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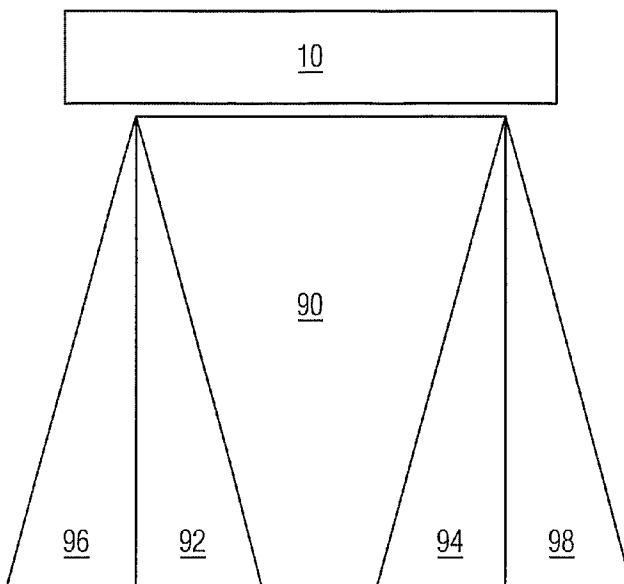
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[Continued on next page]

(54) Title: ULTRASONIC DIAGNOSTIC CONTRAST IMAGING WITH SPATIAL COMPOUNDING



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(57) Abstract: An ultrasonic diagnostic imaging system and method are presented for producing spatially compounded images of harmonic contrast agents which are separated by the pulse inversion technique. Beams with different modulation characteristics are transmitted in different look directions. Aligned beams are combined by a nonlinear signal separator to separate harmonic contrast signal components by pulse inversion. The harmonic contrast signals from the different look directions are combined by a spatial compounding processor to produce a spatially compounded harmonic contrast image. In an illustrated embodiment the spatially compounded harmonic contrast image overlays a tissue image. Different modulation and beam steering techniques such as multiline acquisition are also disclosed for spatial compounding of contrast agent images.



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ULTRASONIC DIAGNOSTIC CONTRAST IMAGING  
WITH SPATIAL COMPOUNDING

5        This invention relates to medical diagnostic imaging systems and, in particular, to ultrasonic diagnostic imaging systems which image contrast agents within the body by spatial compounding.

10      The ultrasonic imaging of blood flow and tissue vasculature within the body can be greatly enhanced by infusing the bloodstream with an ultrasonic contrast agent. Contrast agents are solutions of suspended microbubbles which are highly reflective of ultrasound. As the microbubbles travel through the vasculature and vessels being imaged, the strong echo reflections from the microbubbles cause the blood stream to "light up" in the ultrasound image, enabling the clinician to more clearly diagnose conditions in the heart and blood vessels. See for example US Pat. 5,833,613 (Averkiou et al.) The high harmonic content of echo signals from microbubbles enables the vasculature to be more easily segmented and displayed against the tissue background. See US Pat. 5,951,478 (Hwang et al.)

15      Contrast agents can be used in several different ways. One is to insonify the image field with high energy (high MI) ultrasound which disrupts or breaks the microbubbles. The disruption events produce strong nonlinear reflections which can be readily detected and displayed. See US Pat. 5,456,257 (Johnson et al.) But with the new generation of contrast agents currently being developed, the nonlinear response can be elicited without substantial disruption of the microbubbles, enabling more extended imaging sessions on a single contrast agent infusion. In this technique microbubbles can

be continuously imaged at low transmit energies (low MI). See US Pat. 6,171,246 (Averkiou et al.)

However, low MI contrast images often suffer from very low signal to noise ratios, compromised axial resolution, and overall image aesthetics. This is due to the desire to use the lowest MI possible for minimal microbubble disruption which reduces the intensity of the returning echoes. These adverse effects are also seen when a multi-pulse scheme is used to separate the nonlinear components of the contrast echoes such as those described in US Pats. 5,706,819 (Hwang) and 5,577,505 (Brock-Fisher et al.) These techniques, referred to as pulse inversion, require the transmission of multiple pulses for harmonic separation. Accordingly it would be desirable to improve the quality of contrast images while retaining the advantage of good image aesthetics.

In accordance with the principles of the present invention, an ultrasonic diagnostic imaging system is provided which performs ultrasonic contrast imaging by spatial compounding. The region of interest is interrogated by beams from a plurality of different look directions and the backscattered signals processed for harmonic separation and combined to produce a spatially compounded harmonic contrast image. The spatial compounding not only reduces image speckle and improves the clarity of arcuate anatomical features, but also improves the signal to noise of low MI images. In several illustrated embodiments component images for spatial compounding are acquired in ways which enable the nonlinear signal content to be separated by pulse inversion. In another embodiment the acquisition rate of spatially compounded harmonic contrast images is

improved through pulse inversion separation by interpolation. In yet another embodiment fundamental and harmonic acquisition is interleaved to produce a tissue image with a spatially compounded overlay of contrast enhanced blood flow.

5 In the drawings:

FIGURE 1 illustrates in block diagram form an ultrasonic diagnostic imaging system which produces spatially compounded contrast images in accordance  
10 with the principles of the present invention.

FIGURE 2 illustrates a tissue image with a contrast enhanced overlay of pathology and vasculature.

FIGURES 3a-3c illustrate a technique for  
15 acquiring a tissue image with a spatially compounded overlay of contrast enhanced blood flow.

FIGURES 4a-4c illustrate beam profiles for the multiline acquisition of spatially compounded nonlinear images.

20 FIGURES 5a-5c illustrate component images for spatial compounding which may be acquired by the technique of FIGURES 4a-4c.

FIGURES 6a-6c illustrate a high speed  
25 acquisition technique for spatially compounded harmonic contrast imaging.

FIGURE 7 illustrates the combining of component images for spatial compounding and harmonic separation by pulse inversion.

Referring first to FIGURE 1, an ultrasonic  
30 diagnostic imaging system constructed in accordance with the principles of the present invention is shown in block diagram form. This system operates by scanning a two or three dimensional region of the body being imaged with ultrasonic transmit beams. A scanhead 10 including an array transducer 12

transmits beams at different angles (look directions) over an image field denoted by the dashed rectangle and parallelograms. Three groups of scanlines are indicated in the drawing, labeled A, B, and C with each group being steered at a different angle relative to the scanhead. The transmission of the beams is controlled by a transmitter 14 which controls the phasing and time of actuation of each of the elements of the array transducer so as to transmit each beam from a predetermined origin along the array and at a predetermined angle. As each beam is transmitted along its steered path through the body, the beam returns echo signals with linear and nonlinear (fundamental and harmonic) components corresponding to the transmitted frequency components. The transmit signals are modulated by the nonlinear response of contrast agent microbubbles encountered by the beam, thereby generating echo signals with harmonic components.

