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(74) Agent: **BARKER, Brettell**; 138 Hagley Road, Edgbaston, Birmingham B16 9PW (GB).

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(71) Applicant (*for all designated States except US*): **ISIS INNOVATION LIMITED** [GB/GB]; Ewert House, Ewert Place, Oxford OX2 7SG (GB).

(72) Inventors; and

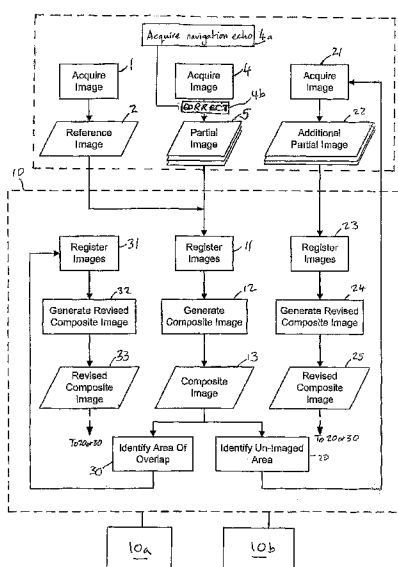
(75) Inventors/Applicants (*for US only*): **BRADY, John, Michael** [GB/GB]; Medical Vision Laboratory, Ewert House, Ewert Place, Oxford OX2 7SG (GB). **NOTERDAEME, Olivier** [BE/GB]; University of Oxford, Department of Engineering Science, Parks Road, Oxford OX1 3PJ (GB).

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(54) Title: ACQUISITION OF MEDICAL IMAGES



(57) Abstract: To acquire images of a region of interest of an individual human or animal body, there are acquired (1) with a first imaging technique, a reference image of the entire region of interest and (2) with one or more further imaging techniques having a different field of view from the first imaging technique, a plurality of partial images of parts of the region of interest including parts at different positions. In respect of each partial image, there is determined a transformation which registers the respective partial image with the reference image. This allows each of the partial images to be accurately registered with each other which provides several further advantages. In many applications, there is generated a composite image combining transformations of each of the partial images.

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ACQUISITION OF MEDICAL IMAGES

The present invention relates to the acquisition of images, in particular
5 medical images, that is images of a region of interest of an individual
human or animal body. Most current commercial applications are in
imaging a human body, but the invention is in technical terms equally
applicable to imaging of an animal body and the term "medical" is used
herein to encompass both. It is understood that images, particularly but
10 not only those used in medical imaging, may be two-dimensional, three-
dimensional, or even more dimensional considering time as a fourth
dimension. We refer throughout to image without prejudicing what the
dimensions are of that image.

15 Images are used to support a range of medical applications, from
diagnosis of disease, monitoring of disease progression, through planning
and evaluation of interventions. There are known a wide range of medical
imaging techniques which each image different physical properties of the
subject and hence are useful for imaging different tissues and structures.
20 Examples of common medical imaging techniques include but are not
limited to Magnetic Resonance Imaging (MRI), Computed Tomography
(CT) imaging and other 3D X-ray imaging, ultrasound imaging, Positron
Emission Tomography (PET) imaging, and Single Photon Emission
Computed Tomography (SPECT) imaging.

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Many medical imaging techniques are applied to imaging of rigid
anatomical structures. In this context, the term "rigid" means that the
structure of interest can be considered to be static, that is neither moving
nor deforming, both over the image acquisition period and between
30 acquisitions of subsequent images. Examples in medical imaging of the

structures which are rigid in this sense include the anatomical structure of the brain and skeletal structures.

There are also applications in imaging of deformable tissues which may be subject to deformation over the image acquisition period which is too large to be ignored. Recent developments in imaging techniques have increased interest in this. In certain applications, the major cause of deformation is the regular breathing cycle which induces motion not only in the lungs but in major structures such as the abdomen containing the liver and spleen. In other applications, the deformation may be caused by the beating of the heart, muscle flexation more generally, or the motion of a limb (although care is usually taken to prevent this).

Deformation of the tissue in the region of interest during the image acquisition period can severely degrade the resulting image. For example, in the case of PET and SPECT such deformation will cause a blurring in the acquired image, whereas in the case of MRI deformation during acquisition typically produces major artefacts such as blurring, ghost artefacts, and parallel bands in the phase-encoding direction.

To minimise the degrading effects of deformation, attempts can be made to constrain the motion of the body part of interest during the acquisition of an image. However, particularly in the case of imaging deformable organs such as the liver, this may not solve the problem. Additionally, images may be acquired at what is assumed to be the same point in a regular cycle where motion occurs (e.g. breathing or heart beating). While this can be effective in cases where image acquisition is relatively rapid, in many cases this is not so. In such cases, to further minimise the effects of deformation during image acquisition, images are typically acquired while the individual holds his or her breath. However imaging during breath holds has numerous limitations. In many applications, for

example, a single breath hold is insufficient to acquire an image of the entire and often large region of interest, particularly as the individual (who may be infirm) may only be capable of holding their breath for a limited period. For this reason, image acquisition over a succession of
5 breath holds is widely practised but difficult to coordinate and often causes some deformation between the breath holds.

The need for the structure to remain static during the image acquisition period places restrictions on the imaging techniques which can be applied
10 to image given regions of interest, particularly large regions of interest. Effectively the choice of available imaging techniques is limited and for a given imaging technique the resolution is limited.

To tackle these limitations, an alternative to acquiring an image of the
15 entire region of interest is to acquire a plurality of partial images of parts of the region of interest at different positions, e.g. in different breath holds. The totality of the set of partial images are intended together to cover the region of interest but there are practical limitations firstly in aligning the imaging apparatus with each successive part of the region of
20 interest of the body and secondly in the occurrence of deformation between each acquisition of a partial image. As a result it is frequently the case that the partial images are not contiguous but instead suffer from relative translation, rotation or deformation causing gaps and/or overlaps between the partial images.

25 It is now established practice for certain kinds of image and certain regions of interest that the region of interest is imaged in a plurality of images, each acquired during a breath hold, where the imaging is designed to minimise overlap between partial images but which may result
30 either in gaps or in (unknown) extensive overlap. Note that, imaging areas with considerable overlap means that the same areas is imaged

repeatedly. Time is thus spent on an aspect which may not provide additional information. In a clinical environment with time constraints this is frequently undesirable. For example in case of imaging the abdominal area, the liver is a highly movable and deformable organ. The liver can thus be at anatomically different positions during each image acquisition in a different breath hold, resulting in gaps in the total coverage from the partial images and/or overlaps between one or more partial images.

To make matters worse any gap and/or overlap between the partial images is not necessarily apparent from the partial images themselves. Common medical practice is for the partial images to be supplied as separate images which are believed to cover the region of interest completely and contiguously for interpretation to a clinician who might not appreciate the presence of any gap and/or overlap. This can lead to the clinician making an inaccurate medical interpretation which in turn can lead to incorrect diagnosis or inappropriate patient management. In the case of an overlap, duplicate information might not be understood as such, leading for example to overestimation of the severity of a condition. Even more seriously in the case of a gap, information that could crucially affect a patient management decision may be missing, in some cases leading to underestimation of a condition or even failure to recognise a condition at all. For example in the case of a tumour lying entirely within the gap the tumour may be missed.

