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(54) Title: ULTRASONIC DIAGNOSTIC IMAGING SYSTEM AND METHOD FOR DETECTING LESIONS OF THE LIVER
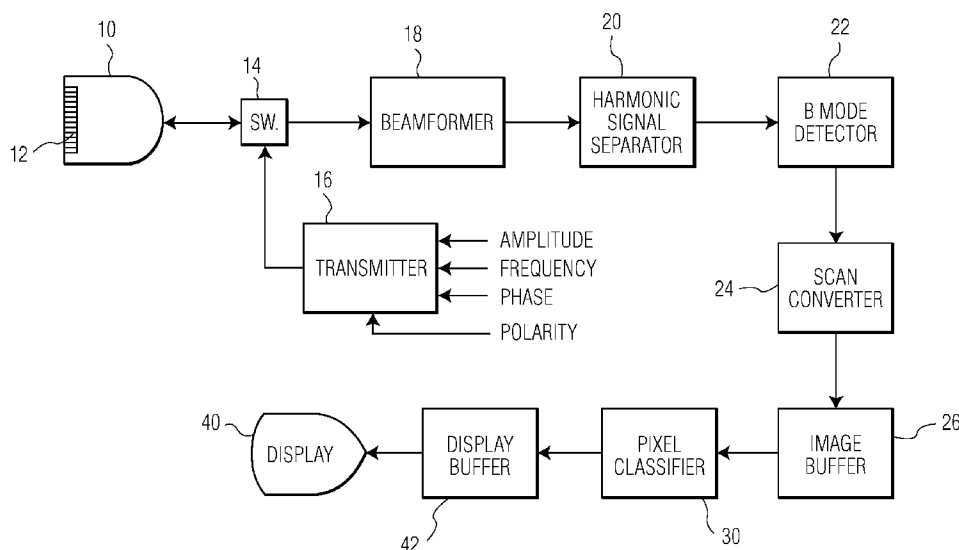
(57) Abstract: Significant liver growths such as HCC lesions are detected during a contrast agent ultrasound exam by their early
reception of contrast and brightening following a bolus injection, as compared with surrounding normal tissue and benign growths.
A pixel classifier looks for and identifies pixel or voxel regions where this early wash-in of contrast occurs and denotes these pixel
or voxel locations in a parametric image. The pixel classifier analyzes pixel or voxel values from a sequence of images and identifies
suspicious regions in an image by uniquely coding the points in a parametric liver image where early wash-in occurs .

ULTRASONIC DIAGNOSTIC IMAGING SYSTEM AND METHOD
FOR DETECTING LESIONS OF THE LIVER

This invention relates to ultrasonic diagnostic
imaging systems and, in particular, to ultrasound
systems and methods for diagnosing lesions of the
liver.

Hepatitis B and hepatitis C patients have been
found to be at an increased risk of developing
primary liver cancer, hepatocellular carcinoma (HCC).
Due to the late discovery that hepatitis C was being
contracted by patients through blood transfusions in
the early 1980's, there remain a significant number
of hepatitis C patients who need to be examined
regularly for the onset of HCC, as the lesions are
best treated in their early stages. The usual
progression of the disease is from hepatitis to liver
cirrhosis to HCC. An easy-to-use monitoring
technique for liver disease progression would have
widespread application in assisting in the early
detection of this serious disease.

There are a number of lesions in addition to HCC
which can develop in the liver. Our paper
"Ultrasound Contrast Imaging Research" by M. Averkiou
et al., published in *Ultrasound Quarterly*, vol. 19,
no. 1 at pp 27 *et seq.* (2003) discusses four primary
liver lesions: hepatocellular carcinoma (HCC),
metastasis from a primary tumor at some other
location, hemangioma, and focal nodal hyperplasia.
The former two are malignant and the latter two are
benign. A technique for identifying lesions in the
liver should be able to detect all four of these
lesions so that more detailed diagnosis can identify
and distinguish between all lesions found in the
liver.

US patent application serial number 60/542,259 entitled "ULTRASONIC IMAGING OF PERFUSION AND BLOOD FLOW WITH HARMONIC CONTRAST AGENTS," of which several of the present inventors are co-inventors, describes a technique for classifying or segmenting ultrasonic signals received during a contrast exam as to the anatomical sources of the signals. This information is used to distinctly depict tissue, capillary beds, and blood flow in larger vessels in the ultrasonic image. The ultrasonic signal information is segmented by using different filters for harmonic Doppler information produced by the signals, then classifying the differently filtered signals by velocity variance to determine whether the signals came from tissue, stationary contrast agent microbubbles in small capillaries, or flowing microbubbles in larger blood vessels. US patent 6,814,703 discusses a different technique for the same problem, classifying ultrasound signals by their Doppler power (P), B mode amplitude (B), and velocity (V) characteristics. Both patents show application of their techniques in liver diagnosis, and both rely on the fact that blood flow velocities in larger vessels such as arteries are greater than blood flow velocities in smaller vessels such as capillary beds. Both techniques thus require Doppler processing in order to determine signal segmentation. However, despite the complexities and versatilities of these techniques, neither patent addresses the unique problem of liver lesion detection and diagnosis.