The ultrasound system of FIGURE 1 utilizes a transmitter 16 which transmits waves or pulses of a selected modulation characteristic in a desired beam direction for the return of harmonic echo components from scatterers within the body. The transmitter is responsive to a number of control parameters which determine the characteristics of the transmit beams as shown in the drawing, including the frequency components of the transmit beam, their relative intensities or amplitudes, and the phase or polarity of the transmit signals. The transmitter is coupled by a transmit/receive switch 14 to the elements of the array transducer 12 of the scanhead 10. The array transducer can be a one dimensional array for planar (two dimensional) imaging or a two dimensional array for two dimensional or volumetric (three

dimensional) imaging.

The transducer array 12 receives echoes from the body containing fundamental and harmonic frequency components which are within the transducer passband.

5 These echo signals are coupled by the switch 14 to a beamformer 18 which appropriately delays echo signals from the different transducer elements then combines them to form a sequence of fundamental and harmonic signals along the receive beam direction from shallow  
10 to deeper depths. Preferably the beamformer is a digital beamformer operating on digitized echo signals to produce a sequence of discrete coherent digital echo signals from a near field to a far field depth of field. The beamformer may be a multiline  
15 beamformer which produces two or more sequences of echo signals along multiple spatially distinct receive scanlines in response to a single transmit beam, which is particularly useful for 3D imaging and for high speed acquisition of spatially compounded  
20 contrast image as described in several of the following embodiments. The beamformed echo signals are coupled to an ensemble memory 22. The transmitter 16 and the beamformer 18 are operated under control of a system controller 60, which in  
25 turn is responsive to the settings of controls on a user interface 20 operated by the user of the ultrasound system. The system controller controls the transmitter to transmit the desired number of scanline groups at the desired angles, transmit energies, frequencies and modulation characteristics.  
30 The system controller also controls the digital beamformer to properly delay and combine the received echo signals for the apertures and image depths used.

35 In accordance with one aspect of the present invention, multiple waves or pulses are transmitted

in each beam direction using different modulation techniques, resulting in the reception of multiple echoes for each scanned point in the image field. The echoes corresponding to a common spatial location 5 are referred to herein as an ensemble of echoes, and are stored in the ensemble memory 22, from which they can be retrieved and processed together. The echoes of an ensemble are combined in various ways as described more fully below by the nonlinear signal separator 24 to produce the desired nonlinear or harmonic signals of the contrast agent. This harmonic separation acts to enhance the nonlinear components by reinforcement and suppress the fundamental components by cancellation due to the 10 different transmit modulation of the echo signals being combined. The modulation techniques used can be amplitude modulation, phase modulation, polarity modulation or a combination thereof. See concurrently filed US patent [application attorney docket ATL-347] entitled "ULTRASONIC SPECKLE 15 REDUCTION USING NONLINEAR ECHO COMBINATIONS" for a description of the various ways in which the echoes of differently modulated signals can be combined for nonlinear separation. The separated signals are 20 filtered by a filter 62 to remove unwanted frequency components. When imaging harmonic contrast agents the passband of the filter 62 is set to pass harmonics of the transmit band. The filtered signals are subjected to B mode or Doppler detection by a 25 detector 64. For B mode imaging the detector 24 will perform amplitude detection of the echo signal envelope. For Doppler imaging ensembles of echoes 30 are assembled for each point in the image and are Doppler processed to estimate the Doppler shift or 35 Doppler power intensity.

In accordance with another aspect of the present invention the digital echo signals are processed by spatial compounding in a processor 30. The digital echo signals are initially pre-processed by a 5 pre-processor 32. The pre-processor 32 can preweight the signal samples if desired with a weighting factor. The samples can be preweighted with a weighting factor that is a function of the number of component frames used to form a particular compound 10 image. The pre-processor can also weight edge lines that are at the edge of one overlapping component image so as to smooth the transitions where the number of samples or images which are compounded changes. The pre-processed signal samples may then 15 undergo a resampling in a resampler 34. The resampler 34 can spatially realign the estimates of one component image to those of another component image or to the pixels of the display space.

After resampling the component images are 20 compounded on a spatial basis by a combiner 36. Combining may comprise summation, averaging, peak detection, or other combinational means. The samples being combined may also be weighted prior to combining in this step of the process. Finally, 25 post-processing is performed by a post-processor 38. The post-processor normalizes the combined values to a display range of values. Post-processing can be most easily implemented by look-up tables and can simultaneously perform compression and mapping of the 30 range of compounded values to a range of values suitable for display of the compounded image.

The compounding process may be performed in estimate data space or in display pixel space. In a constructed embodiment scan conversion is done 35 following the compounding process by a scan converter

40. The compound images may be stored in a Cineloop®  
memory 42 in either estimate or display pixel form.  
If stored in estimate form the images may be scan  
converted when replayed from the Cineloop memory for  
5 display. The scan converter and Cineloop memory may  
also be used to render three dimensional  
presentations of the spatially compounded images as  
described in U.S. Patents 5,485,842 and 5,860,924.  
Following scan conversion the spatially compounded  
10 images are processed for display by a video processor  
44 and displayed on an image display 50.

FIGURE 2 illustrates an overlay contrast image  
70 of the type described in aforementioned US Pat.  
6,171,246 (Averkiou et al.) This image 70 comprises  
15 an echo tissue background 72 with an area bounded by  
76 which is overlaid with a harmonic contrast image  
74 of contrast agent microbubbles. The multiple look  
directions used to acquire the image signals improve  
the ability to discern tumors and masses in the image  
20 field such as that illustrated at 78. The  
combination of signals from different look directions  
improves the signal to noise ratio of the signals  
returned from the mass 78 enabling it to stand out  
more clearly against the background, and the  
25 different look directions provide better definition  
of the contours of the mass 78. In addition, subtle  
masses which may be obscured by image speckle can be  
easier to discern. The harmonic contrast image can  
be colored to better highlight the vasculature in the  
30 mass.

A technique for acquiring this image 70 is  
illustrated in FIGURES 3a-3c. An ultrasound probe 10  
transmits beams 82, 84, 86 into the body at different  
look directions A, B, and C. This can be done by  
35 transmitting all of the beams of a specific look

direction before transmitting beams of another look direction. Alternatively it can done by interleaving transmissions of beams of different look directions. It can also be done by transmitting beams in  
5 different look directions simultaneously as described in US patent application serial number 60/501,795 entitled "ULTRASONIC SPATIAL COMPOUNDING WITH MULTIPLE SIMULTANEOUS BEAM TRANSMISSION." FIGURE 3a shows a group of beams 82 which are transmitted in a  
10 look direction A, FIGURE 3b illustrates a group of beams 84 which are transmitted in a look direction C, and FIGURE 3c illustrates a group of beams 86 which are transmitted in a look direction B.

