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(71) **Applicant** *(for all designated States except US)*: **BRACCO RESEARCH S.A.** [CH/CH]; 31, route de la Galaise, CH-1228 Plan-les-Ouates (CH).

(72) **Inventors; and**
(75) **Inventors/Applicants** *(for US only)*: **ARDITI, Marcel** [CH/CH]; 27, rue Daubin, CH-1203 Geneva (CH). **GORCE, Jean-Marie** [FR/FR]; 198 Rue Henri Grobon, F-01700 Miribel (FR).

(74) **Agents: SAVOYE, Jean-Paul** et al.; Moinas & Savoye SA, 42, Rue Plantamour, CH-1201 Geneva (CH).

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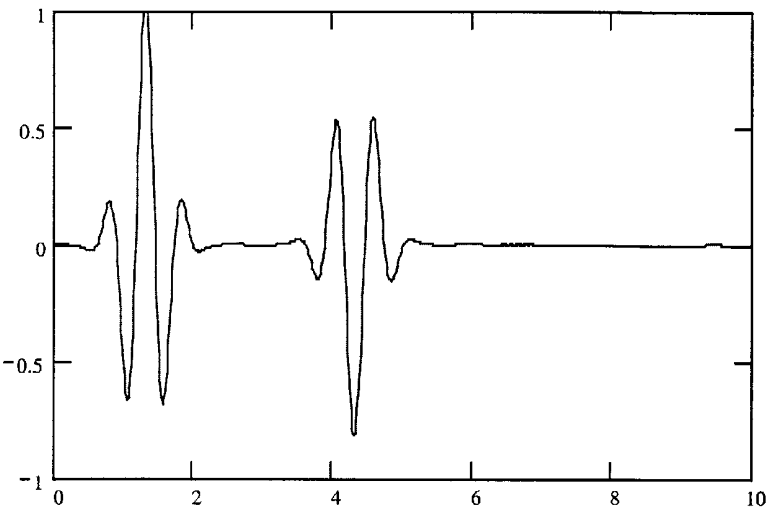
(54) **Title:** ULTRASOUND CONTRAST IMAGING WITH MULTIPLE-PULSE EXCITATION WAVEFORMS



(57) **Abstract:** The method of imaging the nonlinear components of ultrasound echo signals returned from scatterers comprises the steps of constructing a multi-pulse excitation waveform, the pulses composing this waveform having spectra with known relative frequency dependencies, differing in amplitude and phase so that the multi-pulse waveform can be considered as a convolution of any single of said pulses with a known coding function, transmitting said multiple-pulse waveform within a single transmission of an ultrasound beam in the direction of said scatterers, decoding the received rf-waveform by a first appropriate decoding function to obtain a new rf-waveform, decoding said received rf-waveform by a second and different appropriate decoding function to obtain another rf-waveform realigning in time, as required, both decoded rf-waveforms obtained from the same returned echo signal by a time delay as determined by the transmit-coding function, normalizing amplitudes and combining both rf-waveforms to enhance echo components caused by nonlinear scatterers and essentially suppress echo components caused by linear scatterers.

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ULTRASOUND CONTRAST IMAGING WITH MULTIPLE-PULSE EXCITATION WAVEFORMS

The invention relates to a method of ultrasound imaging of organs and tissues by detection of ultrasound backscattered from a region which may contain nonlinear scatterers such as microbubbles used as a contrast agent, the method comprising projecting an ultrasound beam to a zone of tissue to be imaged, receiving the echo reflected from the tissue as a radiofrequency response signal, processing the radiofrequency response into a demodulated video output signal, storing the output in a video scan converter, and scanning the tissue to produce a video image of the region under investigation. The invention also comprises a system for ultrasonic imaging of organs or tissues which may contain nonlinear scatterers such as microbubbles used as a contrast agent, the system comprising an ultrasonic probe for transmitting and receiving ultrasonic signals, signal processing means, means for storing the processed signals and a display element. Use of the system for imaging of organs, tissues and blood vessels is also disclosed.

Background Art

Wide acceptance of ultrasound as an inexpensive non-invasive diagnostic technique coupled with rapid development of electronics and related technology has brought about numerous improvements to ultrasound equipment and ultrasound signal processing circuitry. Ultrasound scanners designed for medical or other uses have become cheaper, easier to use, more compact, more sophisticated and more powerful instruments. However, the changes of acoustic impedance occurring within the living tissue are small and the absorption of ultrasound energy by different types of tissue (blood vessels, organs, etc.) are such that some diagnostic applications remain unmet challenges, despite these technical developments. This situation changed considerably with the development and introduction of administrable ultrasound contrast agents. Introduction of contrast agents made from stabilized suspensions of gas microbubbles or gas-containing microparticles into the bloodstream and organs to be investigated have demonstrated that better and more useful ultrasound images of organs and surrounding tissue may be obtained with ultrasound equipment. Thus, pathologies in organs like the liver, spleen, kidneys, heart or other soft tissues are becoming more readily recognizable, opening up new diagnostic areas for both B-mode and Doppler ultrasound and broadening the use of ultrasound as a diagnostic tool.

Recently, ultrasound techniques, i.e. scanners, electronic circuitry, transducers and other hardware and software components are showing great progresses in their abilities to exploit, to a fuller extent, the specific properties of ultrasound contrast agents. This is made possible by the vision by ultrasound instrument manufacturers of the vast potential offered by these contrast agents towards more accurate diagnosis, thanks to enhanced imaging capabilities and quantification of blood flow and perfusion. Thus, what was almost independent developments of these related segments of the field are now providing opportunity to draw on synergies offered by studies in which the electronic/ ultrasound characteristics of the apparatus and the physical properties of the contrast agent are combined. A few examples of such studies reported improvements from specific agents/equipment combinations, such as harmonic contrast imaging. These synergies are thus opening new areas of experimentation, innovation, and search of more universal methods for producing greater tissue resolution, better image and greater versatility of ultrasound as a diagnostic technique. There is no doubt that, provided their implementation is kept relatively simple, these will be widely accepted.

An attempt towards improved ultrasound imaging is described in WO-A-93/12720 (Monaghan) which discloses a method of imaging of a region of the body based on subtracting ultrasound images obtained prior to injection of a contrast agent from the images of the same region obtained following administration of the contrast agent. Based on this response subtraction principle, the method performs superposition of images obtained from the same region prior to and after administration of the contrast agent, providing an image of the region perfused by the contrast agent freed from background image, noise or parasites. In theory, the method described is capable of providing a good quality images with enhanced contrast. However, in practice, it requires maintenance of the same reference position of the region imaged for a long period of time, i.e. long enough to allow injection and perfusion of the contrast agent and maintenance of an enormous amount of data. Therefore the practical implementation of the method is very difficult if not impossible. The difficulty is partly due to inevitable internal body movements related to breathing, digestion and heart beat, and partly due to movements of the imaging probe by the ultrasound operator. Most realtime imaging probes are commonly handheld for best perception, feedback and diagnosis.

Interesting proposals for improved imaging of tissue containing microbubble suspensions as contrast agent have been made by Burns, P., Radiology 185 P (1992) 142 and Schrope, B. et al., Ultrasound in Med. & Biol. 19 (1993) 567. There, it is suggested that the second harmonic frequencies generated by non-linear oscillation of microbubbles be used as imaging parameters. The method proposed is based on the fact that normal tissue does not display nonlinear responses to the same extent as microbubbles, and therefore the second harmonics method allows for contrast enhancement between the tissues with and without contrast agent.

Although attractive, the method has its shortcomings, as its application imposes several strict requirements. Firstly, excitation of the fundamental "bubble-resonance" frequency must be achieved by fairly narrow-band pulses, i.e. relatively long tone bursts of several radio-frequency cycles. While this requirement is compatible with the circuits and conditions required by Doppler processing, it becomes hardly applicable in the case of B-mode imaging, where the ultrasound pulses must be of very short duration, typically one-half or one-cycle excitation. In this case, insufficient energy is converted from the fundamental frequency to its "second-harmonic", and thus the B-mode imaging mode cannot greatly benefit from this echo-enhancing method. Secondly, the second harmonic generated is attenuated, as the ultrasound echo propagates in tissue on its way back to the transducer, at a rate as determined by its frequency, i.e. at a rate significantly higher than the attenuation rate of the fundamental frequency. This constraint is a drawback of the "harmonic-imaging" method, which is thus limited to propagation depths compatible with ultrasound attenuation at the high "second-harmonic" frequency. Furthermore, in order to generate echo-signal components at twice the fundamental frequency, "harmonic imaging" requires non-linear oscillation of the contrast agent. Such behavior imposes the ultrasound excitation level to exceed a certain acoustic threshold at the point of imaging (i.e. at a certain depth in tissue). During nonlinear oscillation, a frequency conversion takes place, causing in particular part of the acoustic energy to be converted from the fundamental excitation frequency up to its second harmonic. On the other hand, that level should not exceed the microbubble burst level at which the microbubbles are destroyed, and hence harmonic imaging will fail due to the destruction of the contrast agent in the imaging volume. The above constraints require that the imaging-instrument be set-up in such a way as to ensure the transmit-acoustic level to fall within a certain energy band: high enough to generate second harmonic components, but low enough to avoid microbubble destruction within a few cycles.

Thus, methods which treat electronic echo signals during normal realtime ("on the fly") investigations are those most desirable, allowing better imaging and wider use of ultrasound diagnostic imaging. Such methods are based on an enhancement of the echoes signals received from the regions imaged, using signal processing functions which are designed to enhance the contrast between regions containing contrast agent from those without contrast agent, on the basis of nonlinear or frequency-dependent parameters, would be simple to use and implement in new instrument designs.

