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(54) Title: LOCAL INTENSITY METHOD AND SYSTEM FOR PATHOLOGY DETECTION

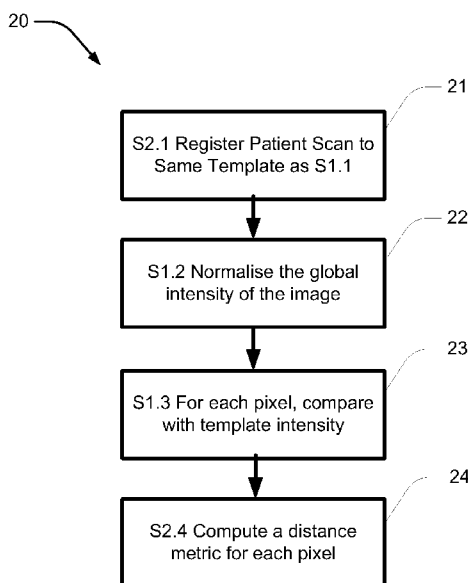


FIG. 2

(57) Abstract: A method of detecting a subject outlier case for a subject image case, the method including the steps of: (a) from a series of non outlier cases, generating a voxel by voxel basis in a template space; (b) testing a new subject image case by spatial and intensity normalization of the subject image case to the template; (c) applying an comparison of the results of step (b) to determine a differential measure between the subject image case and the basis in the template space.

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- 1 -

Local Intensity Method and System for Pathology Detection

Field of the Invention

[0001] The present invention relates to the field of medical image processing, and in particular, to the identification of abnormalities within image scans.

Background

[0002] Any discussion of the prior art throughout the specification should in no way be considered as an admission that such prior art is widely known or forms part of common general knowledge in the field.

[0003] Medical Imaging is becoming a widespread diagnosis tool for many pathologies, and the detection of lesions among normal tissues is a formidable task performed manually and routinely by radiologists. As scanner resolution improves and the number of images increases continuously, the visual inspection and manual delineation of lesions in hundreds of slices per scan becomes a tedious and costly task.

[0004] It would be desirable to be able to detect lesions in any medical image substantially automatically. For example, it would be desirable to be able to detect lesions in the white matter of the brain from Magnetic Resonance Imaging (MRI) scans. With ageing and various diseases (e.g. Alzheimer's disease, Multiple-sclerosis), the white matter of the brain is subject to lesions that appear as hyper-intense (brighter than normal) in a FLAIR MRI scan and hypo-intense (darker than normal) in a T1W MRI scan. Fig. 3 shows an example of these lesions.

[0005] Current approaches to detection of these lesions consist in using a model of the brain as made of a fixed number of tissues, typically three different tissues: white matter (WM), gray matter (GM), and cerebro-spinal fluid (CSF). Each tissue is assumed to have the same intensity across the whole brain for a given patient. To model the noise, the intensity for each tissue (histogram) is fitted using a non-parametric (e.g. Parzen windows) or parametric (e.g. one or more normal distributions or clusters) model. The methods consist then in adapting the intensity models for each patient's scan.

[0006] There are two problems with this approach: 1) if lesions exist, the model would include normal tissues and lesions, and therefore be biased. Specific techniques have been proposed to model each tissue as normal + lesions but this is difficult as the lesions are not known a priori (e.g. Van Leemput and Parastawa). 2) The intensity of a tissue is not constant across the brain. Because of the anatomical complexity and variation in tissue composition, this assumption is wrong and yields to a loose model in order to include the spatial variations in intensity.

[0007] Other recent approaches tried to classify normal tissues from lesions using pattern recognition techniques (e.g. neural networks, support vector machines). Tissues and lesions are modelled as two classes. In addition to the intensity for each tissues, the location can be input as an extra parameter so that the model can learn the variations in tissue intensity across the brain and distinguish lesions from normal tissues. There are generally at least three problems with this approach: 1) the model needs to learn what is a lesion is and therefore examples of lesions need to be defined, often using manual

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segmentation; 2) the training data must be large enough and sufficiently exhaustive of the possible configuration for the model to accurately learn lesions from normal tissues; 3) the processing time is long, although some optimization using hardware or GPGPU implementation exist.