In the embodiment of FIGURES 2 and 3, both  
15 fundamental and harmonic signals are used to produce the overlay contrast image 70. One way to do this is to transmit each beam at a fundamental frequency and receive echoes at both the fundamental and harmonic frequencies. Signals from different look directions at the fundamental are spatially combined and used to form the echo tissue image 72 and signals from different look directions at the harmonic are spatially combined and used to form the harmonic contrast overlay image 74. A variation of this  
20 technique is to use the fundamental frequency signals from only one look direction to form the echo tissue background and the harmonic frequency signals from multiple look directions to form the harmonic contrast overlay image. This variation does not  
25 produce spatial compounding of the tissue image 72, but does spatially compound the harmonic contrast signals in the area 76 where the mass 78 is being diagnosed. In both of these techniques the harmonic frequencies can be separated from the fundamental  
30 frequencies by bandpass filtering.  
35

Another approach is to use pulse inversion for harmonic separation. One way to do this is to transmit at least twice with a different modulation characteristic along each beam 82, 84, and 86. The 5 echo ensembles along each beam direction are temporarily stored in ensemble memory 22, then combined on a spatial basis by the nonlinear signal separator 24. The different modulation of the echoes being combined (e.g., phase modulation, amplitude 10 modulation, polarity, or a combination thereof) causes the fundamental components to be suppressed and the harmonic components to be emphasized. The fundamental signals from at least one look direction are separated by filtering or by inverse pulse 15 inversion (e.g., instead of additively combining the differently modulated echoes, they are subtractively combined to suppress the second harmonic while emphasizing the fundamental frequency component.) The pulse inversion separated harmonic signals from 20 the different look directions are spatially compounded by the spatial compounding processor 30 to produce the harmonic contrast image 74. Fundamental signals from multiple look directions may also be spatially compounded by the processor 30 to produce 25 the echo tissue image 72.

In yet another embodiment the beams of the different look directions are transmitted at different transmit frequencies. For instance, the beams transmitted in look direction A can be 30 transmitted at a nominal frequency of 1.9 MHz and the harmonics received at a frequency of 3.8 MHz and separated by bandpass filtering or pulse inversion (if multiple, differently modulated transmission are used). The beams transmitted in look direction C can be transmitted at a nominal frequency of 3.0 MHz and 35

the echoes received at that fundamental frequency of 3.0 MHz. The beams transmitted in look direction B are done in the same manner as look direction A: transmission is done at a nominal frequency of 1.9  
5 MHz and the harmonics received at a frequency of 3.8 MHz and separated by bandpass filtering or pulse inversion. The echo tissue image is formed from the fundamental frequency echoes received in look direction C and the harmonic contrast image is formed  
10 by spatially compounding the harmonic signals received in look directions A and B. The tissue image, while not spatially compounded, will exhibit good resolution by virtue of the fact that it is formed from the fundamental component, which is  
15 enhanced by the higher transmit frequency used.

A variation of this embodiment which results in a higher frame rate of display is to transmit once along each beam 82 with one modulation characteristic in look direction A and once along each beam  
20 direction 86 with another modulation characteristic in look direction B. Pulse inversion harmonic separation is then performed by the spatial compounding process as the echoes from the differently modulation beams are combined on a  
25 spatial basis, resulting in both spatial compounding and harmonic separation. In this case the harmonic contrast image is of the trapezoidal shape as illustrated in FIGURE 7. In the central area 90 of the image field echoes are present from all three  
30 look directions and combining the echoes from two or three look directions will cause harmonic separation and a high degree of spatial compounding in this area 90. In areas 92 and 94 echoes are present from only two look directions: directions A and C for area 92  
35 and directions B and C for area 94. Thus, with the

1.9MHz-3.0MHz-1.9MHz transmission scheme described above, a lower degree of spatial compounding will occur in these areas, but no pulse inversion harmonic separation can occur. Harmonic separation can be  
5 done in these areas by pulse inversion if each transmit beam is at 1.9MHz with different modulation characteristics so that echoes from any two or more beams can be used for pulse inversion separation. In that case, both spatial compounding and harmonic  
10 separation can be performed for areas 92 and 94. For instance, beams 82 can be transmitted at 1.9MHz with a first phase characteristic, beams 84 can be transmitted at 1.9MHz with a different amplitude characteristic, and beams 86 can be transmitted at  
15 the amplitude of beams 82 but with a different phase characteristic. Combining the echoes from some or all of these beams will result in both spatial compounding and pulse inversion nonlinear separation.  
In areas 96 and 98 only one echo is present from a  
20 three look direction transmit scheme, and neither spatial compounding nor pulse inversion separation can be performed in these areas.

It will be appreciated that using more than three look directions will produce additional areas  
25 and differently shaped areas for both spatial compounding and pulse inversion separation. In a constructed embodiment up to nine look directions were employed.

Another technique for increasing the frame rate of display is to use multiline acquisition when doing both spatial compounding and pulse inversion nonlinear signal separation. One multiline technique mentioned above is to transmit simultaneous beams in different look directions as described in the  
35 aforementioned US patent application serial number

60/501,795. Another multiline technique is illustrated in FIGURES 4 and 5. In FIGURES 4a-4c, beams are transmitted in three different look directions. The beams have beam profiles which 5 encompass multiple receive beams. For instance, in FIGURE 4a each beam profile 102 has a dashed center line and encompasses two receive beams on either side of the center line. The sign "+" denotes a beam transmitted with a given modulation characteristic 10 and the sign "-" denotes a beam transmitted with a different modulation characteristic. In the drawings the paired transmit and receive beam centers are shown parallel to each other for clarity of illustration; in practice, these beams would be 15 aligned with each other. In FIGURE 4a, a + beam is transmitted in a given beam direction and two or more + receive beams are received in response to the transmission and held in the ensemble memory 22. A - beam is then transmitted in the beam direction and 20 two or more - beams received in response. The aligned +/- receive beams are combined by the nonlinear signal separator 24, thereby producing two harmonic contrast beams, one on either side of the dashed center of the transmit beam 102. Thus, two or 25 more harmonic beams are received in response to only two transmit events. This transmit/receive sequence is repeated across the aperture as shown in FIGURE 5a, producing pairs of aligned, differently modulated receive beams which can then be combined to produce 30 pulse inversion separated harmonic contrast signals along each beam 182 in a first look direction.

This same sequence of transmission, reception and combination is then performed in a second look direction as shown by beam profiles 104 and beams 184 35 in FIGURES 4b and 5b. The sequence is repeated a

third time in a third look direction as shown by beam profiles 106 and beams 186 in FIGURES 4c and 5c. The harmonic echo from the different look directions are then processed and combined by the spatial  
5 compounding processor 30 to form a harmonic contrast image.

Another technique for increasing the frame rate with or without multiline reception is by the interpolation technique shown in FIGURES 6a-6c. A  
10 series of beams are transmitted and received across the aperture as shown in FIGURE 6a. These beams have alternating transmit characteristics as indicated by the + and - signs above each beam location. In this example beams 122 are modulated in a first manner and  
15 beams 124 are modulated in a second manner. The receive beams in adjacent beams 122,124 are then combined to interpolate an intermediate scanline 130. The combination of the echoes from the differently modulated beams causes harmonic separation along each  
20 scanline 130. Thus, scanlines 130 comprise a set of harmonic contrast scanlines in a first look direction.