Even though common medical practice is for the partial images to be supplied as separate images, one could consider supplying a composite image which combines the partial images in some manner. In the academic literature, there are disclosed many techniques which attempt to form such a composite image. When forming a composite image, a preliminary step is to register the images with respect to each other.

Techniques to effect the registration of images of rigid bodies are well established. However, the present invention applies in the context of imaging a deformable structure, such as deformable tissue, for which there is no consistent and established approach. Academic literature includes many specific registration algorithms which register a series of images with respect to each other, for example by selecting one image and registering all the other images in the series to that one image or by registering each successive image in the series to the previous image in the series. However, the known techniques make the fundamental assumption that there is sufficient overlap between images that are to be registered. This assumption is not always satisfied, for example it is not satisfied in the case described above in which a region of interest is imaged in a plurality of images, each acquired during a breath hold, where the imaging is designed to minimise overlap between partial images but which may result either in gaps or in overlap of an unknown, possibly substantial, extent.

It would be desirable to alleviate the problems discussed above.

According to the present invention, there is provided a method of acquiring images of a region of interest of an individual human or animal body, the method comprising any one or more of the following steps in any combination:

acquiring, with a first imaging technique, a reference image of the region of interest;

acquiring, with one or more further imaging technique having a different field of view from the first imaging technique, a plurality of partial images of parts of the region of interest including parts at different positions;

determining a respective transformation in respect of each partial image which transformation registers the respective partial image with the reference image; and

5 identifying an un-imaged area of the region of interest which is not imaged by the plurality of partial images.

Thus, the method involves acquiring a reference image of the entire region of interest, in addition to acquiring the plurality of partial images of the part of the region of interest. The partial images are then each
10 registered with the reference image. As a result of this registration with the reference image, the partial images after being transformed by their respective transformations are accurately registered with respect to each other. Crucially this is achieved without the need to perform registration of the partial images with each other and hence the method succeeds even
15 if deformation of the tissue being imaged results in a gap between the coverage of the partial images.

The ability to accurately register the partial images without the need for overlap effectively reduces the limitation on the imaging technique. This
20 makes it possible for the partial images to have a field of view which may be smaller than would be possible if it was required to register the partial images with respect to each other. The ability to reduce the field of view reduces the limitations on the imaging technique. This reduces the limitations of the imaging technique within the constraint that the image
25 acquisition period is sufficiently short that the deformable tissue may be considered to be static, for example not subject to involuntary deformation. This is advantageous. One possible advantage is that the reduced field of view allows the imaging technique to be performed with an increased spatial and/or temporal resolution. This effectively increases
30 the quality of the image. Another possible advantage is that the reduced field of view allows the use of more advanced imaging techniques which

require a longer image acquisition period which prevents their use with a larger field of view within the available time. This effectively allows the use of imaging techniques which would not otherwise be available or commonly used.

5

Furthermore, the accurate registration of the partial images with respect to each other has the very significant advantage of making it possible to identify any gap, that is an area which is not imaged by the plurality of partial images. As previously mentioned, the gap might not be evident
10 from the partial images themselves. However, the registration of the partial images with respect to the reference image allows the coverage of the partial images to be accurately determined.

If any such gap is identified, then it may be covered by the acquisition of
15 additional partial images. As a result, it is possible to achieve complete coverage of the region of interest. This avoids the risk of missing information in a gap which may be crucial to a patient management decision. Accordingly there is a reduction of the risk of underestimation of a condition or even failure to recognise a condition at all.

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The registration of the partial images has particular benefit in the acquisition of parametric images representing a parameter derived from images acquired with the same imaging technique with different acquisition parameters.

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In one example, the composite image is generated as a parametric image representing a parameter derived from the partial images acquired using the different acquisition parameters and transformed by their respective transformations. As the parameters are derived from the partial images by
30 using the different acquisition parameters after transformation, any deformation between the acquisition of the partial images using different

acquisition parameters is compensated for by the transformation and thus does not result in errors in the derivation of the parameters.

In another example, the respective partial images are acquired as parametric images by: acquiring a plurality of initial images with the same further imaging technique using different acquisition parameters while the human holds his or her breath; and generating the respective partial image as a parametric image representing a parameter derived from the initial images. In this case, the reduced field of view provided by the method allows the initial images to be acquired in a sufficiently short period that the initial images needed to generate a single parametric partial image are all acquired during a single breath hold. This means that they are sufficiently aligned to properly generate the parameters. In contrast with a larger field of view it might be necessary to acquire the initial images during different breath holds, resulting in deformation between the initial images which would cause errors in the derivation of the parameters.

For use in many applications, the method may advantageously further comprise generating a composite image combining transformations of each of the partial images. As the transformed partial images are accurately registered with respect to each other, due to the registration with the reference image, the composite image properly combines all the information from the partial images, even where there are gaps and/or overlap between the partial images. This allows a clinician to properly appreciate the extent to which the partial images cover the region of interest. This reduces the risks discussed above in the event that there are gaps and/or overlaps between the partial images.

In the event of overlaps, overestimation by the clinician can be avoided. Indeed, the overlap may be used to improve the quality of the image in

the area of overlap. For example, in an area of overlap, the number of data values for each image point may be increased, thereby improving the signal-to-noise ratio by a factor proportional to the square root of the number of data values. Thus, the acquisition of partial images with overlapping areas can actually improve the image quality, for example by increasing the signal-to-noise ratio, rather than degrading the image quality, for example by introducing blurring or artefacts.

The reference image is acquired with a first imaging technique which may be selected to be sufficiently rapid to acquire an imaging technique of the entire region of interest in an acquisition period over which any deformable tissue in the region of interest may be considered to be not subject to an involuntary deformation, for example a translation, a rotation or a warp. Typically, this will mean that the first imaging technique is of a different type from one or more further imaging techniques used to acquire the partial images, although in principle the first imaging technique could be of the same type as the further imaging technique but with different parameters enabling acquisition with a relatively large field of view in the available time period for acquisition.

In many applications, the plurality of partial images will all be acquired by the same further imaging technique. However, the advantages of accurate alignment of the partial images is equally apparent in applications where the plurality of partial images are acquired by plural, different further imaging techniques.

The invention is applicable to achieve these advantages in a wide range of applications. By way of example, some specific applications which are described in more detail below include breast imaging, imaging of people with breathing difficulties, temporal studies such as contrast-enhanced

studies, studies of moving organs, fast alignment of two studies, and abdominal imaging covering the liver.