References

The prior art includes a number of attempts to automatically detect lesions in medical images, including:

1. Van Leemput K, Maes F, Vandermeulen D, Colchester A, Suetens P. Automated segmentation of multiple sclerosis lesions by model outlier detection. IEEE Trans Med Imaging. 2001 Aug;20(8):677-688.
2. Prastawa M, Bullitt E, Ho S, Gerig G. A brain tumor segmentation framework based on outlier detection. Medical Image Analysis. 2004 Sep;8(3):275-283.
3. Ourselin S, Roche A, Subsol G, Pennec X, Ayache N. Reconstructing a 3D structure from serial histological sections. Image and Vision Computing. 2001 Jan;19(1-2):25-31.
4. Rueckert D, Sonoda LI, Hayes C, Hill DL, Leach MO, Hawkes DJ. Nonrigid registration using free-form deformations: application to breast MR images. IEEE Trans Med Imaging. 1999 Aug;18(8):712-721.

Summary of the Invention

[0008] It is an object of the present invention to provide an improved method and apparatus for the automatic detection of anomalies such as lesions in medical images.

[0009] In accordance with a first aspect of the present invention, there is provided a method of detecting a subject outlier case for a subject image case, the method including the steps of: (a) from a series of non outlier cases, generating a voxel by voxel basis in a template space; (b) testing a new subject image case by spatial normalization of the subject image case to the template; (c) applying an comparison of the results of step (b) to determine a differential measure between the subject image case and the basis in the template space.

[0010] The voxel by voxel basis can comprise a model of normal tissues of each voxel. The method can also provide for quantifying how different can be a voxel from the model of normal tissue.

[0011] In some embodiments the image can comprise a medical scan image such as an MRI image.

[0012] The subject image case preferably can include multiple images of the same object. The model preferably can include forming a histogram of values for each voxel. The quantification preferably can include thresholding the values of each voxel.

[0013] In some embodiments, the voxel by voxel basis preferably can include a temporal component measuring scanning variations for the images. In other embodiments, a model can be built of outlier cases and a relative distance measure between the subject image case and the model can be also calculated.

[0014] In accordance with another aspect of the present invention, there is provided a system for detecting a subject outlier case for a subject image case, the system including: first processing means for generating a voxel by voxel basis in a template space for non outlier cases; second processing means for testing the new subject image by spatial normalization of the subject image case to the template; and, comparison means for comparing the normalized subject image case to the basis in the template space. Preferably, the voxel by voxel basis comprises a model of normal tissues of each voxel. In some embodiments, the comparison means utilizes a model to quantify how different a voxel is from the model of normal tissue. In some embodiments the subject image case includes multiple images of the same object.

Brief Description of the Drawings

[0015] Benefits and advantages of the present invention will become apparent to those skilled in the art to which this invention relates from the subsequent description of exemplary embodiments and the appended claims, taken in conjunction with the accompanying drawings, in which:

Fig. 1 and Fig. 2 illustrates flow charts in the steps the preferred embodiment;

Fig. 3 to Fig. 5 illustrate the application of lesion detection to an image; and

Fig. 6 illustrates the histogram processing of the preferred embodiment.

Detailed Description of the Preferred and Other Embodiments

[0016] Preferred embodiments of the invention will now be described, by way of example only, with reference to the accompanying drawings.

[0017] The preferred embodiments provide a different approach to the detection of anomalies such as lesions in medical images. The preferred embodiments consist of two series of steps. A first series of pre-processing steps (S1), builds an intensity model for each pixel of a template image. In the second series of steps (S2), each pixel intensity of a new scan is compared to the intensity model corresponding to that pixel. If the intensity lies within the normal intensity range for that pixel, then the pixel is labelled as normal. If it falls outside the normal intensity range, it is labelled as abnormal.

[0018] The S1 series are further illustrated in Fig 1 and include the steps of:

[0019] S1.1. register a sufficient number of normal brain scans on a same template (for example using the approaches of Ourselin et al and Rueckert et al);

[0020] S1.2. normalize (e.g. adjust contrast and brightness) the global intensity of the image (histogram) so that for each pixel similar intensity values are found;

[0021] S1.3. for each pixel, construct an approximation to a probability density function of the signal intensity such as by constructing a histogram and store it in memory. The histogram can be built using raw data or estimated using non-parametric or parametric methods.