US 5'632'277 and US 5'706'819 already disclose methods and apparatus for the detection and imaging of harmonic echo components from microbubble-based contrast agents in blood. These methods utilize first and second ultrasound pulses that are alternatively transmitted into the medium being imaged. The first and second ultrasound pulses are amplitude modulated signals in the radiofrequency range, the first ultrasound pulse differing only in sign (polarity) from the second ultrasound pulse transmitted. The echo signals generated by these successive pulses are stored in memory and combined by adding them so that the linear components cancel, leaving only the nonlinear component to be imaged. Accordingly, since tissue generally reflects less harmonic components than microbubbles, such processing enables the microbubble echoes of the contrast agent to be received with a high signal to noise ratio.

In these known approaches, for each " line-of-sight ", or in other words for each transmitted-ultrasound beam steering and focusing properties, a minimum of two successive pulses is required to cancel echoes from tissues while preserving significant signals of echoes from microbubbles. The radiofrequency echo signals are stored in a temporary memory following excitation of each successive pulses.

Alternative methods have been proposed in US 5'961'463, or WO 99/30617 according to which, by alternating the polarity or otherwise coding the successive excitation conditions and taking the sum, difference or other combinations of these rf-echo signals, essentially zero signals are produced from linear reflectors other than the microbubbles, while echo signals from microbubbles produce non-linear signals that can be used to construct images with great sensitivity and enhanced contrast between microbubbles and tissues not containing a significant number of microbubbles.

There are several disadvantages common to these techniques. Firstly, because of the finite propagation velocity of sound in tissues, a time interval of several hundred microseconds must elapse between successive transmit pulses, in order for the echoes from the deepest regions of interest to return to the ultrasound probe before a following transmit pulse can be applied. This requirement limits the achievable frame rate, which is reduced in a proportion depending on the number of pulses fired in each direction, compared to similar imaging conditions without contrast-specific transmit coding. Secondly, the bubbles can move significant distances in the blood vessels in the time interval between pulses. Because of that, the resulting processing is sensitive not only to nonlinear scattering by microbubbles, but also to decorrelation due to movement between pulses. Thirdly, since the bubbles are excited successively by interrogating pulses, they can be destroyed or in other ways altered between successive pulses. As a consequence, the resulting images, Doppler or other signals are not purely dependent on the nonlinear particularities of microbubbles, but also depend on these other possible effects and artefacts.

These techniques are sometimes designated " pulse-inversion imaging ", " phase-inversion imaging ", "wideband harmonic imaging", "non-linear imaging using phase cancellation ", etc.

Summary of the invention

The present invention pertains to a method of coding the transmitted pressure-pulse waveform in such a way as to allow decoding the resulting echo waveforms giving substantially reduced contributions from linear scatterers or tissues which do not contain contrast agent microbubbles, and significant contributions for echoes originating from contrast agent microbubbles.

The present invention relates to a method of nonlinear imaging by coding the transmitted waveforms within single transmit firings of the transducer or imaging probe. It is based on the observation that in the case of reflection by linear or essentially linear scatterers such as most tissues, individual rf-echo signals can be appropriately decoded, or deconvolved, to produce signals of reduced amplitude, while in the case of reflection by more strongly nonlinear scatterers such as contrast agent microbubbles, applying the same decoding algorithms produces comparatively enhanced signals.

In this way, a sensitive method is provided to significantly enhance the contrast between microbubbles and tissues, without paying a penalty of reducing the effective pulse-repetition frequency and frame rate.

The invention also relates to a device for carrying out the above-mentioned method, comprising means for constructing a suitable excitation waveform, comprising two or more pulses, the multiple-pulses composing this waveform having spectra with known relative frequency dependencies with respect to one another, differing in amplitude and phase in a known fashion, this waveform being intended to be applied to an ultrasound transducer to generate an ultrasonic beam, an ultrasound transducer array connected to said excitation means, comprising one or a plurality of transducer elements, a transmitter coupled to said transducer array for pulsing said transducer elements, receiving means coupled to said transducer for receiving said echo signals, means for decoding the returned echo signal by a first appropriate decoding function to obtain an rf-waveform, means for decoding the returned echo signal by a second and different appropriate decoding function to obtain an rf-waveform, means for realigning in time both decoded rf-waveforms, means for normalizing amplitudes of said decoded rf-waveforms, and means for summing or otherwise combining both rf-waveforms to effectively suppress echo components caused by linear scatterers and comparatively enhance echo components caused by nonlinear reflectors.

The invention further relates to the use of the device for detecting and imaging the nonlinear components of ultrasound echo signals returned from scatterers within the body of human patients or animals.

Brief description of the drawings

The following drawings illustrate, schematically, as examples two embodiments of the method and the device according to this invention.

Figure 1 is a diagram of a typical single-shot phase inversion pulse for linear echo cancellation.

Figure 2 is a typical response of a 4μ microbubble to the single-shot phase inversion pulse of Figure 1.

Figure 3 is a diagram of the power spectrum of coded pulse of Figure 1 and of the bubble response of Figure 2.

Figure 4 is a diagram of transmit coding as delta function with respect to the first, "positive" pulse.

Figure 5 is a diagram of transmit coding as delta function with respect to the second, "negative" pulse.

Figure 6 is a diagram of a typical rf-echo signal containing nonlinear echoes in the 20-40 μS interval.

Figure 7 is a diagram of deconvolved rf-waveform with respect to the "positive" pulse of figure 4.

Figure 8 is a diagram of deconvolved rf-waveform with respect to the "negative" pulse of figure 5.

Figure 9 is a diagram of result of single-shot linear echo cancellation processing for a random collection of linear scatterers, except in the 20 to 40 µS time interval which contains harmonic generating nonlinear reflectors.

Figure 10 is a block diagram which illustrates a contrast echography device with single-shot linear echo cancellation imaging.

Figure 11 illustrates one deconvolution kernel used in the first example.

Figure 12 illustrates two deconvolution kernels, noted $w_1(t)$ and $w_2(t)$, respectively used in the estimation of the two components $s'_1(t)$ and $s'_2(t)$.

Figure 13 represents the spectrogram map computed from $s'_1(t)$.

Figure 14 represents the spectrogram map computed from $s'_2(t)$.

Figure 15 is a diagram of local power estimates for the case of similar energy between the linear and nonlinear reflectors considered.

Figure 16 is a diagram of local power estimates for the case of energy in the nonlinear reflectors 24 dB lower than in the linear reflectors.

Figure 17 is a block diagram which illustrates a contrast echography device with single-shot linear echo cancellation imaging based on the SSLF/spectrogram-ratio method.

Detailed description of the invention

In a first disclosed implementation of this invention, a pulse waveform such as illustrated in Fig 1 is generated by a transmit ultrasound transducer, with a center frequency at 1.8 MHz. The horizontal time axis is labeled in microseconds, while the vertical axis is in arbitrary pressure or voltage units. This example illustrates a double-pulse, where the second instance is inverted in polarity, delayed by 3 µS and reduced by 20% in amplitude with respect to the first one. The double-pulse is constructed by summing two instances of the same model pulse, with the indicated changes in polarity, delay and amplitude; thus, the two pulses have spectra with identical relative frequency dependencies, differing only in amplitude and phase. Figure 2 illustrates a typical pressure waveform from a 4 µ microbubble in response to the excitation shown in Figure 1, as can be computed using well known and accepted bubble-oscillation models (e.g. De Jong N., Cornet R. and Lancee C.T., Higher harmonics of vibrating gas-filled microspheres. Part one: simulations, Ultrasonics, 1994 (32), 447-453). The power spectra magnitudes of the double-pulse waveform and the bubble response are given in Figure 3, illustrating first that these spectra display, as expected, a modulation in amplitude given by the inverse of the time delay between the two pulses, i.e. at 1/3 µS = 0.67 MHz in this example, and secondly, that the spectrum of the bubble response exhibit, also as expected, significant energy around harmonics of the excitation center frequency, i.e. around frequencies multiples of the excitation frequency, due to nonlinear microbubble oscillation. From linear-systems theory, the double-pulse waveform of Figure 1 can be considered as a convolution of a model single-pulse with a coding function *c(t)* composed of a pair of delta functions of amplitudes one and -0.8, separated by a time delay of 3 µS, as illustrated in Figure 4. This function can be written as:

$$c(t) = \delta(t) - \alpha \cdot \delta(t - \tau),$$

with $\alpha = 0.8$, $\tau = 3\,\mu\text{S}$.

Deconvolution of the received echo waveforms from a collection of scatterers, such as those obtained in B-mode ultrasound imaging, can be applied in the time domain by convolution with an appropriate deconvolution kernel, or in the frequency domain by complex division by the spectrum of the coding of Figure 3. One can thus obtain the rf-waveforms which would have been obtained from linear echoes to single-pulse excitation by the first pulse of the pulse-pair, by deconvolution of the echoes from the pulse-pair by the appropriate decoding function. Similarly, one can also obtain the rf-waveforms which would have been obtained from linear echoes to single-pulse excitation by the second pulse of the pulse-pair, by deconvolution of the same echoes from the pulse-pair by a different, appropriate, decoding function.

This different decoding function can be obtained from the observation that the pulse pair can also be considered as a convolution of the second, negative phase, pulse component by a different coding of delta function pair, as given by Figure 5, where the first pulse is obtained by a delta function with a negative time shift and a 1/0.8, or 1.25 amplitude relative to the delta function of unity amplitude centered at the origin. In this way, and for any rf-echo signals produced by an ensemble of randomly distributed linear scatterers, it is possible, by deconvolution, to generate two rf-waveforms, equal to those that would have been obtained from the first and second pulses individually. Note that in this example, considering positive and negative pulses of different peak amplitudes allows computing the inverse of the coding spectra without problems of discontinuities at the frequencies where zero amplitudes appear when the pulses are considered identical in amplitudes.