In accordance with the principles of the present invention, pathology is detected during an ultrasonic contrast exam by segmentation on the basis of the time of arrival of the contrast agent at a particular anatomical site in the body. The location of anatomy

exhibiting such a characteristic is uniquely
identified in the ultrasound image as by a particular
color or brightness. Time of arrival information may
be correlated with signal amplitude in the

5   classification process, and curve-fitting techniques
may also be used. In one embodiment frame-to-frame
motion of the anatomy is corrected for better
detection. Embodiments of the present invention are
particularly useful for detecting HCC and other

10   lesions in the liver.
       In the drawings:
       FIGURE 1 illustrates in block diagram form an
ultrasonic diagnostic imaging system constructed in
accordance with the principles of the present

15   invention.
       FIGURES 2 and 3 illustrate comparison of pixel
values over time for normal tissue and lesions in the
liver.
       FIGURE 4 is one embodiment of a signal

20   classifier constructed in accordance with the
principles of the present invention.
       FIGURE 5 is another embodiment of a signal
classifier constructed in accordance with the
principles of the present invention.

25   FIGURE 6 is yet another embodiment of a signal
classifier constructed in accordance with the
principles of the present invention.
       FIGURE 7 illustrates in block diagram form an
ultrasonic diagnostic imaging system which aligns the

30   image data for classification in accordance with the
principles of the present invention.
       Blood flow to the liver comes from two sources:
the hepatic artery and the portal vein. The hepatic
artery is supplied with blood flow from the aorta.

35   The flow of blood through the portal vein comes from

the inferior vena cava. The inferior vena cava in turn receives blood from the kidneys which cleanse a flow of blood supplied by the aorta. Blood flow out of the liver passes through the hepatic vein and to

5 the superior vena cava. The liver receives 20% of its total supply of blood from the aorta and hepatic artery and 80% of its blood supply from the inferior vena cava and the portal vein.

As a result of this vasculature, when a bolus of

10 contrast agent is injected into a vein, it will first begin to appear in the liver by way of the hepatic artery. After being pumped from the heart and into the aorta, some of the contrast agent will flow into the hepatic artery and begin to infuse the liver.

15 But since only 20% of the blood supply to the liver is provided by the hepatic artery, this early infusion will be at a low level. The rest of the contrast agent flow in the aorta flows into the stomach and intestinal vasculature and then is

20 collected in the portal vein which then significantly infuse the liver parenchyma.

It has been found that the vasculature developed by HCC lesions are supplied with their primary source of blood flow from the hepatic artery. Because the

25 contrast agent first appears in the liver by way of the hepatic artery, this means that one of the initial sites of contrast agent detection in the liver after a bolus injection is the locus of an HCC lesion. If no lesion is present, only the usual

30 hepatic artery and normal vessels supplied by it will appear with contrast present. After another 10-20 seconds the remainder of the bolus of contrast will have passed through the gastrointestinal system, the inferior vena cava, and the portal vein and this

35 delayed flow of contrast agent will begin to appear

5

as the capillary bed of the liver becomes infused
with contrast agent. Since about 80% of the bolus
will be delivered to the capillary bed, the delayed
flow of contrast agent in the capillary bed will
quickly overwhelm the appearance of the lesser supply
of contrast in the HCC lesion and the HCC lesion will
begin to appear dimmer in the ultrasound image in
relation to the surrounding brightly appearing normal
tissue of the capillary bed. There are thus only a
few heartbeats and a few seconds in the initial
infusion phase when the HCC lesion will distinctively
stand out with contrast in the image, termed "early
wash-in." It is this early wash-in characteristic
which must be identified in the imaging procedure in
the diagnosis of an HCC lesion, and there is only a
small window of time in which to make it.

In accordance with the principles of the present
invention the diagnosis of HCC lesions is enhanced by
producing a parametric image of the liver based upon
the relative arrival times of contrast agent in the
liver to highlight areas of early wash-in which may
be suspicious of HCC. The overall brightening of the
liver with the arrival of contrast agent is monitored
and areas that become bright early are identified.
These areas are distinctively denoted in the image as
by a unique brightness or color, indicating areas of
suspicion for further investigation. The inventive
technique is particularly suitable for 3D imaging
where a significant volume of the liver can be
diagnosed at one time. The 3D parametric image can
be rendered from the parametric volume using a simple
maximum intensity projection or other known or newly
developed 3D imaging technique.