[0022] The series S2 is illustrated in Fig. 2 and can further include:

[0023] S2.1. register the patient's brain scan to the same template used in S1.1.

[0024] S2.2. normalize that scan histogram to the histogram of the template as in S1.2 (22).

[0025] S2.3. compare each pixel's intensity to the histogram built for that pixel in S1.3 (23).

[0026] S2.3. compute a metric to quantify how far each pixel's intensity is from the normal range of intensity found in normal brain at that pixel (24).

5 [0027] An example is shown in Fig. 3 to Fig. 5. In Fig. 3, there is illustrated a patient brain scan with some lesions e.g. 33 in white. Fig. 4 illustrates a process of manual segmentation and Fig. 5 illustrates a process of automatic segmentation. Three points 31-33 are shown and Fig. 6 illustrates a histogram of the three points. Fig. 6 illustrates histograms 61-63 of the three pixels identified in Fig. 3. Thresholds defined by 96% of normal intensity for the three locations are also showed 64-66 and are indicated by the dashed lines. Any intensity greater than the threshold (right of the dash lines) is considered abnormal and labelled as a lesion.

10 [0028] This threshold step can be at step S2.3 and can be for example a simple threshold at 96% (~ 2 standard deviation) of the normal intensity range, or a probabilistic maximum a posteriori classification method. Different threshold tests can be used. The threshold can be based on detecting higher than the intensity of normal tissue from the FLAIR to detect white matter lesions, but can also be lower to detect pathologies. When multiple images are available and a joint histogram is used, then different areas of the joint histogram threshold can define different pathologies based the distance from the intensity distribution of normal tissues (e.g. multi dimensional thresholding, or level-set),

15 [0029] Instead of a binary decision (normal/lesion) one can also define a distance (using any metric including but not restricted to Euclidian or Mahalanobis) from normal tissue (defined by a threshold) in the histogram space and estimate how strong a lesion is distant from normal tissue. In defining this distance measure, if only one image is available, then a one dimensional histogram is used. When more than one image are available, a joint histogram can be used.

20 [0030] The preferred embodiment thereby provides a method performing outlier detection to segment scan images thorough the generation of a model of normal appearing tissue on a voxel by voxel basis in template space. This is done in a non-parametric manner by computing a histogram at each voxel location. The averaged template is tested with new subject by spatial and intensity normalization of the subject to the template followed by the application of an outlier detection scheme.

25 [0031] As this is an outlier based approach, only a model of normal appearing white matter has to be generated. Therefore as opposed to training based approaches where manual segmentations of the lesions are required to train classifiers, minimal if any manual segmentation is required.

30 [0032] Furthermore the model can incorporate any scanner and sequence specific changes in intensity and contrast. Therefore if a model is generated for the scanner and sequence, than no parameters would need to be chosen or altered beyond the threshold on the distance maps. The approach has the added advantage in that although as proposed it is fully automated, it can in fact be used as a semi-supervised operation. For example, the operator may have the ability to choose the threshold on the distance maps.

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[0033] Although the preferred embodiment has been described particularly with reference to MRI brain scans, it can be applied to other segmentation tasks whereby deviations from the norm are to be detected. As lesions generally result in a change in tissue along with a corresponding change in the grey level intensity of the tissue in scans, this approach could be used to segment other lesion types in medical imaging.

[0034] A number of limitations may exist. First the registration to a single template might be inaccurate and computationally demanding. The segmentation accuracy is not that important if a neighborhood around each pixel is considered to capture the anatomical variation that cannot be capture by non-rigid registration. Second, there might be variation in intensity over time due to the scanner itself. This issue has previously been reported and can be addressed by building a model per scanner and per sequence that adapts over time (using only the last similar 100 scans for example).

[0035] It can therefore be seen that the preferred embodiment includes the spatial registration of many scans from a similar body part to a template. The scans can be global or regional intensity normalized of all the scans intensity, e.g. adjusting the contrast and brightness so that all the histograms are similar.

[0036] Next, where only normal scans have been registered, an estimation of the intensity distribution at each pixel from the database is created. A more robust estimation of the intensity models can be created if lesions might be present in the image database. Where the lesions are labelled, an estimate of the pixel intensity model for the normal tissue and one for each type of lesions can be created.