Figure 6 illustrates the case of a simulated rf-echo signal, for scatterers of random amplitudes and positions along the beam propagation path, in response to the " single-shot " double-pulse coded excitation. These scatterers are considered linear at all positions, except in the time interval from 20 to 40 µS, where they are considered as originating from microbubbles according to their responses shown in Figure 2. Two different deconvolved rf-waveforms can be derived from this signal : one obtained by deconvolution with respect to a first coding sequence, as given by Figure 4, and a second waveform obtained by deconvolution with respect to a second coding sequence, as given by Figure 5. It is emphasized that both these resulting waveforms are derived from echoes originating from a single transmit, coded pulse waveform. The resulting rf-waveforms are illustrated in Figure 7 and Figure 8, respectively. The final step in the single-shot linear echo cancellation processing is to take the sum of both rf-waveforms, following a time shift to realign both rf-waveforms by an amount equal to the delay applied in the transmit double-pulse excitation waveform, amplitude normalization, again determined by that applied within the double-pulse sequence, and highpass filtering to enhance harmonic components vs. fundamental components. These quantities can be accurately known and programmed by the control circuits and software of modern echographic instruments. The result of that sum is an essentially zero time trace signal, except in the time interval containing the nonlinear reflectors, as illustrated in Figure 9.

Thus, in the presence of contrast agent microbubbles following intravenous injection in the organism, this method allows sensitive detection of microbubbles by providing enhanced echo signals available for further demodulation, processing and display as a representative of the presence of contrast agent in this region.

In this way, a sensitive method is found to enhance the contrast between regions not containing in significant amounts nonlinear scatterers, and regions containing contrast agent microbubbles with significant nonlinear scattering properties, without the drawbacks of other known methods, as outlined previously. It becomes evident from the disclosed method of the present invention that it relates to the field of imaging processing from ultrasound echoes reflected by scatterers, so that this method is neither a method for treatment of the human or animal body, nor a diagnostic method practised on the human or animal body. Accordingly, this method is implemented by echographic imaging specialists and not by medical staff.

A block diagram of a typical contrast echography device of the invention, with single-shot linear echo cancellation for carrying out the above disclosed method is illustrated in figure 10. The device includes at least the following modules: central processor unit 1, timing circuits 2, time gain control 3, transmit radiofrequency waveform shaping and coding 4, power transmit circuit 5, Tx/Rx-element multiplexer 6, ultrasound transducer array 7, receive amplifiers with time gain function and analog to digital converter 8, digital beamforming processor 9, a first radiofrequency waveform decoder 10a (a deconvolver in this case), a second radiofrequency waveform decoder 10b, radiofrequency amplitude normalization and time shift module 11a connected to decoder module 10a, radiofrequency amplitude normalization and time shift module 11b connected to decoding module 10b, arithmetic combination, demodulation and one-line memory 12. The output of the module 12 is connected to a video scan converter 13, connected to a video monitor 14.

In operation and under general control of a Central Processor Unit, the timing circuits 2 define a pulse repetition frequency, required for constructing echographic images (B-mode images, Doppler components in one- and two dimensions), based on sequential scanning of the region of the body to be imaged. For each successive coded-pulse excitation waveform, the timing circuits 2 also define the time-origin of a time dependent function used to provide variable amplification gain to echo signals originating from increasing imaging depths. This function is realized by the time gain control module 3, whose output can be a varying voltage, applied to gain control of the receiving amplifier with adjustable gain 8. The timing circuits 2 also allow to define transmit shaped/coded waveform, required for the adequate sequential excitation of the individual elements of the ultrasound transducer array 7 to provide beam focusing and steering to be applied to the electrical excitation power transmit circuit 5. The timing circuits also provide the signals needed to bring predefined groups of array elements into connection with the power transmit circuit 5, by ways of the connections provided by the transmit-receive element multiplexer 6. The output signals from this multiplexer are then routed to the receive amplifiers with time gain function and analog-to-digital conversion means 8, also controlled by the timing circuits 2. The digital output of these circuits 8 is fed to the digital beamforming processor 9, the output of which is fed as a common input to the processing channels for implementing waveform decoding and linear echo cancellation on the returned echoes.

The example of figure 2 implements linear cancellation by feeding the echo signals through respectively first and second radiofrequency decoders 10a, 10b, each followed by a radiofrequency amplitude normalisation and time shift 11a, 11b in order to deconvolve the echo signals from the transmit shaped/coded excitation radiofrequency waveforms. The individual outputs of the processing channels are then routed as input signals to the digital summation and one-line memory 12 for taking the sum of both rf-waveforms to effectively suppress all echo components caused by linear scatterers and produce output signals then fed to the input of the video scan converter 13, setup to write the incoming data, for each sequential pulse, in a pattern corresponding to the selected beam steering and positioning.

Thus, by repeating the above sequence at the specified rate, each time modifying the beam steering and/or focusing to obtain echoes from successive positions in the organs, tissue and blood, the scan converter output signal refreshes the image as displayed on the video monitor 14, in realtime, i.e. at a rate between a few images per second to hundreds of images per second, sufficient for reproducing perception of movement by operator of the instrument. In the process described above, the regions of the echographic images corresponding to regions containing contrast agents appear with a contrast that is vastly enhanced, because tissues reflect minimal harmonic components.

The convolution process may be implemented by spectral Fourier, Chirp-Z or wavelet transform analysis of returning echoes and also by applying the linear echo cancellation processing within a sliding time window of the returning echoes. In a similar manner, the individual signal components may be spectrally analysed or filtered in distinct or similar frequency bands before being compared, added, subtracted, multiplied, divided or otherwise combined arithmetically, as described for example in US 5,526,816, incorporated herein by reference in its entirety.

In a second disclosed implementation of this invention, a similar transmit-coding waveform can be used, but the decoding aimed at detecting the nonlinear components in the received echoes is different than in the first example. In the first implementation above, the length of the input signal is finite, while the deconvolution kernel is of an arbitrarily long and inpractical size (see for example Figure 11). As an alternative and more practical approach, finite-length decoding filters can be considered, as described hereafter, and combined with an approach for Source Separation by Linear Filtering (SSLF) coupled with time-frequency analysis (spectrogram) or time-scale analysis (discrete wavelet transform). Here, the input echo-signal $y_{RF}(t)$ reflected in response to the double-pulse excitation is considered as a linear combination of two signals $s_1(t)$ and $s_2(t)$, corresponding to components responding in an odd and even manner to the coded excitation, as follows:

$$y_{RF}(t) = c_1(t) * s_1(t) + c_2(t) * s_2(t)$$

with the following definitions of $c_1(t)$ and $c_2(t)$:

$$c_1(t) = \delta(t) - \alpha \cdot \delta(t-\tau) \text{ and } c_2(t) = \delta(t) + \alpha \cdot \delta(t-\tau).$$

Here, δ, α, τ are, respectively, Dirac's delta function, the relative amplitude coefficient of the second pulse in Figure 1, and the time separation between the two coding pulses, again as in Figure 1. The $s_1(t)$ component represents the contributions from linear scatterers, responding with a polarity equal to that of the excitation code $c_1(t)$, while the $s_2(t)$ component represents the harmonic contributions from nonlinear scatterers, responding with a positive polarity irrespectively of the polarity of the excitation code (i.e. responding as if they had been coded with the $c_2(t)$function. With this formalism, estimates $s'_1(t)$ and $s'_2(t)$of the $s_1(t)$ and $s_2(t)$ components, respectively, can be approximated by convolutions with appropriate decoding filters, for example as:

$$s'_1(t) = w_1(t) * y_{RF}(t)$$

and

$$s'_2(t) = w_2(t) * y_{RF}(t)$$

where $w_1(t)$ and $w_2(t)$ are deconvolution kernels optimized for the estimates of the $s_1(t)$ and $s_2(t)$ components. Such functions can be for example finite codes of length 2 or 3 coding intervals, with odd and even polarity and weighted by a Bartlett window as shown on Figure 12. As an example of this implementation, a $y_{RF}(t)$ signal is considered for the case of coding by $c_1(t)$ with $\alpha = 1$ and $\tau = 3\mu S$, with nonlinear microbubble reflectors added in the 20 to 40 µS time interval.