To allow better understanding, an embodiment of the present invention
5 will now be described by way of non-limitative example with reference to the accompanying drawings, in which:

Fig. 1 is a flow diagram of a method of acquiring medical images;

10 **Fig. 2** is a schematic view of a reference image of a region of interest;

Fig. 3 is a schematic view of a plurality of partial images of parts of a region of interest at ideal positions; and

15 **Fig. 4** is a schematic view of a plurality of partial images of parts of a region of interest at displaced positions.

Fig. 1 illustrates a method of acquiring medical images in accordance
20 with the present invention. The method is applicable to imaging of a region of interest of an individual human or animal body which comprises tissue which may be deformable by translation, rotation or warping. In general, the method is applicable to any part of the body imaged by any imaging technique capable of providing clinically useful information.

25 In step 1, there is acquired, using an acquisition system 1a, a reference image 2 of the entire region of interest. The nature of the system will depend on the nature of the image and will not be described in detail. In this embodiment the images are acquired using an MRI scanning system.
30 The reference image 2 is illustrated in Fig. 2 in which the reference image 2 is shown as a cuboid and a deformable tissue 3 is shown

schematically as a cylinder. The reference image 2 has three spatial dimensions, but preferably has no temporal dimension.

To acquire the reference image 2, there may be selected a first imaging
5 technique which is sufficiently rapid that it can acquire the reference
image 2 covering the entire region of interest within an image acquisition
period over which the deformable tissue may be considered to be static
and not subject to an involuntary deformation. Thus the structure which is
of interest is effectively static over the image acquisition period. Thus,
10 the choice of the first imaging technique depends on the structures being
imaged. However, as the reference image 2 is used as a reference it does
not necessarily need to provide useful clinical information about the
structures being studied in the region of interest.

15 As an alternative, the reference image 2 could be constructed as a
composite from a plurality of images acquired in different image
acquisition periods, but for which it is guaranteed that there is sufficient
overlap so that registration can be properly performed.

20 The reference image 2 of the entire region of interest has sufficient
spatial resolution to serve as a reference even though it lacks the useful
information content provided by the plurality of partial images 5
discussed below.

25 In the case of a human, many structures of interest are deformable during
the normal breathing cycle. The reference image 2 may be acquired from
a human whilst the human holds his or her breath. In this case, the image
acquisition period is at most the period of time for which the breath hold
can be maintained.

For imaging structures which involuntarily deform more rapidly, for example the heart, the imaging acquisition period must be sufficiently short with regard to the speed of movement, that there is effectively no deformation.

5

As an alternative, the image acquisition may be triggered using a gated imaging approach. The gating detects the same points in a regular cycle, for example a breathing or heart-beating cycle. In this case, the acquisition of the plurality of partial images may be triggered by a gating
10 signal. Alternatively each partial image may be acquired by initially acquiring a plurality of initial images with the same further imaging technique using different acquisition parameters at times triggered using the gating signal and then generating the respective partial image as a parametric image representing a parameter derived from the initial
15 images.

Imaging techniques which have relatively short image acquisition periods and which may therefore be suitable for some applications include MRI and CT imaging. For example in the case of imaging the liver, the first
20 imaging technique may be CT or may be MRI with a pulse sequence such as a T1-weighted, fast spoiled, gradient-echo (SPGR).

In step 4, there are acquired a plurality of partial images 5 of respective parts of the region of interest. The partial images 5 are acquired with one
25 or more further imaging techniques having a different field of view from the first imaging technique used to acquire the reference image 2, usually a smaller field of view than the first imaging technique. The one or more further imaging techniques are selected to provide the desired, clinically useful information about the structures being studied in the region of
30 interest. To ensure that the image acquisition is sufficiently rapid to acquire the partial images 5 without the deformable tissue being subject to

an involuntary deformation, the field of view may be reduced. Thus the structure which is of interest may be considered to be effectively static over the image acquisition period.

- 5 Often all the partial images 5 are acquired with the same further imaging technique. In other applications, studies are performed using different further imaging techniques, since in general no single type of imaging technique provides unambiguous information for the clinician.
- 10 The partial images 5 may be acquired at the same stage of clinical management of the human or animal, for example close in time, or may be acquired at different stages of clinical management including diagnosis and treatment, for example before and after a given treatment. Similarly, the reference image 2 may be acquired at any stage of clinical
- 15 management, before, after or between the partial images.

The partial images 5 include images of parts of the region of interest at different positions. This is achieved by control of the image acquisition, for example by relative movement of the image acquisition apparatus and

20 the individual body, or by control of the operation of the image acquisition apparatus. The intention is for the part of the region of interest imaged by the partial images 5 to cover the entire region of interest. This may be achieved by acquiring images which are intended to image contiguous parts of the region of interest or which are intended to

25 overlap. In general, the partial images 5 may each be an image of a mutually different part of the region of interest, or alternatively partial images 5 may be acquired repeatedly at each of the different positions in order to over-sample the region of interest.

- 30 Each partial image may be corrected in an initial correction step using a navigation echo. The navigation echo may be produced at step 4a by

acquiring a low-resolution coronal two-dimensional image by means of a gradient echo sequence featuring a low flip angle which avoids saturation of magnetisation and therefore dark lines. The navigation echo provides an image which allows location of the diaphragm position. Data
5 regarding the diaphragm position is then used to correct the partial image, to prospectively compensate for respiratory motion at step 4b. One navigation echo is acquired for each partial image at step 4a.

Figs. 3 and 4 schematically illustrate a plurality (in this case three) partial
10 images 5 acquired in respect of the same region of interest as Fig. 2. In this example, three partial images 5 are shown, each having a field of view which is a third the size of the field of view of the reference image 2. Fig. 3 illustrates the case that the partial images 5 are of contiguous parts of the region of interest, so that there are no gaps or overlap
15 between adjacent partial images 5. These are the intended positions of the partial images 5 which the further imaging technique attempts to achieve.

However, as the region of interest contains deformable tissue, the individual partial images 5 can be deformed relative to their intended
20 position, for example by translation, rotation or warping. Whilst the image acquisition may by chance occasionally produce contiguous partial images as shown in Fig. 3, more normally the images are relatively deformed. An example is shown in Fig. 4 in which the central partial image 5 is displaced, producing a gap 6 between the central and upper
25 partial images 5 and an overlap 7 between the central and lower partial images 5. Although Fig. 4 illustrates a linear displacement, more generally the partial images 5 may also be displaced by a combination of translation, rotation and warping.

30 With the purpose of deriving a parametric image, it is possible for the plurality of partial images 5 to include images acquired with the same

image technique but using different acquisition parameters. The purpose is to derive a parametric image representing a parameter derived from the partial images 5 acquired using different acquisition parameters. For example, in the case of MRI, the partial images 5 might include two, 5 three or more partial images 5 of each part of the region of interest, with different flip angles or with different repetition times, from which intrinsic parameters such as T_1 and/or T_2 may be derived. The derivation of the parameters occurs later in the method, as described below.