The sequence is repeated a second time in a second look direction as shown in FIGURE 6b.  
25 Transmit beams of alternate modulation characteristics are transmitted and echoes received along each beam as shown by beams 142 and 144. Adjacent receive beams are used to interpolate intermediate scanlines 150 of separated harmonic signals acquired in a second look direction. The sequence is repeated a third time in a third look direction as shown in FIGURE 6c. Alternating transmit/receive beams 162,164 are acquired and used to interpolate intermediate separated harmonic  
30 scanlines 170. The harmonic scanlines 130, 150, 170  
35

are then spatially compounded to produce a spatially compounded harmonic contrast image. The frame rate of display is relatively high, since each group of n scanlines is acquired by transmitting and receiving 5  $n+1$  beams.

Instead of combining two receive lines  $(+, -)$  to effect pulse inversion separation, three or more laterally adjacent lines can be combined with appropriate weighting to separate the nonlinear 10 signal components. For example, three lines  $(+,-,+)$  can be combined to form nonlinear signals at the location of the center  $(-)$  line. The adjacent line of nonlinear signals would be formed at the location of the adjacent  $(+)$  line from the combination of the 15  $(-, +, -)$  lines, also with appropriate weighting, and so forth.

If multiline acquisition is available the frame rate of display can be increased even higher. Each transmission of a + modulated beam centered along a + beam direction in FIGURES 6a-6c can be followed by 20 acquisition of multiple receive beams on either side of the transmit beam center and aligned with scanline locations 130, 150, or 170. Each transmission of a - modulated beam centered along a - beam direction is followed by acquisition of multiple receive beams on 25 either side of the transmit beam which are aligned with the scanline locations. The receive beams aligned with the same scanline location are combined to separate nonlinear signals by pulse inversion along the scanlines 130, 150, and 170. When two receive beams are received for each transmit beam, 30 the frame rate will be the same as in the previous embodiment:  $n+1$  beams are transmitted for each n beams in a look direction. When higher order 35 multiline is employed, e.g., 4x, 6x or 8x multiline

reception, greater frame rates will be obtained. These higher acquisition rates may be accompanied by multiline artifacts, temporal artifacts, or both, however, and may not be suitable in a given application.

## WHAT IS CLAIMED IS:

1. A method for ultrasonic imaging with contrast agents comprising:

5 insonifying a region of interest from a plurality of look directions;  
separating nonlinear signal components from received echo signals; and  
combining the signals from different look  
10 directions to produce a spatially compounded image of the contrast agent in the region of interest.

2. The method of Claim 1, wherein separating nonlinear signal components further comprises  
15 separating nonlinear signal components by pulse inversion harmonic separation.

3. The method of Claim 2, wherein insonifying further comprises insonifying the region of interest  
20 with differently modulated transmit signals.

4. The method of Claim 3, wherein insonifying further comprises insonifying the region of interest with transmit signals which are differently modulated  
25 in one or more of phase, amplitude, or polarity.

5. The method of Claim 1, wherein insonifying further comprises insonifying the region of interest with differently modulated transmit signals; and  
30 wherein separating the nonlinear signal components and combining the signals from different look directions are both performed by a spatial compounding processor.

35 6. The method of Claim 1, wherein combining

further comprises combining nonlinear signal components from different look directions to produce a spatially compounded image of the contrast agent in the region of interest.

5

7. The method of Claim 6, wherein combining further comprises combining fundamental frequency signals from different look directions to produce a spatially compounded tissue image; and

10

further comprising producing an image of the spatially compounded tissue image overlaid with the spatially compounded image of the contrast agent.

15

8. The method of Claim 6, further comprising producing a tissue image; and

further comprising producing an image of the tissue image overlaid with the spatially compounded image of the contrast agent.

20

9. The method of Claim 3, wherein insonifying further comprises transmitting multiple times with different transmit characteristics along each beam direction in two or more look directions.

25

10. The method of Claim 9, wherein insonifying further comprises:

transmitting and receiving multiple times with different transmit characteristics along each beam direction in two look directions; and

30

transmitting and receiving at a fundamental frequency along each beam direction in a third look direction.

35

11. The method of Claim 9, wherein insonifying further comprises transmitting multiple times with

different transmit characteristics along each beam direction in two or more look directions and receiving along multiple, spatially different receive beam directions in response to each transmit event.

5

12. The method of Claim 3, wherein insonifying further comprises transmitting spatially interleaved beams of different transmit characteristics in two or more beam directions;

10

wherein separating nonlinear signal components further comprises interpolating scanlines intermediate the centers of the interleaved transmit beams.

15

13. An ultrasonic diagnostic imaging system for imaging a region of interest containing a harmonic contrast agent comprising:

20

an ultrasonic array transducer which acts to transmit beams in differently steered look directions;

a transmitter coupled to the array transducer which acts to differently modulate the transmit beams;

25

a receive beamformer coupled to the array transducer to receive echo signals from microbubbles in the region of interest;

a detector coupled to the beamformer;

30

a spatial compounding processor, responsive to echoes from microbubbles which produces spatially compounded harmonic contrast agent image signals; and

a display coupled to the spatial compounding processor for displaying a spatially compounded harmonic contrast agent image.

35

14. The ultrasonic diagnostic imaging system of

Claim 13, wherein the detector further comprises a nonlinear signal separator responsive to echoes from differently modulated transmit beams which acts to separate harmonic contrast agent signals by pulse inversion.

15. The ultrasonic diagnostic imaging system of Claim 13, wherein the receive beamformer further comprises a multiline receive beamformer which acts to receive multiple, spatially different receive beams in response to one transmit event.

10 16. The ultrasonic diagnostic imaging system of Claim 13, wherein the detector further comprises a Doppler detector.

15 17. The ultrasonic diagnostic imaging system of Claim 14, wherein the detector further comprises a B mode detector which acts to detect tissue image signals,

20 wherein the display further acts to display a tissue image overlaid with a harmonic contrast agent image.