In the context of this implementation, it is also beneficial to consider processing the individual signal components by spectral analysis or filtering in distinct or similar frequency bands before being compared, added, subtracted, multiplied, divided or otherwise combined arithmetically. A preferred approach is described hereafter. The instanteneous power content within the estimated $s'_1(t)$ and $s'_2(t)$ is computed as a function of frequency within a gaussian time window of length equal to one code. Spectrograms $S_1(f,t)$ and $S_2(f,t)$ are thus computed from these components, as a function of time-of-arrival of the echoes, proportional to depth, and illustrated in Figures 13 and 14, respectively. In these two figures, the x-axis represents time, the y-axis represents the frequency and the gray level at each x-y point represents the magnitude of the spectral energy within a Gaussian time window. It represents a time-localized frequency content of the signal. A comparison between the two spectrograms illustrates how the $s'_1(t)$ estimate achieves suppression of the harmonic components of the nonlinear reflectors (between 3.5 and 4.5 MHz), while the $s'_2(t)$ estimate preserves a comparatively much larger contribution from the harmonic components of nonlinear reflectors. For each frequency component of S_1 and S_2, local power estimates are computed within a sliding time interval of width τ, thus generating two functions the $P_1(f,t)$ and $P_2(f,t)$ representing sub-band local power distributions. Computing the ratios of $P_2(f,t)$ over $P_1(f,t)$ provides a surprizingly sensitive method of detecting the contributions from nonlinear reflectors. These ratios can be individually computed over the whole frequency spectrum considered or limited to frequencies around frequencies of interest, for example around the fundamental or harmonic bands of the transmit frequency. As an illustration of that ability of the "SSLF/spectrogram-ratio linear echo cancellation processing" to detect the presence of nonlinear reflectors, two cases are considered. One where the average energy of the nonlinear reflectors is similar to the energy of the linear-scatterers (designated the 0dB case), and the other where the average energy of the nonlinear reflectors is 24 dB below the energy of the linear-scatterers (designated the -24dB case). Figure 15 illustrates the 0dB case. A comparison is made between the computation of P_2/P_1 within the harmonic frequency band between 3.5 and 4.5 MHz (upper trace) and the case of sub-band local power distributions $P_{RF}(f,t)$ computed on a $y_{RF}(t)$ obtained from a single pulse excitation, again in the same frequency band (lower trace). Both approaches are here able to extract correctly the nonlinear reflector portion of the signal between 20 and 40 µs. Figure 16 illustrates the -24dB case. The comparison between the two approaches shows a clearly higher sensitivity of the approach based on the SSLF/spectrogram-ratio linear echo cancellation processing.

Figure 17 is a block diagram illustrating a contrast echography device with single-shot linear echo cancellation imaging based on the SSLF/spectrogram-ratio method. Elements 1 to 9, as well as 12 to 14, are identical to those included in Figure 10. Elements 10a and 10b represent the operations of linear and nonlinear component estimation, as described above. Elements 11a and 11b represent the optional spectrogram, as well as the local power estimation, computed on the resulting signals from elements 10a and 10b, respectively. These estimations can be performed over bandwidths (1) and (2) which may be selected independently over limited or extended frequency bands. In the example above, these bandwidths (1) and (2) were identical, and chosen around the harmonic frequency band of interest. Alternatively, they could be chosen in arbitrary ways, for example around the fundamental frequency for bandwidth (1) and around the second harmonic for bandwidth (2).

The benefits of the method and the implementations disclosed may equally be exploited in systems in which the processing channels are part of the receiver of a one- or two-dimensional pulsed-Doppler ultrasound system, which may further incorporate a video output representing a spectrum of velocity distribution and/or an audible signal output which is preferably a loudspeaker but it may also be any convenient sound reproducing device. Various useful options may be incorporated in the pulsed-Doppler ultrasound system such as a two-dimensional map of velocity distribution which may further be colour coded, or it may incorporate a two-dimensional map of echo amplitude or energy derived from Doppler echo components from moving targets, optionally at predetermined thresholds for velocities inferior or superior to a given value.

While the above described embodiments only use double-pulse excitation waveform, the invention may also be implemented using excitation waveform comprising more than two pulses.

CLAIMS

1. A method of detecting and imaging the nonlinear components of ultrasound echo signals returned from scatterers, characterized in that it comprises the steps of:

a) constructing a multiple-pulse excitation waveform, the pulses composing this waveform having spectra with known relative frequency dependencies with respect to eachother, differing in amplitude and phase in a known fashion so that the multiple-pulse waveform can be considered as a convolution of any single of said pulses with a known coding function, the time delay separating the pulses being shorter than the time interval needed for ultrasound echo signals to be returned from the most distant said scatterers to be imaged, and longer than or equal to one half period of the fundamental central frequency of any single of said pulses,

b) transmitting said multiple-pulse waveform within a single transmition of an ultrasound beam in the direction of said scatterers,

c) receiving the echo signals in response to said transmitted beam, returned from said scatterers to form a received rf-waveform,

d) convolving said received rf-waveform by a first appropriate decoding function to obtain a new rf-waveform,

e) convolving said received rf-waveform by a second and different appropriate decoding function to obtain another rf-waveform,

f) realigning in time both resulting rf-waveforms obtained from the same returned echo signal by a time delay,

g) generating two signals by normalizing amplitudes of said resulting rf-waveforms,

h) combining arithmetically both resulting signals to effectively suppress echo components caused by linear scatterers and produce output signals, and

i) further processing in known ways the ouptut signals and storing in a scan conversion memory for display on a video monitor as a two-dimensional map of echo-amplitudes.

j) repeating the sequence b) to i) above in order to project ultrasound energy in a different direction.

2. A method of detecting and imaging the nonlinear components of an ultrasound signal as described in claim 1, characterized in that the multiple-pulse excitation waveform is composed of pulses having spectra with identical relative frequency dependencies and differing only in amplitude and phase in order to correspond to a convolution of a single of said pulses with delta functions of similar or slightly different amplitudes and separated by a known time delay.

3. A method according to claims 1-2, wherein a demodulation step includes computing estimations of radiofrequency spectrogram or Discrete Wavelet Transforms for each of the rf-waveforms,

4. A method according to claims 1-2, wherein a demodulation step includes computing local power estimates for each of the signals in a given bandwidth,

5. A method according to claims 1-2, wherein a summation algorithm is used for processing said output signals.

6. A method according to claims 1-2, wherein the amplitude of said output signals is coded by different video colours, to be superimposed on an otherwise conventional grey-scale video image obtained by the usual processing methods applied in B-mode imaging.

7. A method according to one of the preceding claims, wherein it comprises the step of constructing a double-pulse excitation waveform.

8. A device for carrying out the method according to claim 1, wherein it comprises:

means for constructing a multiple-pulse excitation waveform, the pulses composing this waveform having spectra with known relative frequency dependencies with respect to one another, differing in amplitude and phase in a known fashion, this waveform being intended to be applied to an ultrasound transducer to generate an ultrasonic beam,

an ultrasound transducer array connected to said excitation means, comprising one or a plurality of transducer elements,

a transmitter coupled to said transducer array for pulsing said transducer elements,

receiving means coupled to said transducer for receiving said echo signals,

means for convolving returned echo signal by a first appropriate decoding function to obtain an rf-waveform,

means for convolving returned echo signal by a second and different appropriate decoding function to obtain an rf-waveform,

means for realigning in time both computed signals,

means for normalizing amplitudes of said computed signals, and

means for combining arithmetically both rf-waveforms to effectively suppress echo components caused by linear scatterers.

9. A device according to claim 8 further comprising means for computing radiofrequency spectrograms or Discrete Wavelet Transforms,

10. A device according to claim 8 further comprising means for estimating local power in given bandwidths,

11. A device according to claim 8 comprising a video scan converter.

12. A device according to claim 8, comprising analog-to-digital converter circuits connected to said transducer elements, whose purpose is to digitize the returned echo signals to allow processing of the returned echo signals by digital electronic processing circuits, and computing means.

13. A device according to claim 8, wherein the returned

echo signal processing means are part of a receiver of a pulsed-Doppler ultrasound system.

14. A device according to claim 13, wherein said pulsed-Doppler ultrasound system incorporates an audible signal output by means of a loudspeaker.

15. A device according to claim 13, wherein said pulsed-Doppler ultrasound system incorporates a spectral video output representing a spectrum of velocity distribution.

16. A device according to claim 13, wherein said pulsed-Doppler ultrasound system incorporates a two-dimensional map of velocity distribution.

17. A device according to claim 16, wherein said two-dimensional map of velocity distribution is colour coded.

18. A device claim 13, wherein said pulsed-Doppler ultrasound system incorporates a two-dimensional map of echo-amplitude or energy derived from Doppler echo components from moving scatterers.

19. A device according to claim 13, wherein said pulsed-Doppler ultrasound system incorporates a two-dimensional map of Doppler echo components from scatterers moving with a velocity inferior to a predetermined threshold.

20. A device according to claim 13, wherein said pulsed-Doppler ultrasound system incorporates a two-dimensional map of Doppler echo components from scatterers moving with a velocity superior to a predetermined threshold.

21. A device according to claim 8, wherein the required convolution processes of said returned echo signals are obtained by spectral Fourier, Chirp-Z, wavelet transform analysis or direct time convolution with a convolution function applied within a sliding time window on the returning echoes.

22. A device according to claim 8, wherein it comprises means for constructing a double-pulse excitation waveform.

23. Use of the device of one of claims 8-22 for detecting and imaging the nonlinear components of ultrasound

echo signals returned from scatterers within the body of human patients or animals.