10 Step 1 of acquiring the reference image 2 and step 4 of acquiring the plurality of partial images 5 may be performed in any order, at times spaced closely or far apart.

The reference image 2 and the partial images 5 are processed in further 15 steps described below which are conveniently performed by a computer program executed on a computer system 10 illustrated schematically by a dotted line in Fig. 1. The computer system 10 may be of any type but is typically a conventional personal computer. The computer program may be written in any suitable programming language. The computer program 20 may be stored on a computer-readable storage medium, which may be of any type, for example: a recording medium which is insertable into a drive of the computing system and which may store information magnetically, optically or opto-magnetically; a fixed recording medium of the computer system such as a hard drive; or a computer memory.

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As an alternative, the computer system 10 could be a system dedicated to the present analysis, for example associated with a system used to acquire the reference images 2 in step 1, and the partial images 5 in step 4 and the partial images 22 in step 21. In this case the computer system 10 30 could be optimised for performing the analysis, for example by running various processes in parallel.

As an another alternative, some or all of the functions of the computer system 10 could be performed by hardware.

5 In step 11, each of the partial images 5 is registered with the reference image 2. In particular, step 11 is performed by determining in respect of each partial image 5 a respective transformation which registers the partial image 5 with the reference image 2. In general terms, registration of images is well known and this step may be performed using any known
10 technique, for example those described in Maintz, J.B. and M.A. Viergever, "A survey of medical image registration", Med Image Anal, 1998. 2(1): p. 1-36 or in Hill, D.L., et al., "Medical image registration", Phys Med Biol, 2001. 46(3): p. R1-45.

15 Typically, the registration in respect of a given partial image 5 is performed by determining a transformation Tr which maximises a measure of similarity between the given partial image 5 and the reference image 2. Mathematically, this is represented in the equation (1) which is implemented in step 11:

$$20 \quad Tr = \arg \max \sum_k \text{sim}(I(x_k), J(Tr(x_k)) \downarrow) \quad (1)$$

where:

x_k is the set of points of the reference image indexed by k ;

the summation is performed over the area of the partial image 5 (or $\text{sim}(a,b)$ has a value of zero outside the area of the partial image 5);

25 $I(x)$ is the value of the reference image 2 at point x ;

$J(x)$ is the value of the partial image 5 at point x ;

$Tr(x)$ represents the transformation of the partial image 5 at point x ;

$\downarrow$ represents an interpolation which maps the points of $J(Tr(x))$ to
30 the points of $I(x)$;

$\text{sim}(a,b)$ represents a measure of similarity between the values a and b (it is often more convenient mathematically to use a measure of error which may be considered as the inverse case and requires the argmax operation to be replaced by an argmin operation).

5

Depending on the nature of the reference image 2 and the partial images 5, considerable variation in the implementation of equation (1) in step 11 is possible. For example:

the values $I(x)$ and $J(x)$ may be any type of image values, for example intensity values, feature values (such as local phase, local orientation, local energy, degree of phase congruency, degree of edginess), or parametric values;

the interpolation $\downarrow$ may use any interpolation technique, for example a bilinear technique or a spline technique;

the transform $Tr(x)$ may be of any class, for example rigid, affine or deformable (e.g. spline warps), thus incorporating different combinations of translation, rotation and warping;

the measure of similarity $\text{sim}(a,b)$ may be of various types for example the magnitude of the difference, the root of the difference squared, a measure such as mutual information, any measure described in Maintz, J.B. and M.A. Viergever, "A survey of medical image registration", Med Image Anal, 1998. 2(1): p. 1-36 or in Hill, D.L., et al., "Medical image registration", Phys Med Biol, 2001. 46(3): p. R1-45; and

the search algorithm used to derive argmin (or argmax) may be of various types.

As each one of the partial images 5 is registered with the reference image 2, this means that the partial images 5 are effectively accurately registered with each other. This allows the exact physical position and

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orientation of each partial image 5 to be established. Such knowledge provides advantages when the partial images 5 are interpreted.

Thus, a further consideration in the selection of the first imaging technique is that it should provide a reference image 2 with a resolution which is sufficiently high to provide a high accuracy in the registration of each of the partial images 5 with the reference image 2. Preferably the resolution of the first imaging technique used in step 1 is at least as high as the resolution of one or more further imaging techniques in step 4. Alternatively, the first imaging technique in step 1 may provide a high degree of resolution in respect of an anatomical structure present in the region of interest and which is rigid, for example a skeletal structure. In this case, the registration of the partial images 5 may be performed relative to the skeletal structure. This has the consequence that it is not necessary for the reference image 2 to properly image the deformable tissue of interest which is imaged by the partial images 5. In this case, it is not necessary that the image acquisition period in step 1 is sufficiently short to prevent the deformable tissue from being subject to an involuntary deformation.

20

The registration in step 11 is useful in itself and in this sense the method could cease with step 11. However, for many if not most applications it is desirable to proceed with step 12 in which a composite image 13 is generated from the partial images 5. Step 12 is performed taking account of the registration of the partial images 5 with respect to the reference image 2. Thus step 12 is performed by combining the partial images 5 after they have been transformed by their respective transformations derived in step 11. Step 12 may be performed in two stages, firstly transforming each of the partial images 5 by its respective transformation and secondly by combining the transformed partial images 5, or by an equivalent mathematical operation which incorporates both stages. The

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composite image 13 may of course be output from the computer system 10, for example by display on a display device 10a or by printing on a printer 10b.

- 5 The combination of the transformed partial images 5 may be performed by any suitable technique, and may include interpolation of data values if the data points of the transformed partial images 5 do not overlie one another. In areas of the region of interest where only a single partial image 5 is present, then the composite image 13 may simply take the
10 value of that single partial image 5. In areas of the region of interest where two or more transform partial images 5 overlap, the combination may use a number of different techniques, for example as follows.

One possibility is that the partial images 5 which overlap represents the
15 same type of feature, for example when both of the partial images 5 have been acquired by the same imaging technique. In this case, the area of overlap is over-sampled. The over-sampling can be an unintentional, but can equally be intentional, for example in the case described above that the plurality of partial images 5 include plural different images acquired
20 at each position across the region of interest. In this case, the combination uses the additional information to improve the image quality. This type of combination technique is well established, for example as described in R.H., W.G. Bradley, and C.J. Lisanti, "*MRI : the basics*", 2nd ed. ed. 2003, Philadelphia, Pa. ; London: Lippincott Williams &
25 Wilkins. xiii, 353 p.142/179. Any known combination technique may be applied. The combination will improve the image quality. For example, if a number n of partial images 5 are combined, then the signal-to-noise ratio of the composite image 13 will be increased by factor of $\sqrt{n}$ at points where the n images overlap.