25 18. The ultrasonic diagnostic imaging system of Claim 17, wherein the detector further comprises a Doppler detector,

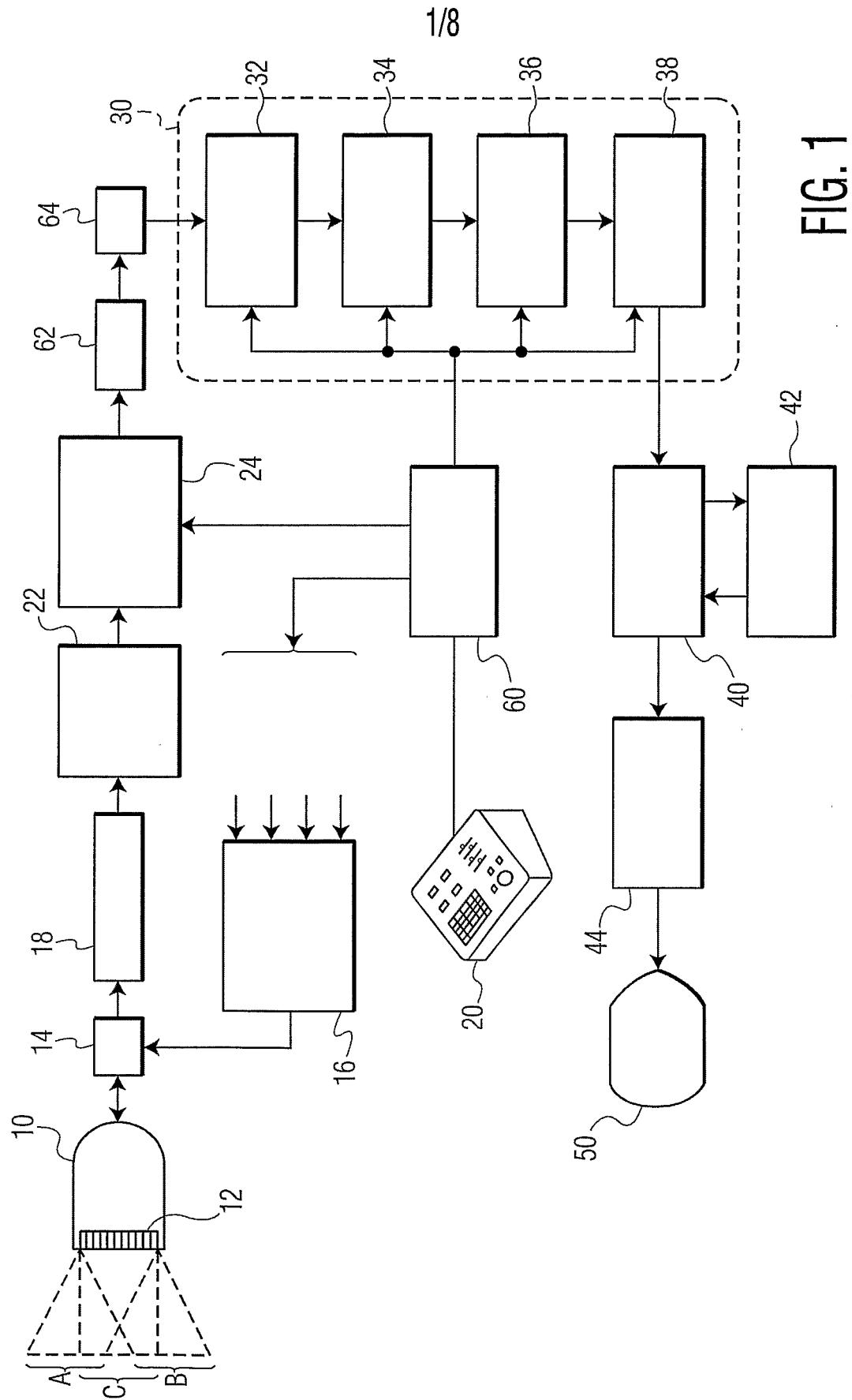
30 wherein the display further acts to display a tissue image overlaid with a color Doppler harmonic contrast agent image.

35 19. The ultrasonic diagnostic imaging system of Claim 13, wherein the transmitter further comprises a transmitter coupled to the array transducer which acts to differently modulate the transmit beams in

one or more of phase, amplitude, or polarity.

20. A method for ultrasonic imaging with contrast agents comprising:

- 5        insonifying a region of interest from a plurality of look directions, wherein transmit signals for different look directions are differently modulated; and
- 10      combining echo signals received from different look direction transmissions to separate nonlinear signal components of received echo signals and to produce a spatially compounded image of the contrast agent in the region of interest.



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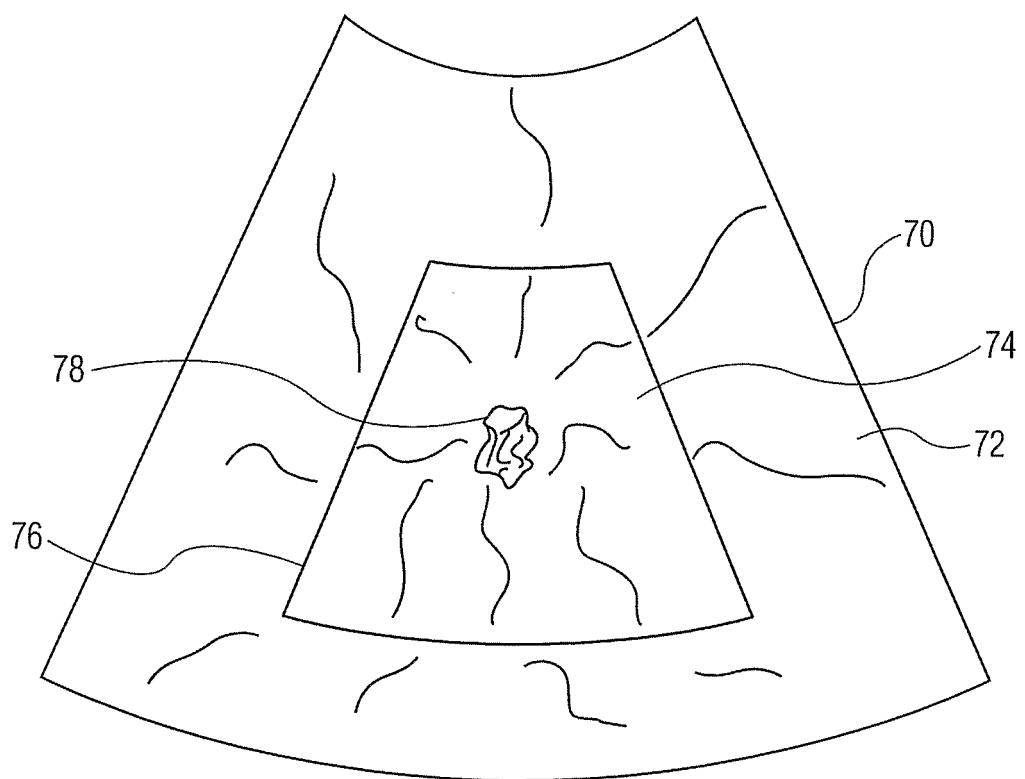


