwidth of today's state-of-the-art transducer technologies. High frequency imaging offers spatial resolution on the order of several hundred microns – which may be applied to areas such as the human breast, thyroid, testicle, or carotid arteries. The emerging field of small animal imaging for use in genomics, pharmaceutical, or other research studies can also benefit from improved resolution at high frequencies with excellent agent-to-tissue specificity.



High frequency Cadence CPS display of perfusion in rabbit kidney, utilizing current generation contrast agent

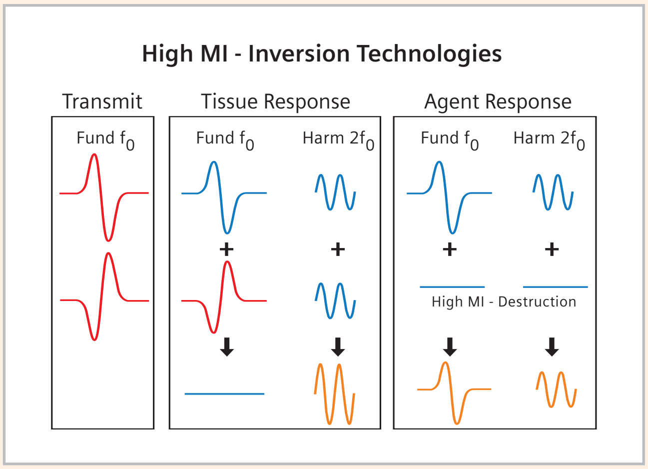


Figure 4

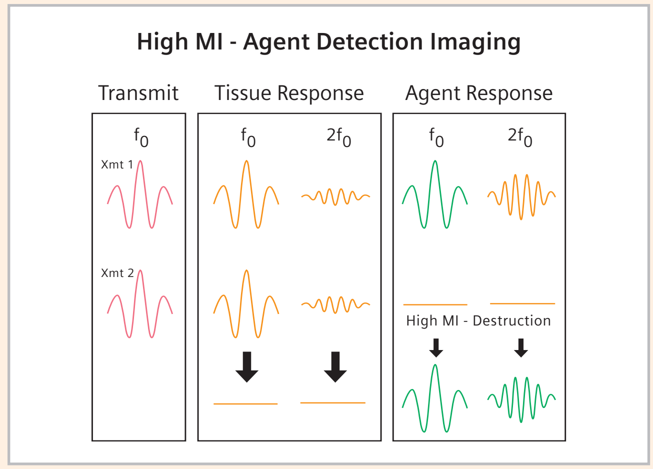
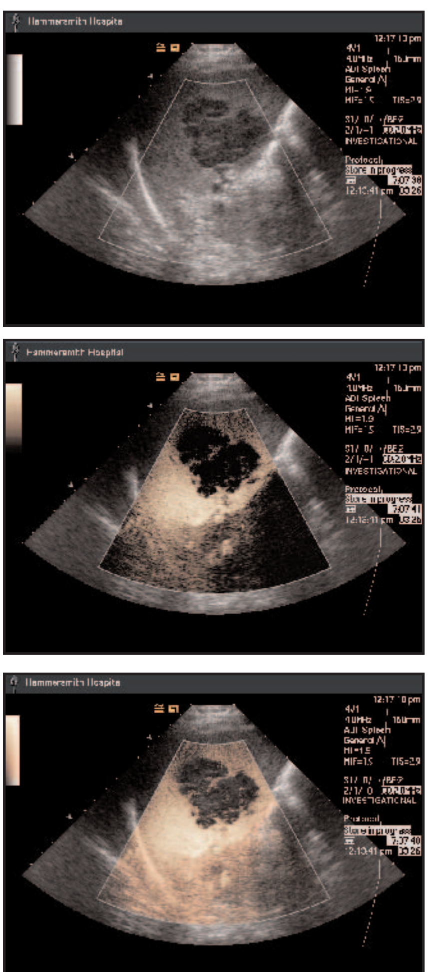


Figure 5

Understanding Cadence Agent Detection Imaging Technology

High MI imaging that provides "tissue only, contrast only, or both together"



Cadence ADI display selection of tissue-only image, contrast agent-only perfusion image, or both together.