Of course, as an alternative where plural partial images 5 are acquired at each position, it would be possible to combine the plural partial images 5 acquired at each position to generate a composite partial image 5 prior to registration in step 11. The composite partial images 5 from each position could then be used in steps 11 and 12. However, this alternative suffers from the disadvantage that deformations between the acquisitions of each partial images 5 at a given position can lead to reduction in the image quality of the composite partial image 5, for example leading to blurring or imaging artifacts depending on the imaging techniques. It may be preferable to combine all the acquired partial images 5 in step 12 after the registration in step 11 has been performed.

Another possibility in the case that the partial images include partial images acquired using the same further imaging technique but using different acquisition parameters, is that the combination generates the composite image 13 as a parametric image representing a parameter derived from partial images 5 acquired using different acquisition parameters. Such derivation of the parameters is known in itself and may be performed within step 12 using known techniques.

20

The method allows very accurate estimation of the parametric images, because the partial images acquired using different acquisition parameters are used to derive the parameters after the registration performed in step 11. This effectively compensates for any deformation of the partial images between the acquisition using the different acquisition parameters, where deformation would cause errors in the derivation of the parameters. Of course, as an alternative, the partial images 5 can be derived as parametric images in advance of being registered with the reference image 2 in step 11, but this suffers from the risk that deformation occurring between the initial images used to derive the parametric partial images 5 can degrade the quality of the parametric images.

30

Another possibility is that the partial images 5 represent different types of feature in the region of interest, for example because the partial images are acquired using different imaging techniques. Many such types of feature are known in the field of image analysis. In this case, the composite image 13 may combine the partial images simply by aggregating the partial images 5 so that the composite image 13 includes in respect of each point, a value derived from each type of partial image 5. This may be used for segmentation purposes as well as for characterisation of tissue. Should this aggregation make evident that the alignment of the partial images 5 with the reference image 2 is not accurate enough (e.g. by obtaining physically unrealistic values in the aggregate image), then the alignment can be improved in an iterative procedure until physically meaningful values are obtained. As an alternative, the partial images 5 of different types may be combined in a manner that they are distinguishable when the image is displayed or printed, for example by representing the information from the partial images 5 of different types in different colours.

Two further aspects of the method which operate on the composite images 13 will now be described.

The first further aspect concerns identification of areas of the region of interest which have not already been imaged by the partial images 5. Such un-imaged area can be caused by deformation (translation, rotation or warping) of deformable tissue in the region of interest between the acquisitions of the respective partial images 5.

It is a particular advantage of the present method that the accurate alignment of the partial images 5 in step 11 allows such un-imaged areas

to be accurately identified. The identification of the un-imaged areas occurs in step 20.

Step 20 may be performed automatically by the computer system 10
5 comparing the volume imaged by the transformed partial images 5 with the volume imaged by the reference image 2. In this case, step 20 may be performed without performing step 12 of generating the composite image 13.

10 Alternatively, step 20 may be performed by the user visually inspecting the composite image 13, in which case step 20 can be performed outside the computer system 10.

In the event that un-imaged areas are identified in step 20, then in step 21
15 there are acquired one or more additional partial images 22 of parts of the region of interest covering the identified un-imaged area. Step 21 employs the same one or more further imaging techniques as used in step 4, as described above.

20 The control of the position of the parts of the region of interest imaged in step 21 may be performed automatically by the computer system 10 in the event that step 20 is performed in the computer system, or alternatively may be selected by the user.

25 In step 23, the additional partial images 22 are each registered with the reference image 2. Step 23 employs identical techniques to step 11 as described above.

Subsequently, in step 24 a revised composite image 25 is generated. The
30 revised composite image 25 combines both the original partial images 5 transformed by their respective transformations derived in step 11 and

also the additional partial images 22 transformed by their respective transformations derived in step 23. The manner of generating the revised composite image 25 in step 24 is identical to that of step 12 as described above.

5

The second further aspect, which is optional, concerns the possibility that there is an area of overlap between a subset of two or more of the partial images 5 after being transformed by their respective transformation derived in step 11. It has been appreciated that although step 11 allow
10 each of the partial images 5 to be registered with the reference image 2 to a high degree of accuracy, in some cases there remains a small degree of mis-alignment between the partial images 5 after being transformed by their respective transformations. This is a relatively small effect but can cause the composite image 13 to include some dislocation between parts
15 derived from different partial images 5, thereby reducing the quality of the composite image 13. However, it can be appreciated that such an area of overlap between the transformed partial images 5 can be used to improve the relative registration of the transformed partial images 5. This is performed in the present method as follows.

20

In step 30, an area of overlap between a subset of two or more of the transformed partial images 5 is identified. Step 30 is performed automatically in the computer system 10 by comparison of the volumes in each of the partial images 5 after having been transformed by their
25 respective transformations. Thus, step 30 may be performed without performing step 12 of generating the composite image 13.

In the event that such an area of overlap is identified, in step 31, there is determined a revised transformation in respect of any or all of the partial
30 images 5 in the sub-set which overlap. The revised transformations combine (a) the registration of the respective partial image 5 with the

reference image 2 in the same manner as occurs in step 11, and also (b) the registration of the sub-set of the partial images 5 in the area of overlap. This may be performed by using similar techniques to those implemented in step 11, but additionally taking account of the alignment of the sub-set of partial images 5 in the area of overlap.

In a first example, step 31 may implement equation (2):

$$Tr_1 = \arg \max \left(\sum_k sim(I(x_k), J_1(Tr_1(x_k)) \downarrow) \otimes \sum_o sim(J_2(Tr_2(x_o)), J_1(Tr_1(x_o)) \downarrow) \right) \quad (2)$$

where:

- 10 the various terms have the same meaning as in equation (1) but with the subscripts 1 and 2 identifying the two overlapping images; the $\otimes$ represents a combination operator; and the second summation is performed over the area of overlap.

- 15 The first summation corresponds to the summation performed in step 11 initially to derive transformation and by itself in equation (1) has the effect of registering the respective partial image 5 with the reference image 2. The second summation derives a measure of the similarity in the area of overlap between the sub-set of the partial images 5 after being transformed by their respective transformations. An equivalent equation
- 20 can be formed for Tr_2 . These equations are generally solved in an iterative procedure until a convergence criterion is satisfied.

- 25 The combination operator combines the two summations and the combination of the summations is maximised to derive the respective transformation Tr_1 in respect of the partial image 5 in question. A number of different combination operators may be selected depending on the desired contributions of (a) the registration with the reference image 2

and (b) the registration in the area of overlap. One possibility for the combination operator is to combine the two summations linearly, in which case the linear coefficients may be equal or may depend on the magnitude of the area of overlap.