FIG. 2

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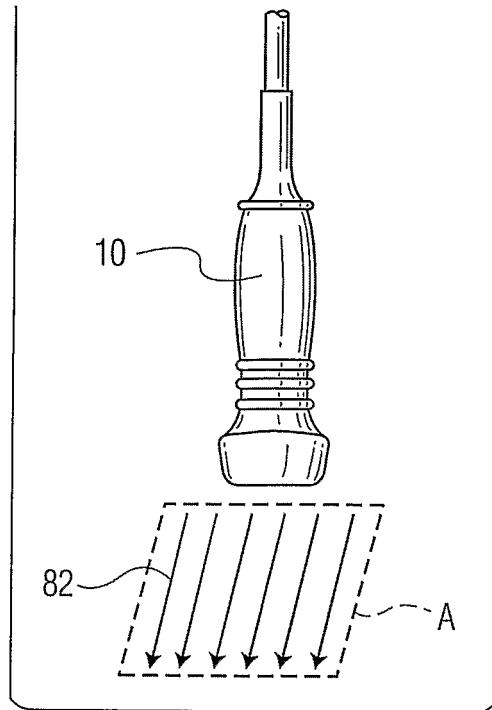


FIG. 3A

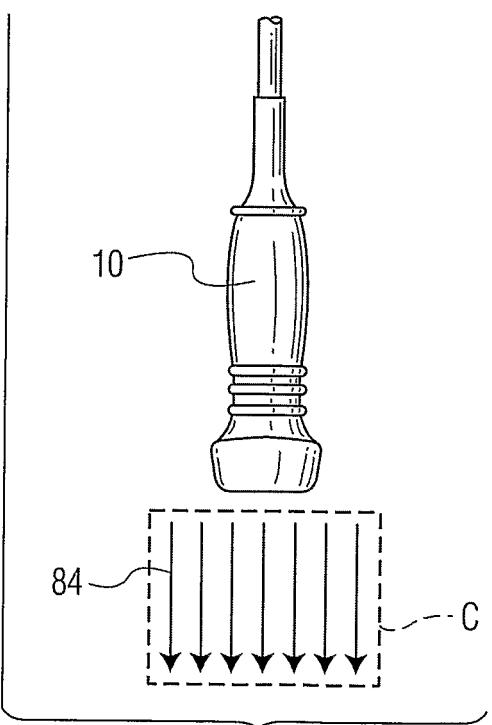


FIG. 3B

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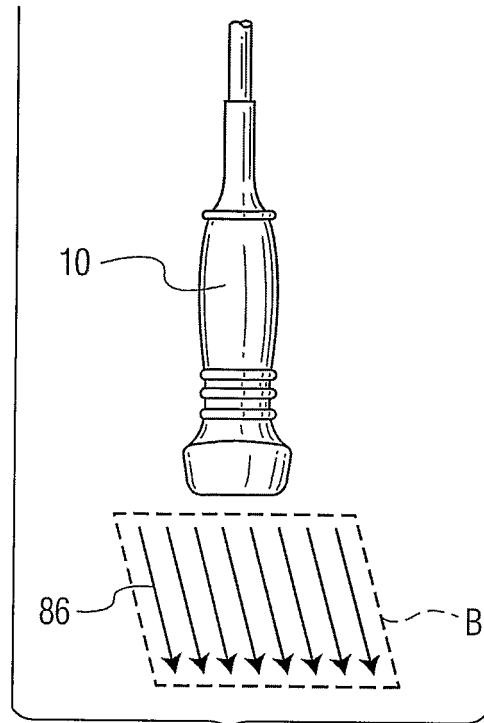


FIG. 3C

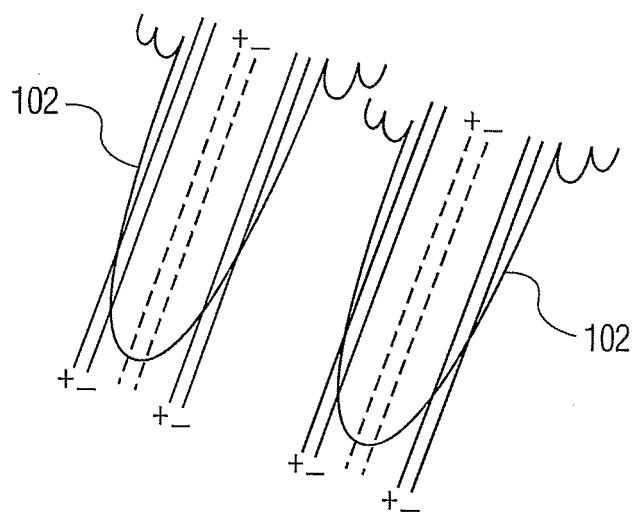
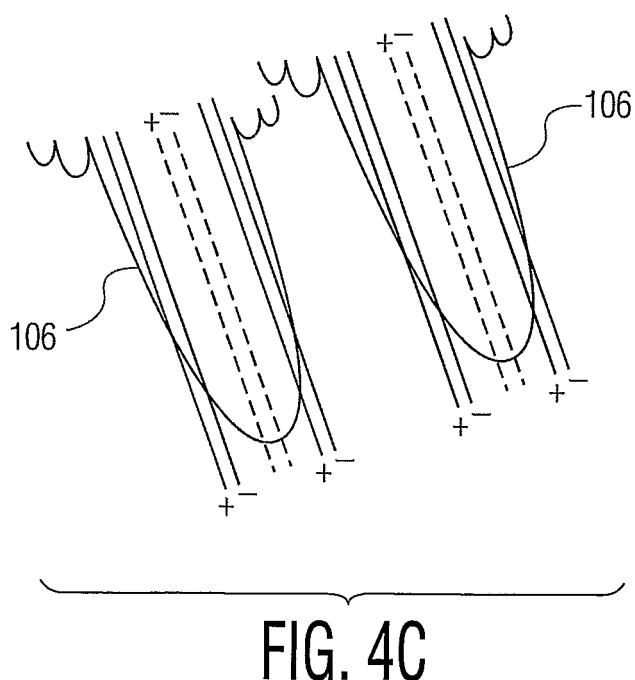
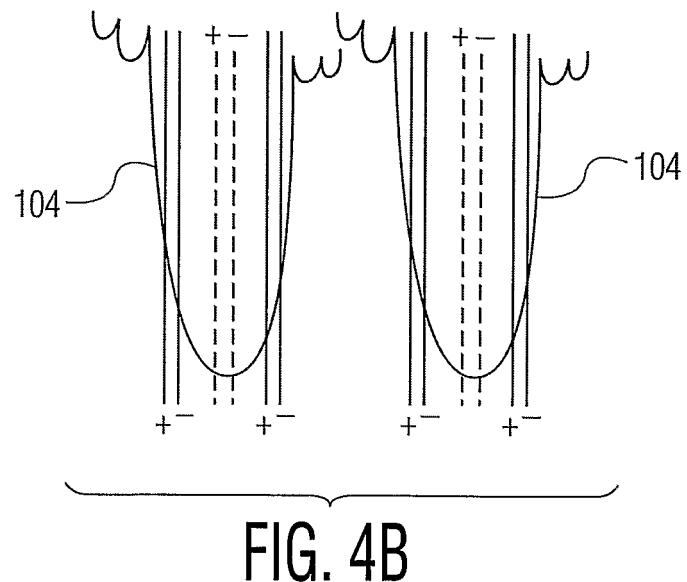