A second Sequoia platform technology for contrast is Cadence™ agent detection imaging technology, (ADI). This method is ideal for investigations where higher transmit powers may be used and some agent depletion is acceptable. Higher transmit levels deliver more energy to the bubbles and force more dramatic changes. High MI imaging may also be referred to as "Emission" imaging as signals are emitted by the contrast bubbles when ultrasound energy causes them to be dramatically altered unlike with low MI imaging. With higher energy insonation, bubbles change shape, merge with other bubbles, and burst open. Cadence ADI technology is a multipulse technology that provides very high resolution images that capture the effect of microbubble emission. The dramatic nonlinear effects create many broad frequency components that contribute to fine spatial resolution and unique bubble signatures that support high specificity detection. One very interesting aspect is that Cadence ADI technology, like Cadence CPS technology, effectively separates the tissue image from the contrast agent image. You can perform a scan and then from the same dataset, view the tissue (as if without contrast agent), only the contrast agent, or both together. In effect, you can view the baseline scan at the same time as the contrast scans.

Although there are other emission techniques being investigated, only Cadence ADI and Cadence CPS technology let you review the functional "contrast" image, the anatomical "tissue" image or both together, all from the same acquisition.

Here is a representation of how "inversion" techniques interact with tissue and contrast agent at high MI, or high power, and are limited for high MI imaging (Figure 4).

When scanning at high MI, it is especially important to understand the properties encountered with inversion methods. A pulse is transmitted with a certain polarity. The received signal contains tissue fundamental, tissue harmonics, contrast agent fundamental, and contrast agent harmonic components. (The degree of fundamental vs. harmonic contrast agent response depends on a number of properties, including the properties of each type of contrast agent.)

An inverted signal is then transmitted into the body [with Coherent Contrast Imaging, (CCI)], the inverted signal is sent down a spatially distinct and different scanline from the original signal). The received signal includes tissue fundamental and tissue harmonic components. There is no (or minimal) contrast agent component because the first pulse interrogates the agent with High MI and depletes the area of agent. The signal from the two pulses are added together.

When traditional inversion techniques are used at high MI, the tissue and contrast agent responses are mixed together. Thus detection is less contrast agent specific. It is therefore not possible to examine the signal received from the contrast agent separately from the signal received from the patient's anatomy. If the clinician needs to examine the "tissue only" image, this image must be obtained prior to administration of the contrast agent. Alternately if the "tissue only" image is needed after the administration of the contrast agent, the clinician must wait until the agent leaves the area of interest. Both methods extend the patient examination time.

Cadence agent detection imaging technology utilizes an entirely different technology which also makes use of the Sequoia system's flexible design. The hallmark of the Cadence ADI technology method is its excellent spatial resolution. The first high resolution pulse is transmitted. The Sequoia ultrasound system receives fundamental tissue signal, harmonic tissue signal, fundamental contrast agent signal, and harmonic contrast agent signal.

The second high resolution pulse is transmitted but is not inverted. It has the same polarity as the first pulse. The signals that come back on receive are fundamental tissue and harmonic tissue. Since the contrast agent was exposed to high MI during the first pulsing, there is no (or little) fundamental or harmonic signal coming back from the contrast agent on this second received pulse.

Rather than adding the results of the receive pulses together, with Cadence ADI technology they are subtracted (Figure 5). Even if some contrast agent signal remains during the second pulse contrast signals are still effectively detected as a difference still exists between the first and second pulses while the tissue signals between the two pulses are identical and cancel out. This results in only the fundamental and harmonic contrast agent signals remaining. This is what forms the "contrast only" Cadence ADI technology image. Cadence ADI technology detects the unique emission signature from contrast agents to simultaneously display co-registration of anatomical and functional images. Cadence ADI technology is the first high MI contrast agent imaging to effectively separate and display tissue, contrast, or both together.

In summary, the Sequoia system provides an exciting new level of contrast agent detection for clinical or research use. Unique contrast agent technologies such as Cadence contrast pulse sequencing and Cadence agent detection imaging technologies allow clinicians to display the tissue image, the contrast agent only image, or both together – all from the same acquisition dataset.

* At the time of publication, the U.S. Food and Drug Administration has cleared ultrasound contrast agents only for use in LVO. Check the current regulation for the country in which you are using this system for contrast agent clearance.

Siemens AG Medical Solutions
Henkestrasse 127
D-91052 Erlangen
Germany
Tel: + 49 9131 84-0
www.siemens.com/medical

Siemens Medical Solutions USA, Inc.
Ultrasound Division Headquarters
P.O. Box 7393
Mountain View, CA 94039-7393 USA
Tel: 1 888-826-9702

Europe: +44 20 8479 7950
Asia Pacific: +65 6341 0990
Latin America: +1 786-845-0697

Siemens **Medical Solutions** that help

A91004-M2430-B284-1-4A00
SD 0305 10.0
Printed in USA