5

In a second example, step 31 may implement equation (3):

$$Tr_1 = \arg \max \left(\begin{array}{l} \sum_k sim(I(x_k), J_1(Tr_1(x_k)) \downarrow) \\ \otimes \sum_o sim(J_2(Tr_2(x_o)), J_1(Tr_1(x_o)) \downarrow) \\ \otimes \sum_l sim(I(x_l), J_2(Tr_2(x_l)) \downarrow) \end{array} \right) \quad (3)$$

and an equivalent equation for Tr_2 , where the various terms have the same meaning as in equation (2) and the third summation is performed over the area of overlap of the second partial image 5. In this case, the equations for Tr_1 and Tr_2 are dependent on each other and are solved by an iterative process until a desired degree of accuracy has been achieved, for example in the manner disclosed in Geng, Kumar and Christensen, "Transitive inverse-consistent manifold registration", Lecture Notes in Computer Science, 2005. At each iteration, the area of overlap is re-computed to account for the iteratively changing transformations Tr_1 and Tr_2 . The second example provides a more accurate result than the first example at the expense of additional computation.

Subsequently, in step 32 a composite image 33 is generated combining the partial images 5 transformed by their effective transformations. Step 32 uses the revised transformation where they have been derived in step 31, but in respect of partial images 5 for which revised transformations have not been derived in step 31, then step 32 uses the respective transformation already derived in step 11.

The two further aspects of the present invention may be used in combination, for example by step 20 being performed in respect of the

revised composite image 33 derived in step 32, or by the step 30 being performed on the revised composite image 25 derived in step 24. Thus the method may proceed from either of steps 24 or 32 to either of steps 20 or 30. The two further aspects may each be performed repeatedly or
5 iteratively until a desired degree of accuracy of registration has been achieved.

The method described above may be used in a wide range of imaging applications which vary both in terms of the structure being imaged in the
10 region of interest and varying in terms of the first and further imaging techniques applied. Some specific examples will now be described to illustrate the advantages of the method, but it must be understood that these examples are by no means limitative.

15 The first example is in breast imaging. The human breast is highly deformable as a result of both muscle flexation and also breathing movement. These deformations degrade the image quality and change the appearance of images. Thus, the advantages of the present invention of allowing accurate alignment of partial images 5 and the ability to identify
20 an un-imaged area are particularly advantageous in the context of breast imaging.

Another area with advantages is imaging using technique requiring a breath hold in the case of individuals with breathing difficulties who are
25 unable to hold their breath for a long period. The present method allows the individual to hold their breath for a very short time whilst respective partial images 5 of small areas are acquired. As the partial images 5 can be accurately registered, this allows the projection of a composite image
13 of sufficiently high quality. The method thus improves patient
30 comfort, image quality and facilitates a correct diagnosis.

The present method may also be applied to temporal studies. The partial images 5 illustrated in Fig. 4 may have three spatial dimension, but the method is equally applicable to images having three spatial dimensions and a temporal dimension. The invention may be applied to several different types of temporal studies, some examples being as follows.

One type of temporal study is a contrast-enhanced study.

To assess the effectiveness of new therapeutic agents it is often desirable to acquire parametric images and/or estimate physiological parameters. It may technically not be possible to acquire parametric images of the complete volume at a temporal resolution sufficiently high for a given clinical application. With the present method it is sufficient for the partial images 5 to be of only a small part of the region of interest. A given part would be re-imaged at a number of time points (it may be desirable to obtain as many as possible) in step 4 and registered with the reference image 2 in step 11. The parts which overlap for all (or a sufficiently high number of) time points can be used so that the composite image 13 provides accurate estimation of the evolution of parametric images and/or physiological properties. Of course the intentional overlap can be used in step 31 to improve the accuracy of registration of each partial image 5 to the reference image 2. Equation (2) may in that case be extended with additional terms if that proves to be useful.

The partial images 5 can also be acquired in different orientations. The physical relation to the body part of interest can be established by registering the partial images 5 with the reference image 2 in step 11. In the case of abdominal imaging for example it would be possible to acquire partial images 5 in the coronal direction even though the reference image 2 and normal imaging is (predominantly) acquired in the axial orientation. Another example of a temporal study is the study of a moving organ.

The present method can also be used to image the deformation of organs over time. The deformation may be due to breathing and/or to muscles. In this application a static reference image 2 is acquired in step 1. As
5 before, the image acquisition technique would have to be sufficiently fast. Partial images 5 are acquired in step 4 and registered with the reference image 2 in step 11. By imaging parts of the region of interest at a high temporal resolution and calculating the deformation field, a good knowledge of the deformations for various regions can be obtained. This
10 can be useful for diagnosis for example in the study of heart motion over cardiac cycles. Acquiring all parts can yield in step 12 a complete image 13 of the body part of interest using an imaging technique identical or different to the one used to create the reference image 2.

15 Where objects are subject to periodic motion (for example due to the heart beat or breathing) the acquisition of partial images 5 in step 4 can be triggered by detection of an event which we will refer to as a reference time point (e.g. a respiratory event or an ECG event). Partial images 5 would always be acquired at the same reference time point. The
20 combination in step 12 of partial images 5 acquired at several of these reference time points would allow the high resolution visualisation of the state of the body part of interest at each of these reference time points. This approach allows for example the study of motion across time with high precision.

25

Another application of the present method is in the fast alignment of two temporal studies, the studies being a set of images, each study being acquired at different times, for example before and after a treatment. The study may consist of several images acquired using different imaging
30 techniques (PET, CT, MRI) and/or using various different image

acquisition parameters prior to this (for example different pulse sequences) at the same or different time points.

5 All the partial images 5 acquired during a study are aligned to the reference image 2 of the study. To compare two studies (for example to see/analyse the effect of treatment, disease progression) it is necessary to align the two studies. With the present method it is only necessary to perform one further alignment operation, namely to align the two reference volumes.

10

The usage of a reference image 2 thus considerably speeds up the availability for comparison of two datasets. The computational cost and time involved is very favourable compared to currently used methods where every image for the two studies has to be aligned. Because the
15 partial images 5 may be of parts which do not overlap there might not be a solution to the problem with the currently used approach. Alignment of two studies allows the analysis of temporal changes, thus improving the diagnosis in the medical field.

20 Another application is in abdominal imaging with the specific example of the liver. One possible approach for liver imaging is as follows. It is understood that a series of different approaches using the invention described previously could be used to obtain similar results, and the following outline is only illustrative.

25

Images of the abdominal area are typically taken after exhale while the patient holds his/her breath. Breath hold is used to minimise artefacts due to motion. Imaging on exhale is used with the hope that the position of the deformable and movable organs, such as for example the liver is
30 identical at different points in time during the study. However, it has been observed that this is not always the case.

It is proposed to acquire a reference image 2 in step 1 in one breath hold with a MRI technique that allows doing so, for example fast SPGR in/out of phase imaging. This sequence enhances the boundary of fat/non-fat tissue. Abdominal organs are commonly surrounded by such a boundary. Alternative sequences which can be acquired in one breath hold are for example an axial (spoiled) gradient echo sequence or 3D ultra fast volume interpolated gradient echo sequence.

Partial images 5 are acquired in step 4 using an imaging technique which cannot cover the entire region of interest in one breath hold. The parts covered by the partial images 5 can consist of several slices or a single slice and are registered with the reference image 2 in step 11.