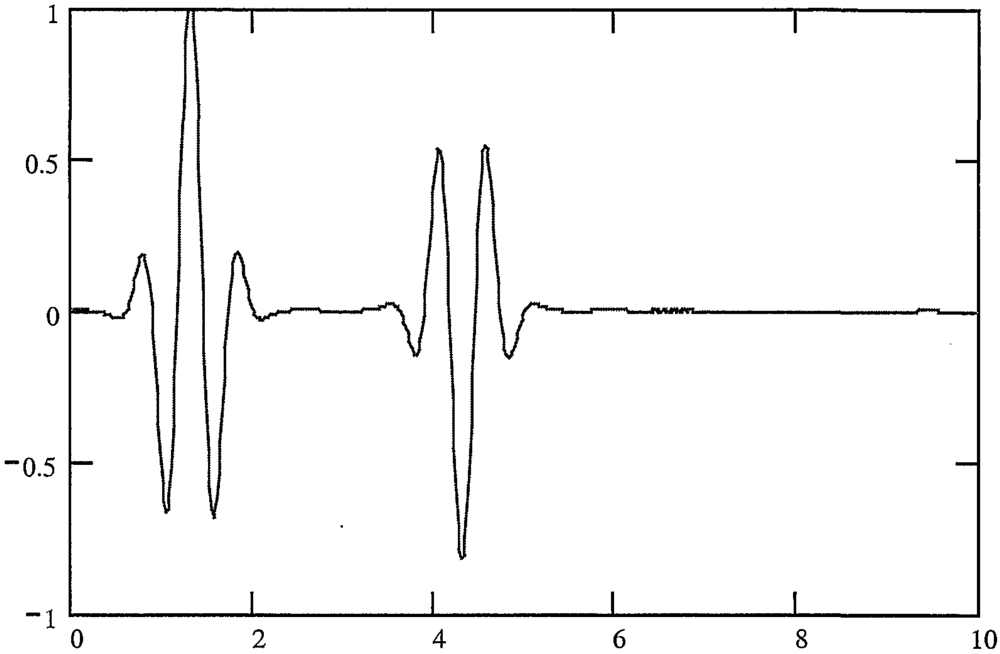


FIGURE 1

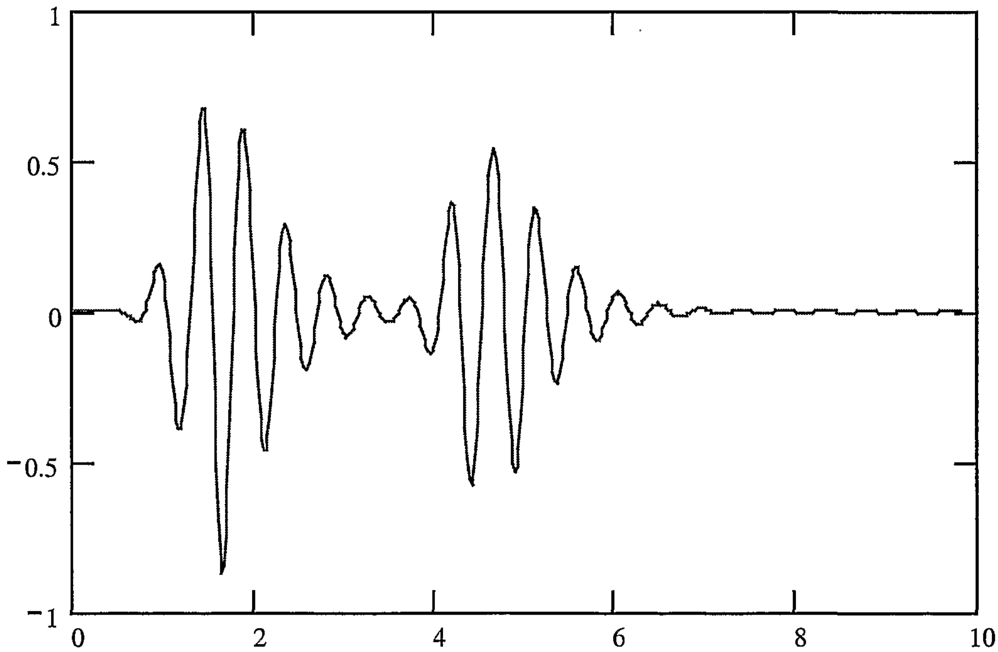


FIGURE 2

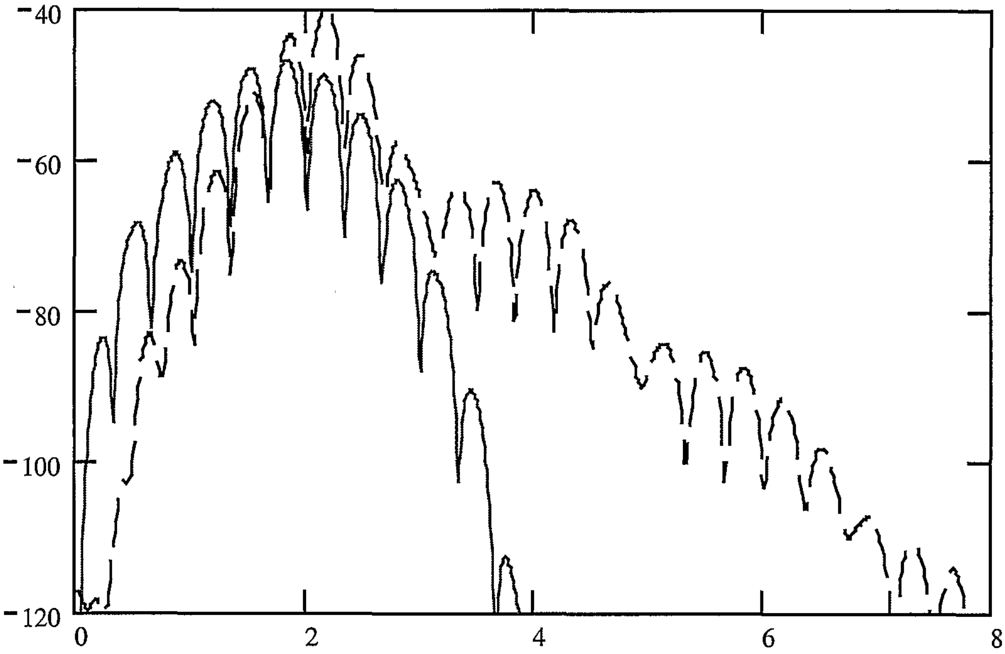


FIGURE 3

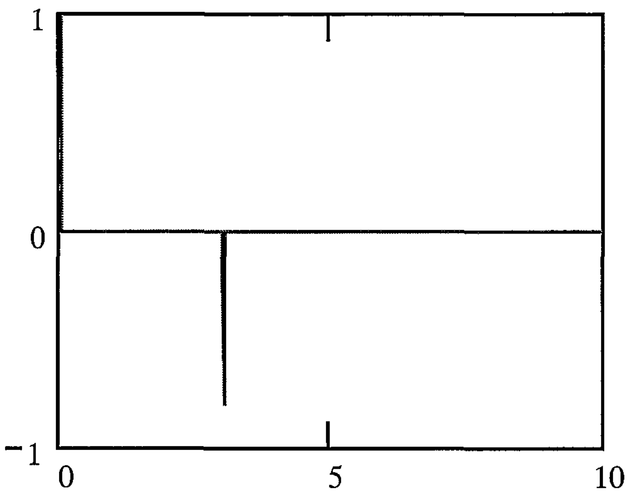


FIGURE 4

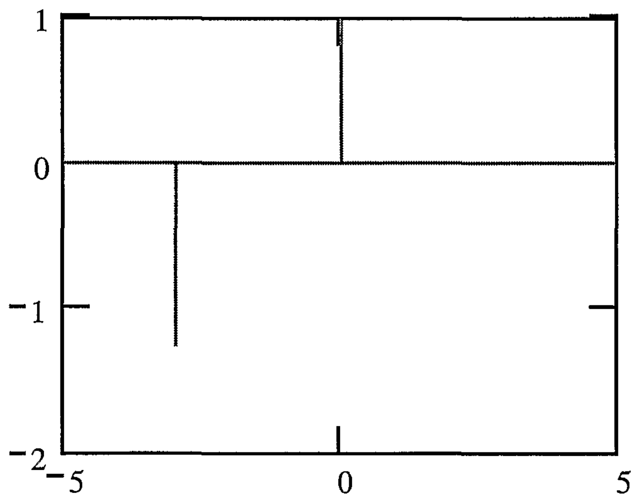


FIGURE 5

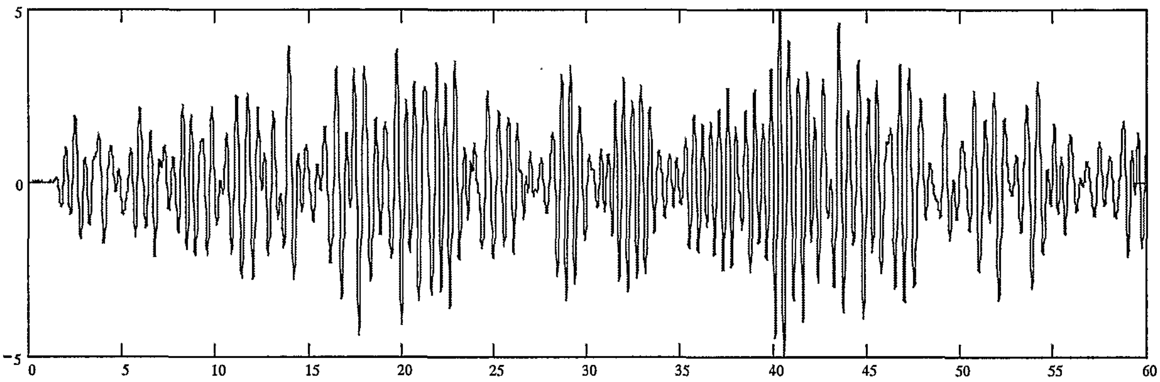


FIGURE 6

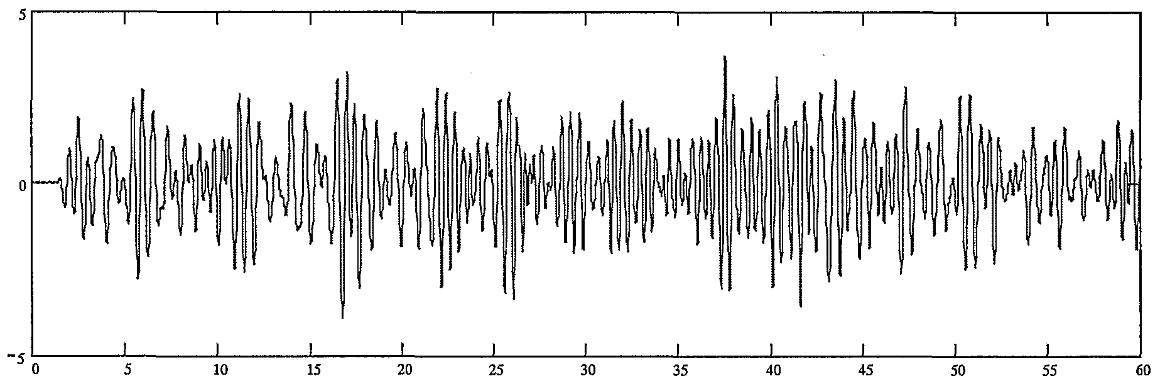


FIGURE 7

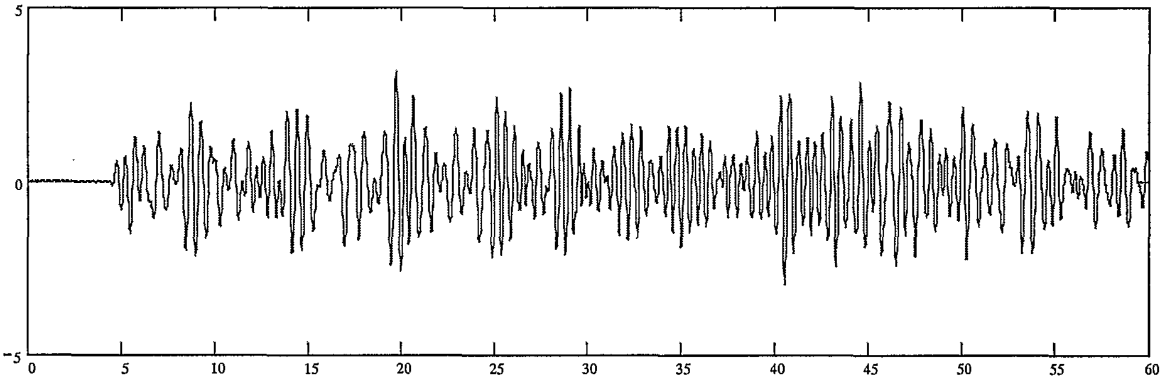


FIGURE 8

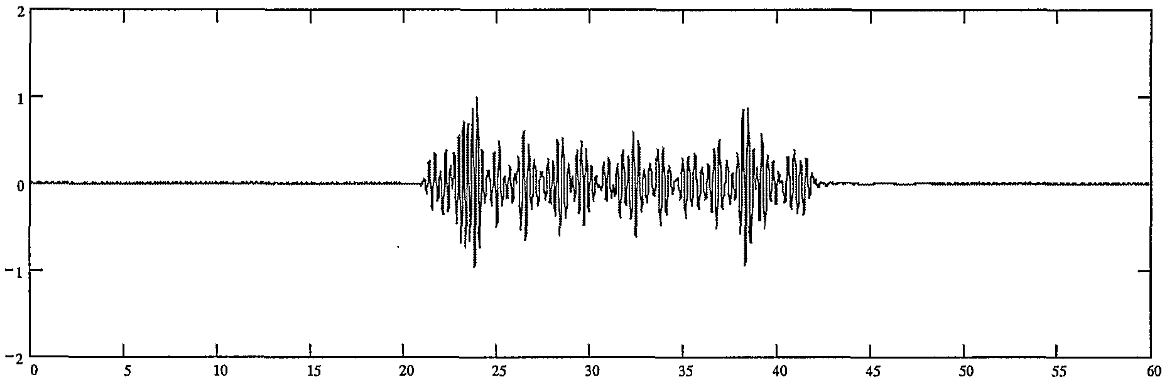
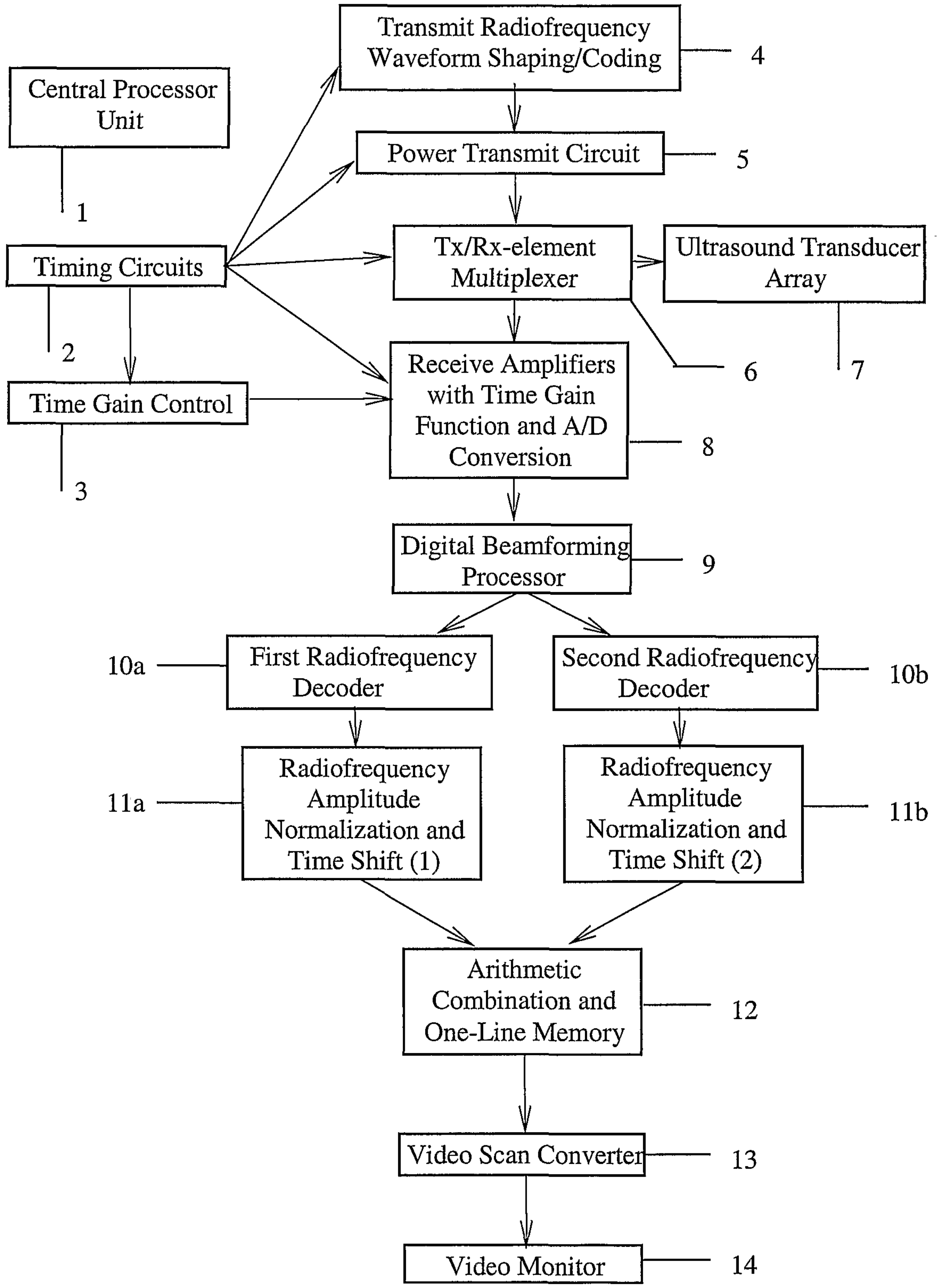


FIGURE 9



Transmit Radiofrequency Waveform Shaping/Coding
4
Central Processor Unit
1
Power Transmit Circuit
5
Timing Circuits
Tx/Rx-element Multiplexer
Ultrasound Transducer Array
2
Receive Amplifiers with Time Gain Function and A/D Conversion
6
7
Time Gain Control
8
3
Digital Beamforming Processor
9
10a
First Radiofrequency Decoder
Second Radiofrequency Decoder
10b
11a
Radiofrequency Amplitude Normalization and Time Shift (1)
Radiofrequency Amplitude Normalization and Time Shift (2)
11b
Arithmetic Combination and One-Line Memory
12
Video Scan Converter
13
Video Monitor
14