Turning first to FIGURE 1, an ultrasonic
diagnostic imaging system constructed in accordance

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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. As

5   each beam is transmitted along its steered path
through the body, the tissue and blood flow in the
body return echo signals with linear and nonlinear
(or fundamental and harmonic) components
corresponding to the transmitted frequency

10   components. The transmit signals are reflected from
the microbubbles of a contrast agent which exhibit a
nonlinear response to ultrasound. The nonlinear
response will cause the echo signals returned from
the contrast agent to contain nonlinear components.

15   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

20   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

25   of the transmit signals. The transmitter is coupled
by a transmit/receive switch 14 to the elements of an
array transducer 12 of a probe 10. The array
transducer can be a one dimensional array for planar
(two dimensional) imaging or a two dimensional array

30   for two dimensional or volumetric (three dimensional)
imaging.

The transducer array 12 receives echoes from the
body containing linear and nonlinear components which
are within the transducer passband. These echo

35   signals are coupled by the switch 14 to a beamformer

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18 which appropriately delays echo signals from the
different transducer elements, then combines them to
form a sequence of coherent echo signals along the
beam from shallow to deeper depths. Preferably the
5   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 beamformer which produces two or
10   more sequences of echo signals along multiple
spatially distinct receive scanlines in response to
the transmission of one or more spatially distinct
transmit beams, which is particularly useful for 3D
imaging. The beamformed echo signals are coupled to
15   a harmonic signal separator 20.

The harmonic signal separator 20 can separate
the linear and nonlinear components of the echoes
signal in various ways. One way is by filtering.
Since certain nonlinear components such as the second
20   harmonic are at a different frequency band ($2f_o$) than
the fundamental transmit frequencies (f_o), the
harmonic signals which are the signature of the
contrast agent can be separated from the linear
components by band pass or high pass filtering.
25   There are also a number of multiple pulse techniques
for separating nonlinear components which are
generally referred to as pulse inversion techniques.
In pulse inversion the image field is insonified by
the transmission of multiple, differently modulated
30   transmit signals in each beam direction, returning
multiple echoes from the same location in the image
field. The transmit signals may be modulated in
amplitude, phase, polarity, or a combination thereof.
When the received echoes from a common location are
35   combined, the linear signal components are canceled

and the nonlinear signal components reinforce each other (or *vice versa*, as desired), thereby producing separated nonlinear (*e.g.*, harmonic) echo signals for imaging.

5   The echo signals are detected by a B mode detector 22. An advantage of the inventive technique over the prior art techniques discussed above is that Doppler processing is not necessary. The present invention may be carried out using Doppler processing

10   if desired in a given embodiment, however the use of B mode signals avoids the reduction in real time frame rate caused by the acquisition of long Doppler ensembles. The detected echo signals are then converted into the desired image format such as a

15   sector or pyramidal image by a scan converter 24. The scan converted image is temporarily stored in an image buffer 26 from which it can undergo further processing.

In accordance with the principles of the present

20   invention a pixel classifier 30 classifies the pixels or voxels in the ultrasound image, looking for those that are characteristic of HCC lesions. FIGURE 2 gives a graphical appreciation of this analysis. Most of the flow of blood with contrast agent to

25   normal tissue in the liver is delayed from the time of a bolus injection at time t_0 by its passage through the kidneys and thereafter its arrival at the liver at a time t_2 by way of the inferior vena cava (IVC), as illustrated by the dotted curve 74. There may be

30   a small, perceptible increase in contrast in the normal tissue at time t_1 from the much smaller amount of blood with contrast agent delivered by the hepatic artery. However the flow of blood with contrast agent in the hepatic artery and into the vasculature

35   developed around an HCC lesion will appear earlier

than the main IVC flow as shown by the rise of solid
line curve 72 at time t_1. The lesser flow delivered
by the hepatic artery may result in achievement of a
lesser concentration of contrast agent as indicated
by the lower peak of the curve 72. It is therefore
the function of the pixel classifier 30 to identify
pixel or voxel data which is characteristic of the
cross-hatched area 70 between curves 72 and 74, as
shown in FIGURE 3, the early wash-in of contrast to
the vasculature of an HCC lesion.

When the pixel classifier 30 identifies such
data it highlights the subject pixels or voxels in a
distinctive shade, brightness, or color. This
creates a parametric image in which the parameter
characteristic of suspect pathology is highlighted to
the user. The parametric image is put into a display
buffer 42, from which it is shown on a display 40.