The present method allows the whole body part of interest, in this case the liver, to be sampled even if the partial images 5 have been acquired in multiple breath holds. Should it be identified in step 20 that part of the volume has been sampled sparsely it would be possible to re-image these areas. The alignment process can compensate for movements and rotations in any direction and gives confidence about the exact anatomical position of the parts covered by the partial images 5. The results may be improved in step 31.

A possible process is to acquire four partial images 5 with a considerable overlap between the imaged parts of the region of interest. Each partial image is registered with the reference image 2. This allows identification of slices which are sampled repeatedly and improvement of the image quality, e.g. the SNR, by the combination in step 12. If un-imaged areas are identified in step 20, additional partial images 22 are acquired in step 21. The composite image 13 or if needed the revised composite image 25

provide proper sampling of the entire liver. By performing step 31 a better sampling of the entire liver may be obtained.

Sequences which typically have to be taken in multiple acquisitions
5 include sequences taken in the coronal direction as well as Fat Saturation and short Tau inversion recovery (STIR) sequences in the axial direction.

Another application involves modification of commonly used MRI pulse sequences. Instead of acquiring complete volumes with one setting (in
10 multiple breath holds) before changing the settings the present method can be applied to change the acquisition parameters after each acquisition of a partial image 5. For example, in one breath hold, partial images 5 of the first anatomical slice can be acquired with several acquisition parameters. One could for example obtain the same anatomical slice with different flip
15 angles allowing the estimation of T1. The advantage of this approach is that the partial images acquired during one breath hold are aligned because the amount of deformation within the breath hold may be considered as negligible, allowing a very accurate estimation of tissue parameters without the need for any registration procedure.

20

It might only be possible to cover a smaller anatomical area in one breath hold (due to the multiple settings taken for each slice). This however does not pose a problem as the present method allows the partial images 5 to be registered with the reference image 2, allowing one to ensure that the
25 whole region of interest has been sampled and to be confident about the exact anatomical position of the information.

Although the method has been described with reference to medical images of a human or animal body, the method could equally be applied to any
30 type of images including non-medical images.

CLAIMS

1. A method of acquiring images of a region of interest of an individual human or animal body, the method comprising:

5 acquiring, with a first imaging technique, a reference image of the region of interest;

acquiring, with one or more further imaging technique having a different field of view from the first imaging technique, a plurality of partial images of parts of the region of interest including parts at different
10 positions;

determining a respective transformation in respect of each partial image which transformation registers the respective partial image with the reference image; and

15 identifying an un-imaged area of the region of interest which is not imaged by the plurality of partial images.

2. A method according to claim 1, further comprising:

acquiring, with the one or more further imaging technique, one or more additional partial images of parts of the region of interest covering
20 the identified un-imaged area; and

in respect of each additional partial image, determining a respective transformation which registers the additional partial image with the reference image.

25 3. A method according to claim 1 or 2, further comprising:

identifying an area of overlap between a subset of two or more of the partial images transformed by their respective transformations; and

determining a revised transformation in respect of at least one of the partial images in said subset which revised transformation combines at
30 least (a) registration of the respective partial image with the reference

image and (b) registration of the subset of the partial images in the area of overlap.

4. A method according to claim 3, wherein said step of determining a revised transformation in respect of at least one of the partial images in said subset comprises determining a revised transformation in respect of all the partial images in said subset which revised transformation combines (a) registration of each of the respective partial images with the reference image and (b) registration of the subset of the partial images in the area of overlap.

5. A method according to claim 3 or 4, wherein said step of determining a revised transformation in respect of at least one of the partial images in said subset comprises determining a respective transformation which maximises a combination of (a) a measure of similarity between the respective partial image after being transformed by its respective transformation and the reference image and (b) a measure of similarity in the area of overlap between the subset of the partial images after being transformed by their respective transformations.

20

6. A method according to any one of the preceding claims, further comprising generating a composite image combining each of the plurality of partial images transformed by its respective transformation and each of the additional partial images transformed by its respective transformation.

25

7. A method according to claim 6, wherein said step of acquiring a plurality of partial images comprises acquiring a plurality of initial images with the same further imaging technique using different acquisition parameters, the composite image being generated as a parametric image representing a parameter derived from the partial

30

images acquired using different acquisition parameters and transformed by their respective transformations.

8. A method according to any one of the preceding claims, wherein
5 said step of determining a respective transformation in respect of each partial image comprises determining a respective transformation which maximises a measure of similarity between the respective partial image after being transformed by its respective transformation and the reference image.

10

9. A method according to any one of the preceding claims, wherein said one or more further imaging technique have a smaller field of view than the first imaging technique.

15 10. A method according to any of the preceding claims, wherein the region of interest of the human or animal body includes deformable tissue.

11. A method according to claim 10, wherein the one or more further
20 imaging techniques have an image acquisition period over which the deformable tissue is not subject to an involuntary deformation.

12. A method according to claim 10 or 11, wherein the one or more further imaging techniques have an image acquisition period over which
25 the deformable tissue can be considered to be static.

13. A method according to any of the preceding claims, being a method of acquiring images of a region of interest of a human body, the human holding his or her breath during the acquisition of the reference image
30 and each of the plurality of partial images.

14. A method according to claim 13, wherein the step of acquiring a plurality of partial images comprises acquiring respective partial images by:

5 acquiring a plurality of initial images with the same further imaging technique using different acquisition parameters while the human holds his or her breath; and

generating the respective partial image as a parametric image representing a parameter derived from the initial images.

10 15. A method according to claim 13, wherein the step of acquiring a plurality of partial images comprises acquiring respective partial images by:

15 acquiring a plurality of initial images with the same further imaging technique using different acquisition parameters, triggered by a gating signal; and

generating the respective partial image as a parametric image representing a parameter derived from the initial images.

16. A method according to any one of claims 1 to 12, wherein the plurality of partial images are acquired triggered by a gating signal.

17. A method according to any one of claims 1 to 12 wherein the acquisition of at least one of the partial images is prospectively corrected using a respective navigator echo.

25

18. A method according to any of the preceding claims, wherein the first imaging technique has a resolution which is at least as high as the resolution of the one or more further imaging techniques.

30 19. A method according to any of the preceding claims, wherein the one or more further imaging techniques comprise any of Magnetic

Resonance Imaging, ultrasound imaging, dynamic Positron Emission Tomography imaging, or dynamic Single Photon Emission Computed Tomography imaging.

5 20. A method according to any of the preceding claims, wherein the first imaging technique comprises one of Magnetic Resonance Imaging and Computed Tomography imaging.

21. A method according to any of the preceding claims, wherein the
10 reference image and the partial images have three spatial dimensions.

22. A method according to claim 21, wherein the partial images have three spatial dimensions and a temporal dimension.

15 23. A method according to any of the preceding claims, wherein the plurality of partial images are acquired by a single further imaging technique.