FIGURE 10

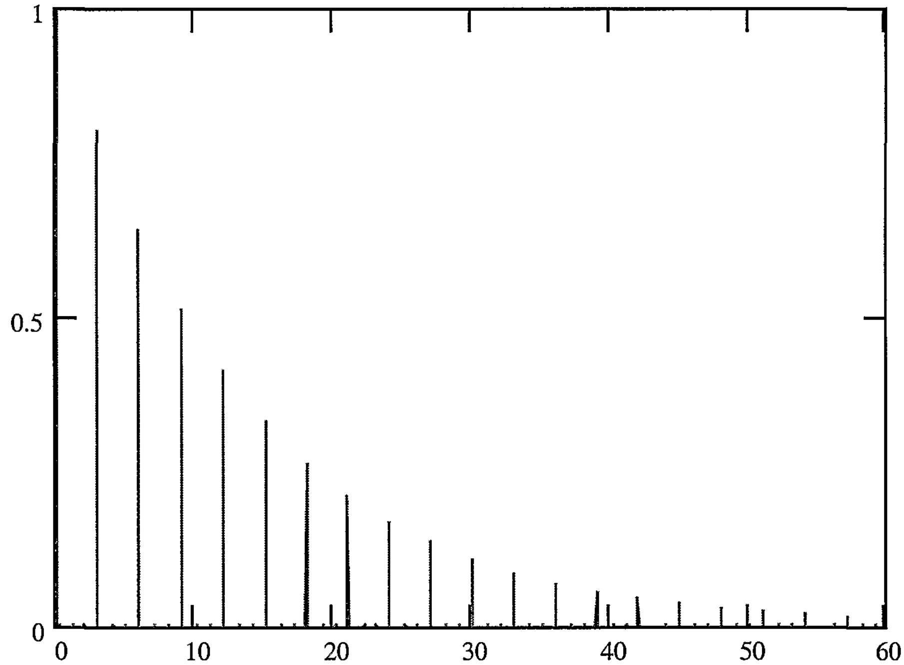


FIGURE 11

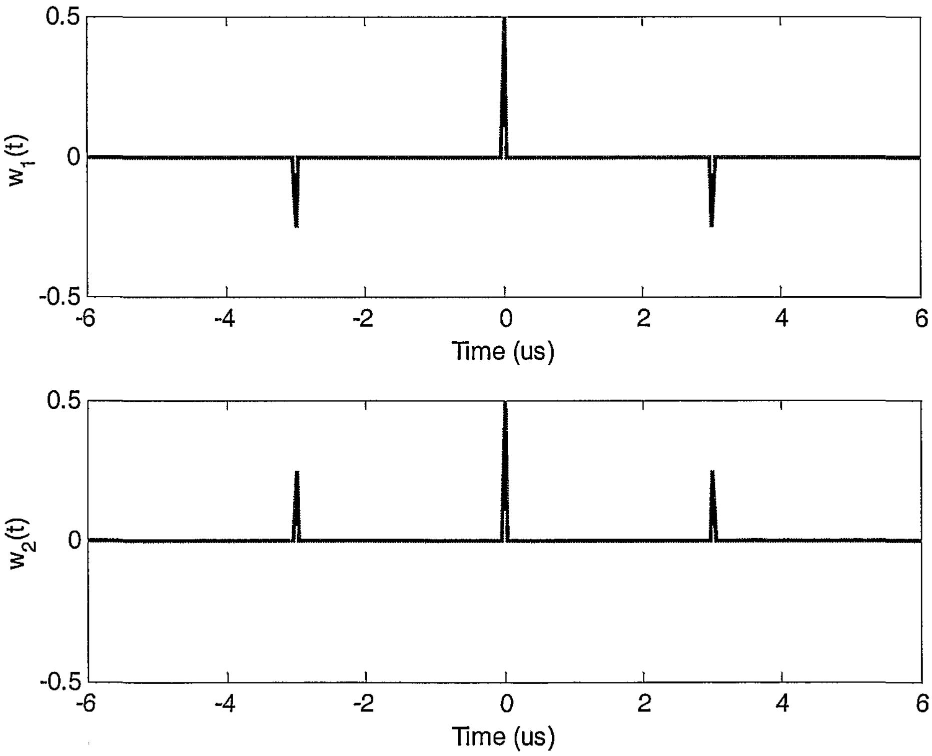


FIGURE 12

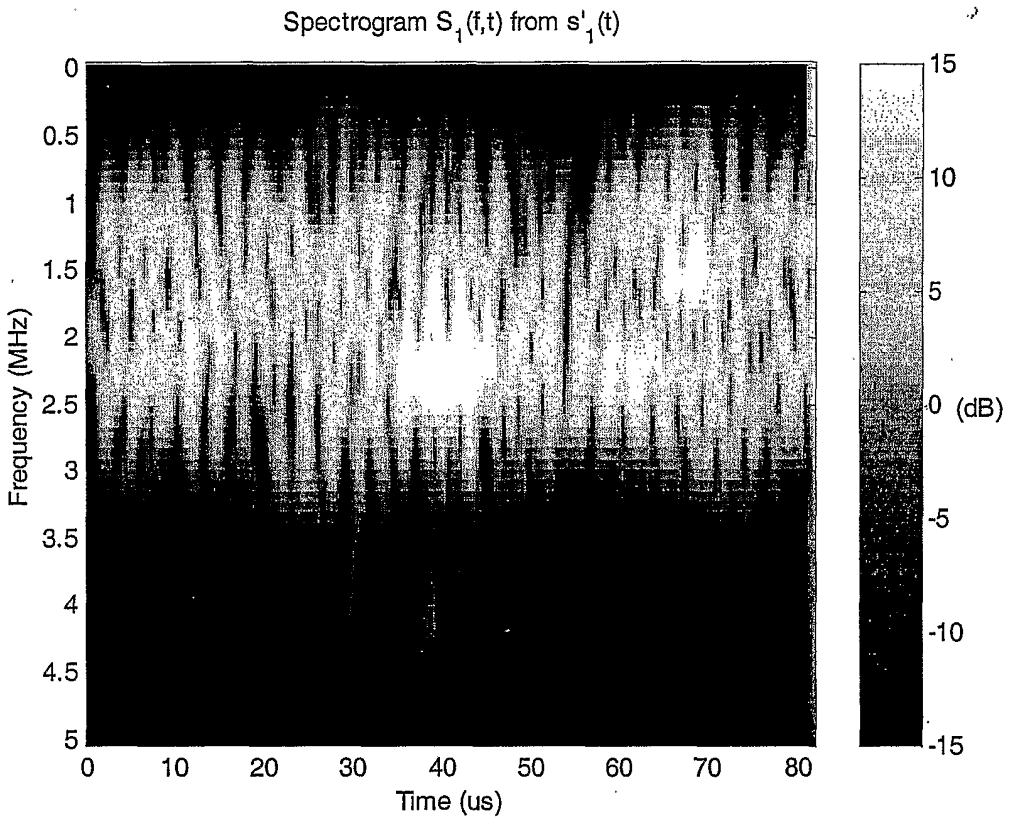


FIGURE 13

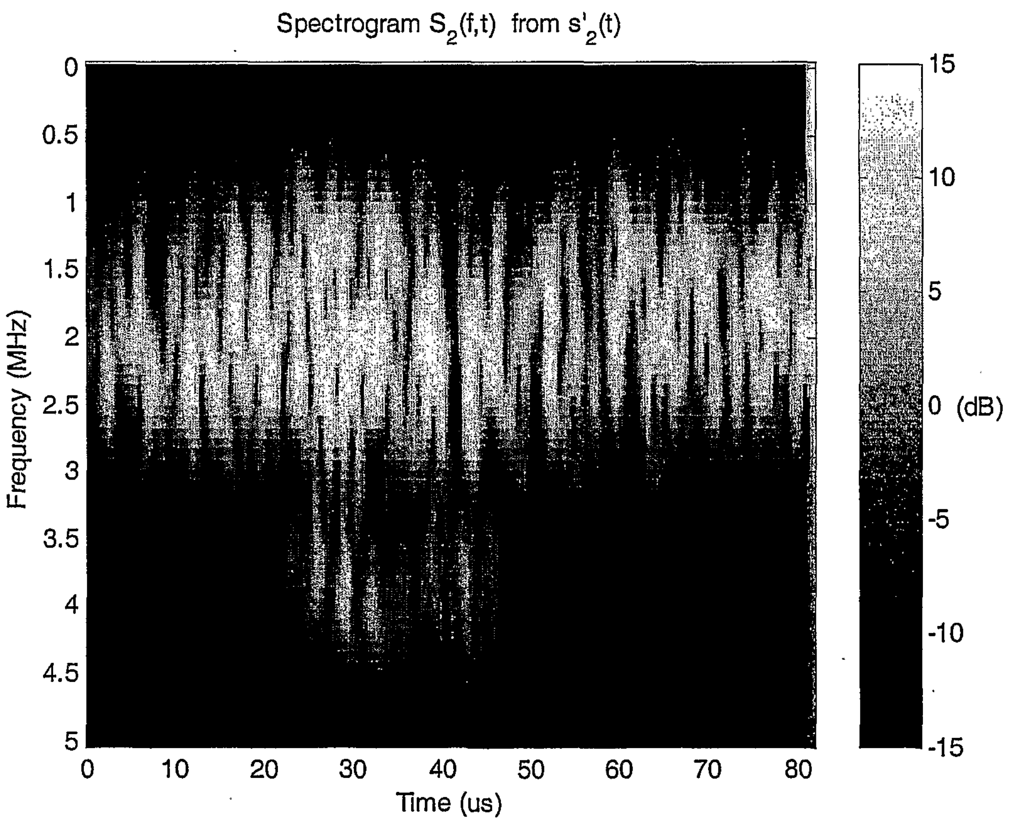


FIGURE 14

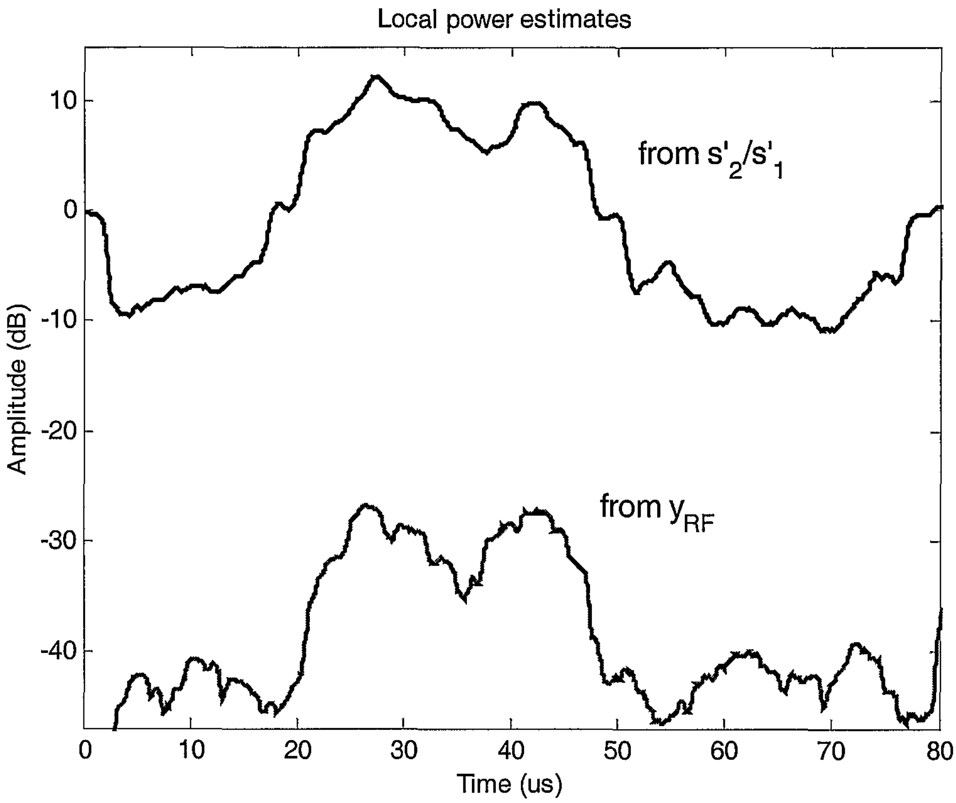


FIGURE 15

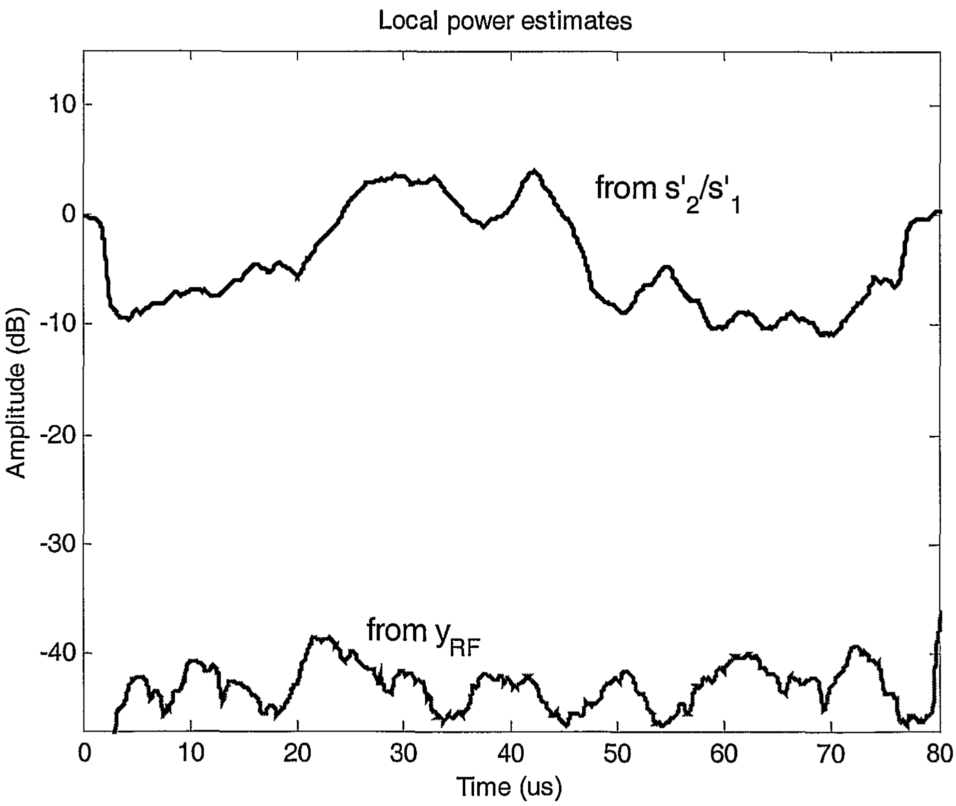


FIGURE 16

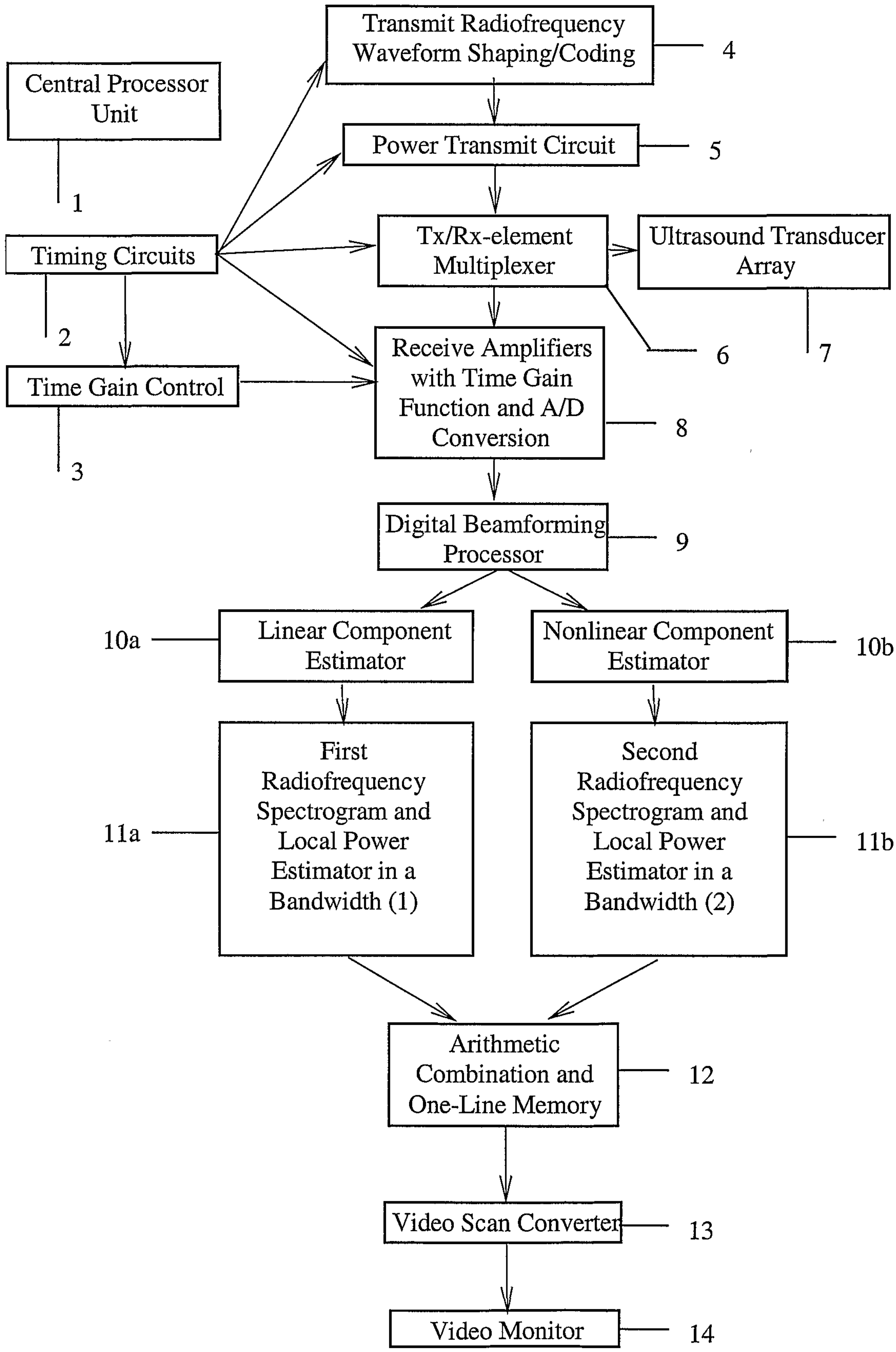

Transmit Radiofrequency Waveform Shaping/Coding
4
Central Processor Unit
1
Power Transmit Circuit
5
Timing Circuits
Tx/Rx-element Multiplexer
Ultrasound Transducer Array
2
Time Gain Control
Receive Amplifiers with Time Gain Function and A/D Conversion
6
7
8
3
Digital Beamforming Processor
9
10a
Linear Component Estimator
Nonlinear Component Estimator
10b
11a
First Radiofrequency Spectrogram and Local Power Estimator in a Bandwidth (1)
Second Radiofrequency Spectrogram and Local Power Estimator in a Bandwidth (2)
11b
Arithmetic Combination and One-Line Memory
12
Video Scan Converter
13
Video Monitor
14

FIGURE 17

INTERNATIONAL SEARCH REPORT

Interna l Application No
PCT/IB 01/00612

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 G01S7/52

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 G01S A61B

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 224 482 A (NIKOONAHAD MEHRDAD ET AL) 6 July 1993 (1993-07-06) column 7, line 22-49; figures 3,4	1,8
P,X	WO 00 57769 A (ACUSON) 5 October 2000 (2000-10-05) page 34, line 8-16; figures 14,25 page 37, line 12 -page 39, line 24	1,8
P,X	US 6 120 448 A (BRADLEY CHARLES E ET AL) 19 September 2000 (2000-09-19) column 4, line 10-21	1,8
A	US 5 902 243 A (HEDBERG DAVID J ET AL) 11 May 1999 (1999-05-11) column 3, line 58 -column 4, line 11; figure 4	1,8

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[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

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"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

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Date of the actual completion of the international search	Date of mailing of the international search report
20 July 2001	01/08/2001

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Jonsson, P.O.

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INTERNATIONAL SEARCH REPORT

Interni il Application No
PCT/IB 01/00612

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

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A	EP 0 916 967 A (ATL ULTRASOUND INC) 19 May 1999 (1999-05-19) paragraphs ‘0017!,‘0018!; figures 5A,5B	1,8

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

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Information on patent family members

Intern l Application No
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