The pixel classifier 30 may operate in a variety
of ways, one embodiment of which is illustrated in
FIGURE 4. The pixel or voxel data from a succession
of acquired images is applied to a threshold detector
32, which compares the levels of the image signals on
a location-by-location basis. When a received pixel
or voxel which is characteristic of the applied
contrast agent, such as a second harmonic signal,
exceeds a lower Threshold 1 during a given time
window, such as the t_0-t_2 time interval in FIGURES 2-
3, the pixel at that image location is classified as
an early wash-in contrast pixel or voxel and is coded
as such in the parametric image in the parametric
image buffer 34. As signals at other pixel or voxel
locations exceed the Threshold 1 level during the
time window the liver image in the parametric image
buffer builds up with a characteristic color or
brightness in the hepatic artery and in the vicinity

of any HCC lesions present. The build-up of the
distinctive early wash-in of contrast can be observed
in real time by periodically displaying the
parametric image of the buffer, or the ultrasound

5   system can wait until the time window closes and the
build-up of early wash-in is completed before
displaying the final early wash-in parametric image.
The parametric image is limited to displaying only
the desired early wash-in of contrast by closure of

10   the time window before the later arrival of contrast
from the IVC (i.e., before the rise of curve 74 in
FIGURES 2-3), and by preventing the detection of
signal levels above a higher Threshold 2 (see
FIGURE#) which is a level anticipated to be achieved

15   by only later-arriving contrast agent.
FIGURE 5 illustrates another embodiment of a
pixel classifier. In this embodiment pixel or voxel
data from a succession of acquired images is compared
with a Threshold, and those exceeding the Threshold

20   (which are assumed to be above a noise level) are
applied to a time of arrival detector 52. The time
of arrival detector 52 is operative during the
interval when a timer 56 is running. The timer 56
may be initiated by the first pixel value to exceed

25   the Threshold, which would be anticipated to occur at
time t_1 of FIGURE 3, and will time out after running
for the t_1-t_2 interval. Thus, early signal levels
characteristic of early wash-in pixels or voxels are
identified during this time interval. If the

30   identification of early wash-in pixels or voxels
ended before the timing out of the timer 56, the
timer would shut down earlier to prevent the
detection of later-arriving contrast pixels or voxels
by the time of arrival detector 52. As before, the

35   early wash-in pixel or voxel locations identified are

coded in the parametric image of the image buffer 54
and the parametric image is displayed either in real
time as it is built up or after the build-up of early
wash-in pixel or voxel areas is complete.

Another embodiment of a pixel classifier is
shown in FIGURE 6. In this embodiment the pixel or
voxel values of a succession of acquired images are
stored in a temporal pixel data map 60 while the
contrast agent begins to flow into and then recedes
from the liver. The data map stores the temporal
signal values for each spatially different location
in the image field. The result is a succession of
values at each location in the data map which, when
plotted, may resemble a curve such as curves 72 and
74 in FIGURES 2-3. Each curve is analyzed by a
curve-fit processor 62 which analytically compares
the data curve at each pixel or voxel location with
characteristic curve data stored in a perfusion curve
data source 66. If the curve at a given pixel or
voxel location fits characteristic curve 72, for
instance, that location is classified as an early
wash-in location in the image of the parametric image
buffer 64. If the curve at a given location matches
curve 74, that pixel or voxel location is classified
as normal tissue. The result will be a parametric
image developed in the buffer 64 which highlights
early wash-in areas in the liver. This embodiment,
like the others, may be constructed to analyze the
whole image region to identify points where the liver
experiences an initial lighting with contrast as
compared with normal tissue in the rest of the liver
image.

It will be appreciated that the sensitivity and
accuracy of many of these techniques will be
dependent upon being able to reliably receive a

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sequence of signal data from the same image point
over a period of time so that the temporal data from
the same point will be analyzed and suspect locations
accurately denoted in the parametric image. This
capability will be compromised in the presence of
motion, including probe motion and patient motion
such as that resulting from breathing. An ultrasound
system which addresses this problem is shown in
FIGURE 7, which is a variation of FIGURE 1 in which
like reference numbers denote the same functionality
in the two drawings. The embodiment of FIGURE 7
contains an image alignment processor 28 which
operates to spatially align successive images in a
sequence of acquired images, thereby reducing or
eliminating the image-to-image motional effects. A
number of techniques may be employed to realize the
image alignment processor, including those shown and
described in US Pat. 6,589,176 entitled "Ultrasonic
Image Stabilization System and Method," and US Pat.
5,538,004 entitled "Method and Apparatus for Tissue-
Centered Scan Conversion In An Ultrasound Imaging
System." In general, each of these two approaches
extract inter-frame motion by a comparison of
successive images or by motional data provided by a
device such as a probe motion sensor. In either
case, the measured motion is used to align the
successive images. It may be preferable to conduct
image alignment with fundamental frequency tissue
images as there may be times when the harmonic signal
levels are too low to confidently align images. In
this manner, the same pixel or voxel location in a
succession of images will correspond to the same
point in the body, thereby producing accurate,
spatially correlated temporal data from each location
in the field of an image for analysis.