24. A method according to any one of claims 1 to 23, wherein the
20 plurality of partial images are acquired by plural, different further imaging techniques.

25. A method according to any of the preceding claims, wherein at least some of the plurality of partial images are images of parts of the
25 region of interest which overlap.

26. A method according to any of the preceding claims, wherein the plurality of partial images are all images of parts of the region of interest at mutually different positions.

27. Apparatus for acquiring images of a region of interest of an individual human or animal body comprising:-

an acquisition system operable to acquire, using a first imaging technique, a reference image of the region of interest, and further
5 operable to acquire, using one or more further imaging techniques having a field of view different from the first imaging technique, a plurality of partial images of parts of the region of interest, including parts at different positions; and

a processing system operable to determine a respective
10 transformation in respect of each partial image, which transformation registers the respective partial image with the reference image; and to identify an un-imaged area of the region of interest which is not imaged by the plurality of partial images.

15 28. Apparatus arranged to carry out the method of any one of claims 1 to 26.

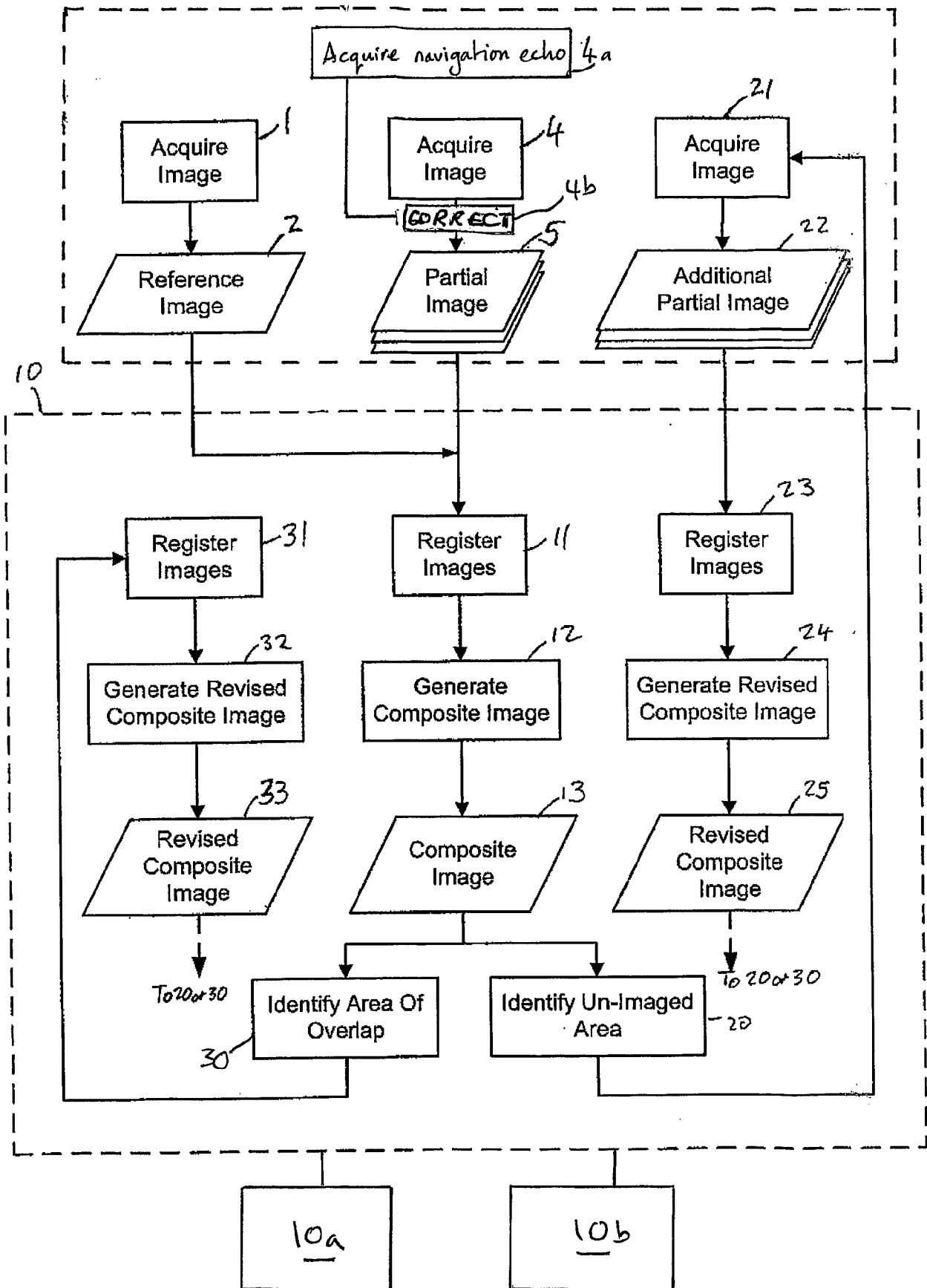


Fig 1

Fig.2

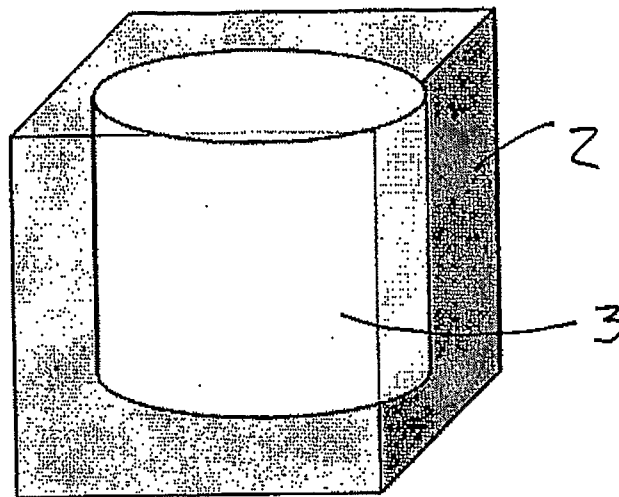


Fig.3

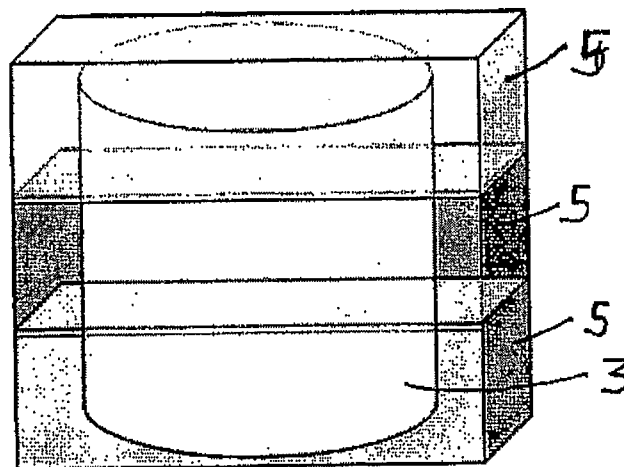


Fig.4