FIG. 4A

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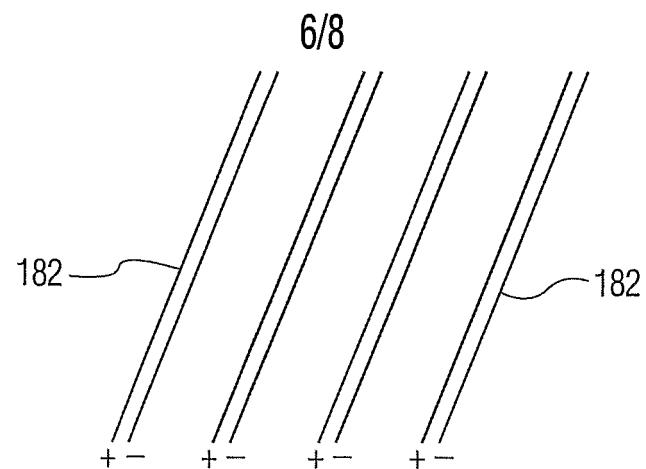


FIG. 5A

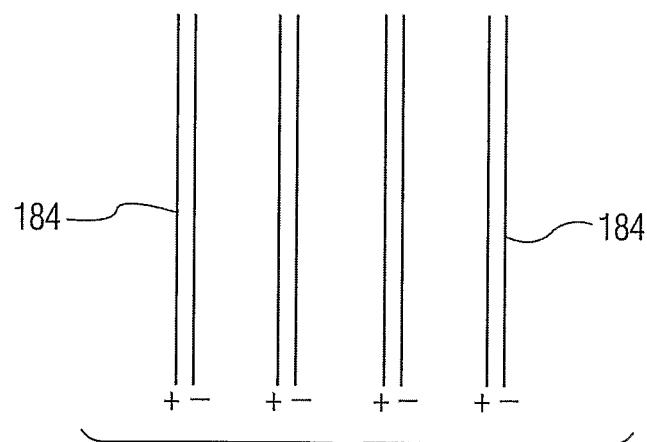


FIG. 5B

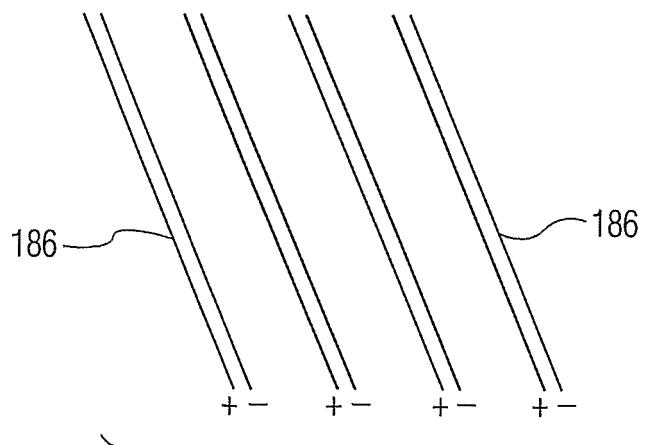


FIG. 5C

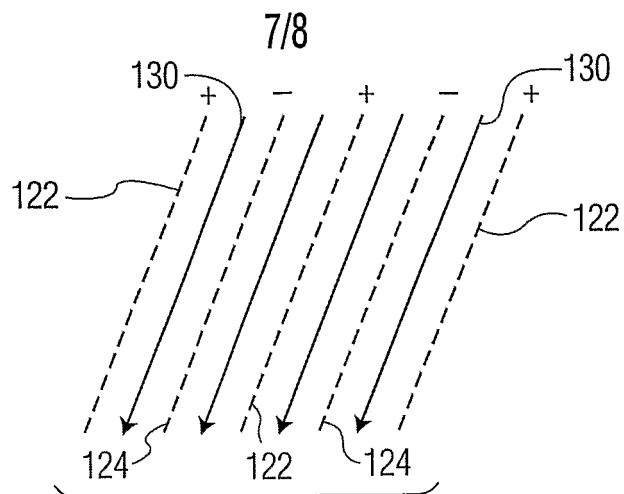


FIG. 6A

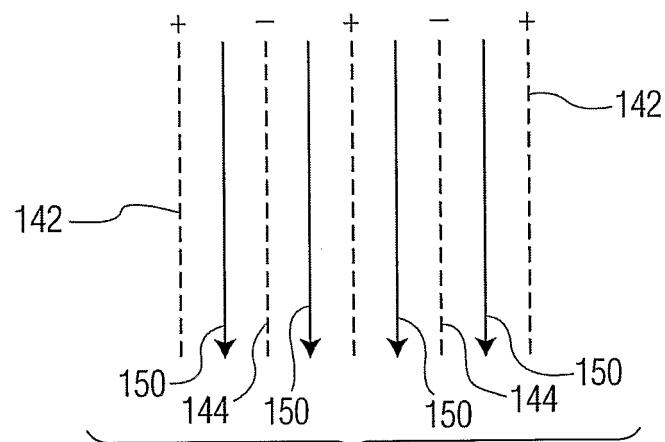


FIG. 6B

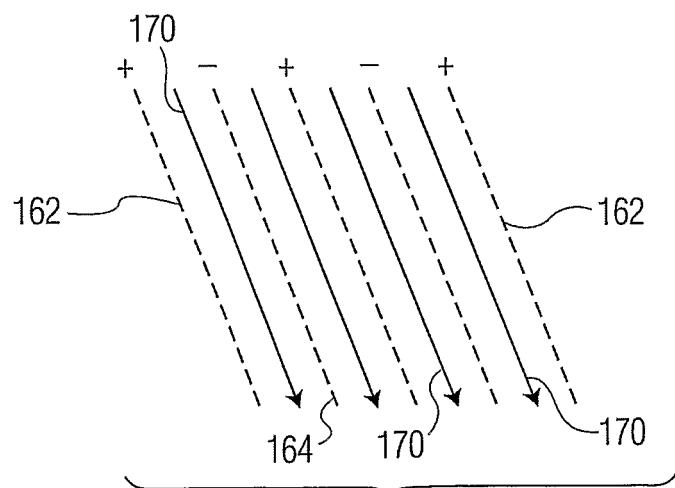


FIG. 6C

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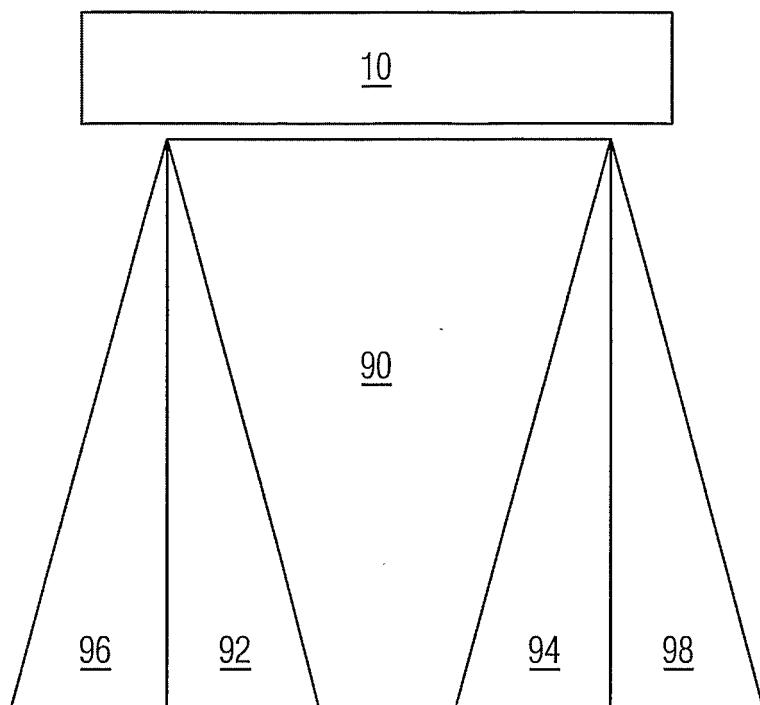


FIG. 7

## INTERNATIONAL SEARCH REPORT

IB2004/052698

A. CLASSIFICATION OF SUBJECT MATTER  
 IPC 7 G01S15/89 G01S7/52 A61B8/14

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, WPI Data

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 530 885 B1 (ENTREKIN ROBERT R ET AL) 11 March 2003 (2003-03-11)	13-18
Y	column 2, line 46 - column 5, line 9 column 8, line 18 - column 10, line 24 figures 1,7-10 -----	19
Y	US 2002/042576 A1 (AVERKIOU MICHALAKIS) 11 April 2002 (2002-04-11) abstract paragraphs '0004!, '0019! -----	19
A	US 2003/004414 A1 (MC LAUGHLIN GLEN ET AL) 2 January 2003 (2003-01-02) paragraphs '0010!, '0011!, '0026! figure 2 ----- -/-	19

Further documents are listed in the continuation of box C.

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
- \*E\* earlier document but published on or after the international filing date
- \*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.
- \*&\* document member of the same patent family

Date of the actual completion of the international search

16 February 2005

Date of mailing of the international search report

25/02/2005

Name and mailing address of the ISA

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Authorized officer

Willing, H

## INTERNATIONAL SEARCH REPORT

IB2004/052698

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	JESPERSEN S K ET AL INSTITUTE OF ELECTRICAL AND ELECTRONICS ENGINEERS: "ULTRASOUND SPATIAL COMPOUND SCANNER FOR IMPROVED VISUALIZATION IN VASCULAR IMAGING" 1998 IEEE ULTRASONICS SYMPOSIUM PROCEEDINGS. SENDAI, MIYAGI, JP, OCT. 5 - 8, 1998, IEEE ULTRASONICS SYMPOSIUM PROCEEDINGS, NEW YORK, NY : IEEE, US, vol. VOL.2, 5 October 1998 (1998-10-05), pages 1623-1626, XP000871850 ISBN: 0-7803-4096-5 the whole document -----	13-19
A	ENTREKIN R ET AL: "Real time spatial compound imaging in breast ultrasound: technology and early clinical experience" MEDICAMUNDI, PHILIPS MEDICAL SYSTEMS, SHELTON, CT,, US, vol. 43, no. 3, September 1999 (1999-09), pages 35-43, XP002181821 ISSN: 0025-7664 the whole document -----	13-19

**FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210**

Continuation of Box II.1