     Thus, an embodiment of the present invention can distinguish potential HCC lesions by highlighting early contrast wash-in areas in a two or three dimensional ultrasound image, as compared to normal tissue and benign structures such as hemangiomas which often fill more slowly with contrast. In a typical diagnosis potential HCC lesions will brighten with contrast first, and normal liver tissue will brighten some 10-20 seconds later, with hemangiomas generally taking a full 120 seconds to fill and brighten.

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WHAT IS CLAIMED IS:

1.   An ultrasonic diagnostic imaging system comprising:

      a probe which acts to transmit and receive signals from a region of the body where time of arrival of a contrast agent may be characteristic of a disease state;

      a detector which detects characteristic signals received from a contrast agent;

      an image processor responsive to the detector;

      a pixel classifier, responsive to the image processor, which identifies signals from the early wash-in of contrast agent;

      a parametric image processor responsive to the pixel classifier, which produces an ultrasound image in which an area of early contrast agent arrival is highlighted; and

      an image display for displaying the parametric image.

2.   The ultrasonic diagnostic imaging system of Claim 1, wherein the probe acts to transmit and receive ultrasonic signals to and from the liver where time of arrival of a contrast agent may be characteristic of a liver lesion.

3.   The ultrasonic diagnostic imaging system of Claim 1, wherein the pixel classifier classifies pixel or voxel data received from a sequence of images by at least one of a threshold level and a time of reception.

4.   The ultrasonic diagnostic imaging system of Claim 1, wherein the pixel classifier classifies

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pixel or voxel data received from a sequence of images by a curve-fitting process.

5.   The ultrasonic diagnostic imaging system of Claim 1, wherein the detector comprises a nonlinear signal component detector.

6.   The ultrasonic diagnostic imaging system of Claim 5, wherein the nonlinear signal component detector comprises a harmonic signal detector.

7.   The ultrasonic diagnostic imaging system of Claim 5, wherein the nonlinear signal component detector comprises a pulse inversion signal processor.

8.   The ultrasonic diagnostic imaging system of Claim 1, further comprising:
an image alignment processor, responsive to a sequence of received images, which acts to spatially align the content of the images.

9.   The ultrasonic diagnostic imaging system of Claim 8, wherein the image alignment processor further acts to align the tissue shown in a sequence of images to the same pixel or voxel locations from image to image.

10.   A method for diagnosing liver lesions by ultrasonic imaging with a contrast agent comprising:
introducing a flow of contrast agent into the bloodstream of a body;
ultrasonically detecting the presence of the contrast agent in the liver by means of the hepatic artery; and thereafter

ultrasonically detecting the presence of the
contrast agent in the liver by means of the inferior
vena cava,

5   wherein the presence of the contrast agent by
means of the hepatic artery may be characteristic of
a liver lesion.

11.   A method for diagnosing liver lesions by
ultrasonic imaging with a contrast agent comprising:

10   introducing a flow of contrast agent into the
bloodstream of a body;
ultrasonically imaging the liver;
ultrasonically detecting the presence of the
contrast agent in the liver by means of the hepatic

15   artery;
highlighting a region in an ultrasound image in
which the presence of the contrast agent by means of
the hepatic artery was detected; and
displaying the ultrasound image with the

20   highlighted region.

12.   The method of Claim 11, wherein
ultrasonically detecting comprises analyzing at least
one of the amplitude and time of reception of a

25   signal from contrast agent in the liver.

13.   The method of Claim 12, wherein
highlighting comprises distinguishing a region in an
image field where the signal from contrast agent

30   meets at least one of a threshold and a time of
arrival test.

14.   The method of Claim 13, wherein
highlighting comprises at least of one of

35   distinctively brightening, coloring, or shading the

region in the ultrasound image.

15. The method of Claim 11, further comprising
spatially aligning a succession of ultrasound images
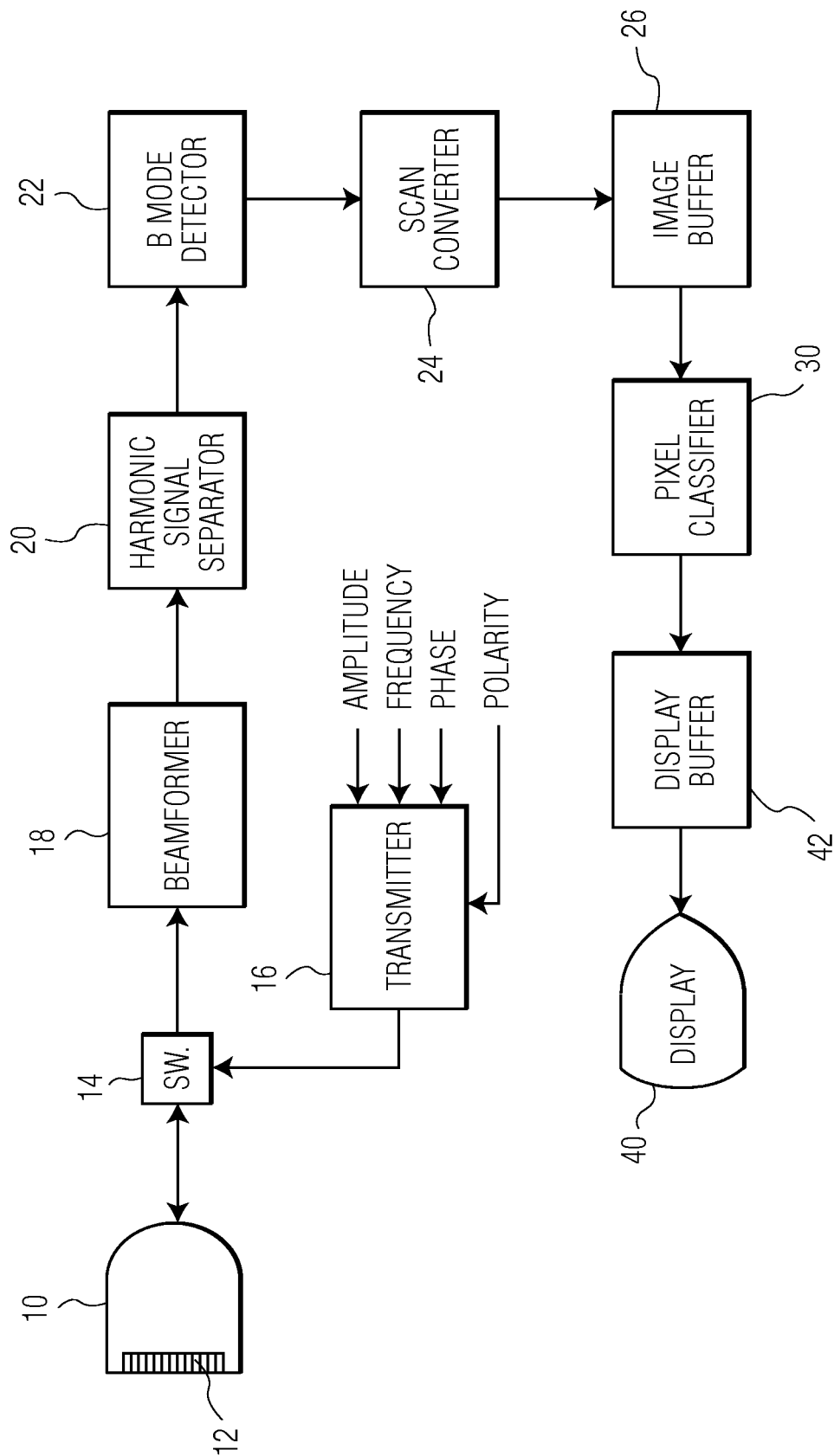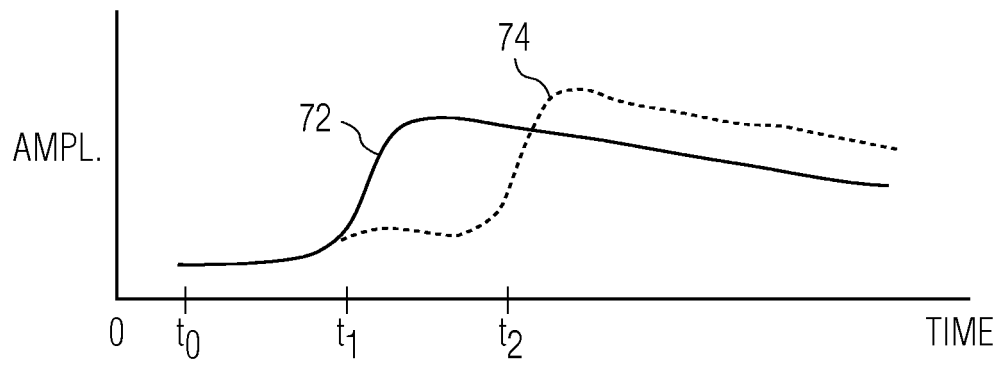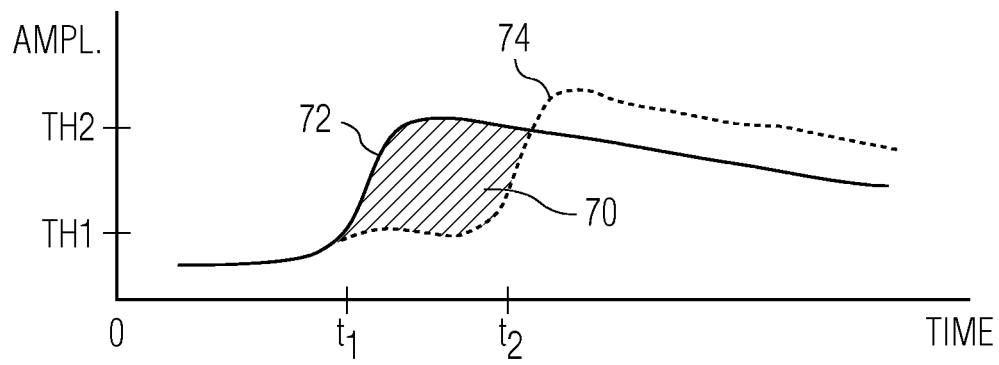5   prior to the ultrasonically detecting.