Claims Nos.: 1-12,20

Rule 39.1(iv) PCT – Method for treatment of the human or animal body by surgery

The methods claimed in independent claims 1 and 20 implicitly require the administration of an ultrasound contrast agent to the living human or animal body. The administration of ultrasound contrast agents is generally performed by way of injection or infusion, for instance intravenously. The administration of the ultrasound contrast agent is, therefore, considered a surgical step, by means of which the claimed methods as a whole are considered to be methods for treatment by surgery.

# INTERNATIONAL SEARCH REPORT

PCT/IB2004/052698

## Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.: 1-12, 20 because they relate to subject matter not required to be searched by this Authority, namely:  
see FURTHER INFORMATION sheet PCT/ISA/210
2.  Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3.  Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1.  As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4.  No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

### Remark on Protest

- The additional search fees were accompanied by the applicant's protest.  
 No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

IB2004/052698

Patent document cited in search report		Publication date		Patent family member(s)		Publication date
US 6530885	B1	11-03-2003	WO EP JP	0169282 A2 1194790 A2 2003527178 T		20-09-2001 10-04-2002 16-09-2003
US 2002042576	A1	11-04-2002	US WO EP JP US	6319203 B1 0210795 A2 1315981 A2 2004504911 T 2002032382 A1		20-11-2001 07-02-2002 04-06-2003 19-02-2004 14-03-2002
US 2003004414	A1	02-01-2003	US CN DE JP TW US	2002188199 A1 1389178 A 10224234 A1 2003038490 A 531407 B 2004158149 A1		12-12-2002 08-01-2003 09-01-2003 12-02-2003 11-05-2003 12-08-2004

专利名称(译)	超声诊断造影成像与空间复合		
公开(公告)号	<a href="#">EP1697765A1</a>	公开(公告)日	2006-09-06
申请号	EP2004801491	申请日	2004-12-07
[标]申请(专利权)人(译)	皇家飞利浦电子股份有限公司		
申请(专利权)人(译)	皇家飞利浦电子N.V.		
当前申请(专利权)人(译)	皇家飞利浦N.V.		
[标]发明人	AVERKIOU MICHALAKIS JENSEN SETH		
发明人	AVERKIOU, MICHALAKIS JENSEN, SETH		
IPC分类号	G01S15/89 G01S7/52 A61B8/14 A61B8/00 A61B8/08		
CPC分类号	G01S15/8995 A61B8/08 A61B8/14 A61B8/463 A61B8/481 A61B8/488 A61B8/5238 A61B8/54 G01S7/52039 G01S7/52095 G01S15/8959 G01S15/8963		
优先权	60/529781 2003-12-16 US		
其他公开文献	<a href="#">EP1697765B1</a>		
外部链接	<a href="#">Espacenet</a>		

#### 摘要(译)

提出了一种超声诊断成像系统和方法，用于产生由脉冲反转技术分离的谐波造影剂的空间复合图像。具有不同调制特性的光束以不同的观察方向传输。通过非线性信号分离器组合对准的光束，以通过脉冲反转分离谐波对比度信号分量。来自不同观察方向的谐波对比度信号由空间复合处理器组合以产生空间复合的谐波对比度图像。在示出的实施例中，空间复合的谐波对比图像覆盖组织图像。还公开了不同的调制和波束控制技术，例如多线采集，用于造影剂图像的空间复合。