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FIG. 1

FIG. 2
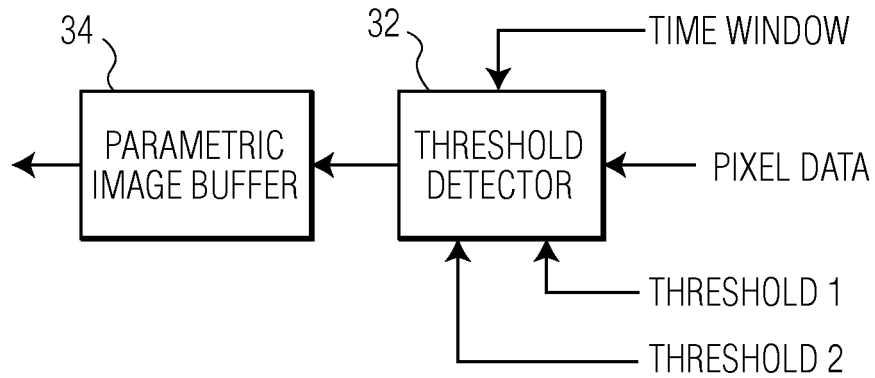

FIG. 3

FIG. 4
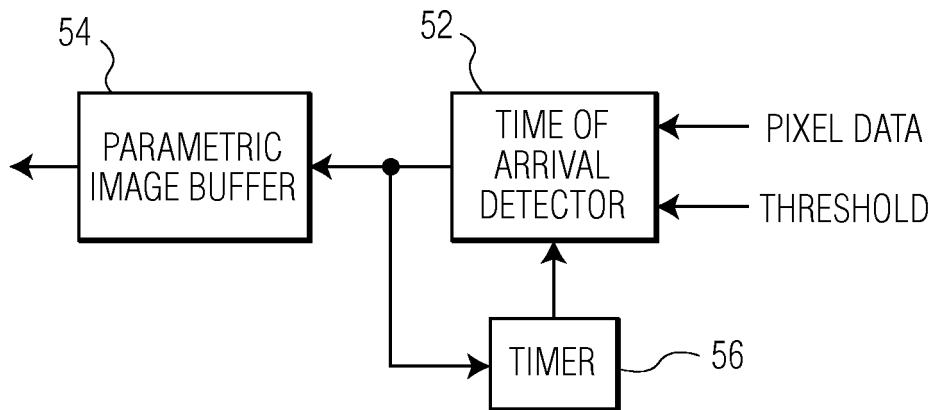
FIG. 5
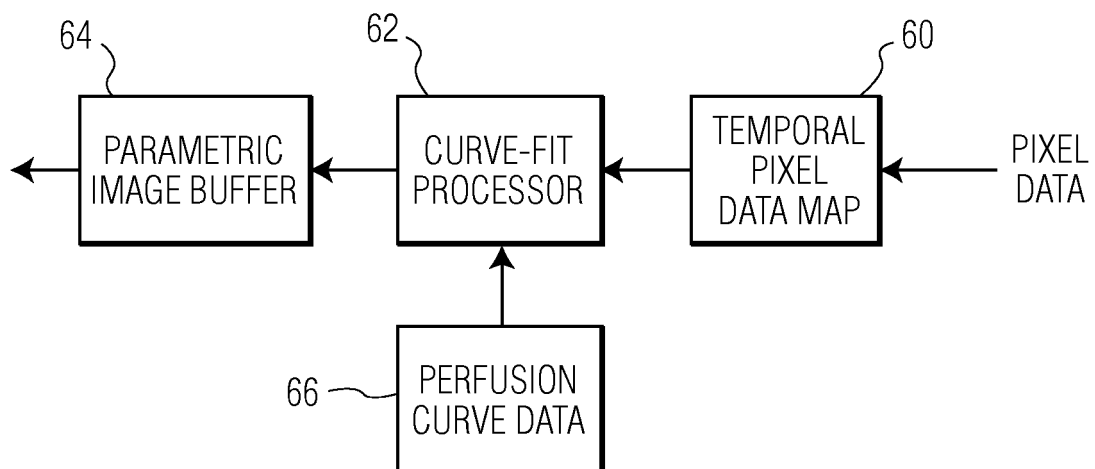
FIG. 6

4/4
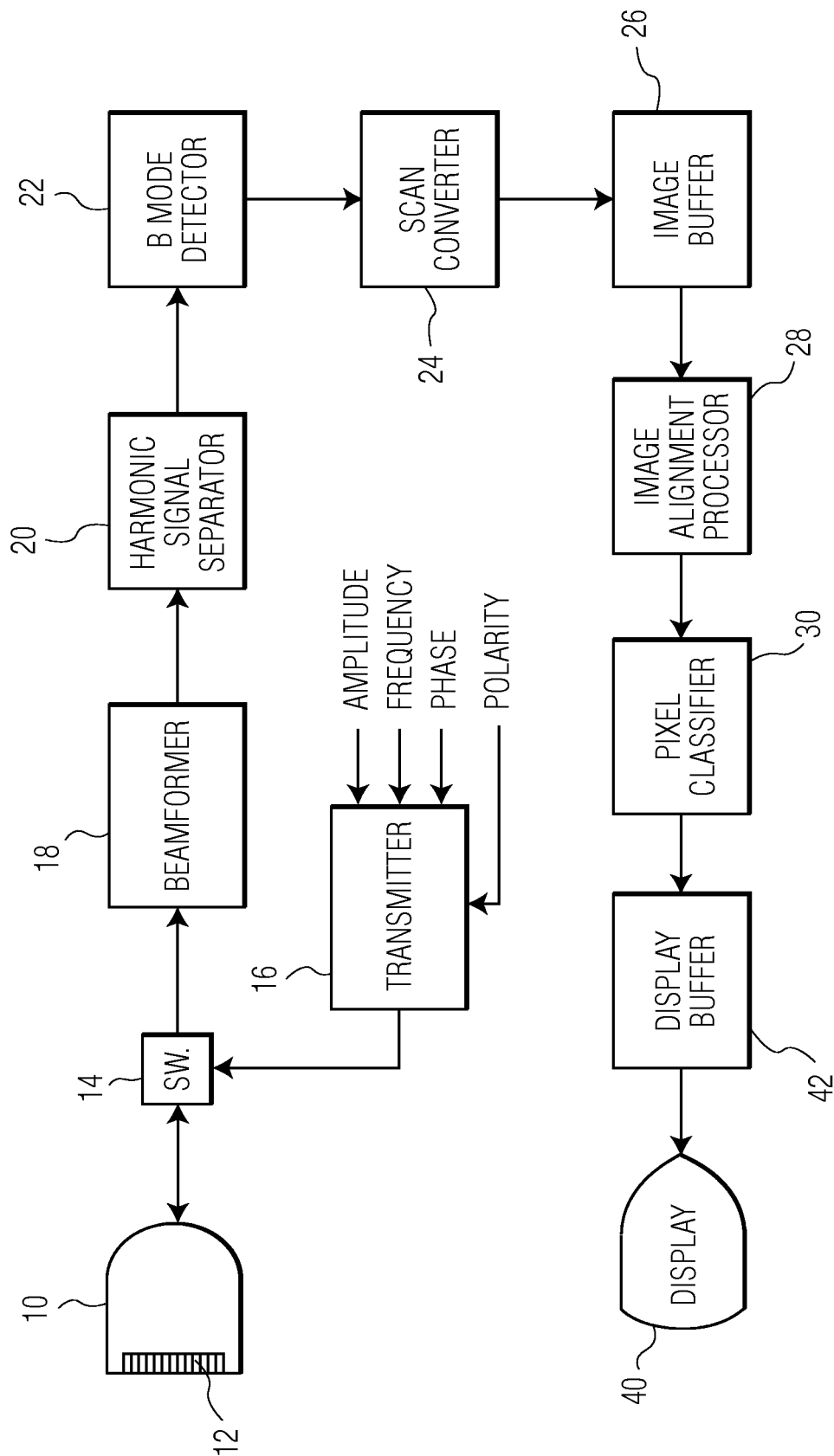
FIG. 7

专利名称(译)	超声诊断成像系统和检测肝脏损伤的方法		
公开(公告)号	EP1855596A2	公开(公告)日	2007-11-21
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[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)	皇家飞利浦电子N.V.		
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外部链接	Espacenet		

摘要(译)

与周围正常组织和良性生长相比，在造影剂超声检查期间通过其早期接受对比和在推注注射后增亮来检测显着的肝脏生长，例如HCC病变。像素分类器查找并识别像素或体素区域，其中对比度的这种早期洗入发生并且表示参数图像中的这些像素或体素位置。像素分类器分析来自图像序列的像素或体素值，并通过对参数肝脏图像中的点进行唯一编码来识别图像中的可疑区域，其中早期洗入发生。