[0037] A new scan is registered to the same template and normalized the same way the model was built. Next, for each model location, detect if the intensity fits or not the intensity variation recorded in the database, and label the corresponding location as normal or pathologic, respectively. In some embodiments, detection can be done by simple thresholding on intensity level. In other examples, detection can be done using probabilistic model such as maximum a posteriori classification, or other detection schemes. A model location can be a single pixel, a pixel and its neighbours, or an area around each pixel. Where multiple images are available, multiple images can be used by using joint histogram.

[0038] The method of the preferred embodiment can be applied to any parts of the body as long as a enough scan exists exist to record in a database an intensity model for each location. The method can be applied to any imaging modalities such as MRI or CT. In some embodiments, the intensity model at each pixel can be made scanner and acquisition specific to capture the intensity variation due to each scanner. The intensity model at each pixel can be adapted over time to capture the variation in intensity due to the time drift of a scanner.

Interpretation

[0039] Reference throughout this specification to “one embodiment” or “an embodiment” means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment of the present invention. Thus, appearances of the phrases “in one

embodiment” or “in an embodiment” in various places throughout this specification are not necessarily all referring to the same embodiment, but may. Furthermore, the particular features, structures or characteristics may be combined in any suitable manner, as would be apparent to one of ordinary skill in the art from this disclosure, in one or more embodiments.

5 [0040] Similarly it should be appreciated that in the above description of exemplary embodiments of the invention, various features of the invention are sometimes grouped together in a single embodiment, figure, or description thereof for the purpose of streamlining the disclosure and aiding in the understanding of one or more of the various inventive aspects. This method of disclosure, however, is not to be interpreted as reflecting an intention that the claimed invention requires more features than
10 are expressly recited in each claim. Rather, as the following claims reflect, inventive aspects lie in less than all features of a single foregoing disclosed embodiment. Thus, the claims following the Detailed Description are hereby expressly incorporated into this Detailed Description, with each claim standing on its own as a separate embodiment of this invention.

[0041] Furthermore, while some embodiments described herein include some but not other features
15 included in other embodiments, combinations of features of different embodiments are meant to be within the scope of the invention, and form different embodiments, as would be understood by those in the art. For example, in the following claims, any of the claimed embodiments can be used in any combination.

[0042] Furthermore, some of the embodiments are described herein as a method or combination of
20 elements of a method that can be implemented by a processor of a computer system or by other means of carrying out the function. Thus, a processor with the necessary instructions for carrying out such a method or element of a method forms a means for carrying out the method or element of a method. Furthermore, an element described herein of an apparatus embodiment is an example of a means for carrying out the function performed by the element for the purpose of carrying out the invention.

25 [0043] In the description provided herein, numerous specific details are set forth. However, it is understood that embodiments of the invention may be practiced without these specific details. In other instances, well-known methods, structures and techniques have not been shown in detail in order not to obscure an understanding of this description.

[0044] As used herein, unless otherwise specified the use of the ordinal adjectives "first", "second",
30 "third", etc., to describe a common object, merely indicate that different instances of like objects are being referred to, and are not intended to imply that the objects so described must be in a given sequence, either temporally, spatially, in ranking, or in any other manner.

[0045] In the claims below and the description herein, any one of the terms comprising, comprised of
35 or which comprises is an open term that means including at least the elements/features that follow, but not excluding others. Thus, the term comprising, when used in the claims, should not be interpreted as being limitative to the means or elements or steps listed thereafter. For example, the scope of the expression a device comprising A and B should not be limited to devices consisting only of elements

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A and B. Any one of the terms including or which includes or that includes as used herein is also an open term that also means including at least the elements/features that follow the term, but not excluding others. Thus, including is synonymous with and means comprising.

[0046] Similarly, it is to be noticed that the term coupled, when used in the claims, should not be interpreted as being limitative to direct connections only. The terms "coupled" and "connected," along with their derivatives, may be used. It should be understood that these terms are not intended as synonyms for each other. Thus, the scope of the expression a device A coupled to a device B should not be limited to devices or systems wherein an output of device A is directly connected to an input of device B. It means that there exists a path between an output of A and an input of B which may be a path including other devices or means. "Coupled" may mean that two or more elements are either in direct physical or electrical contact, or that two or more elements are not in direct contact with each other but yet still co-operate or interact with each other.

[0047] Although the present invention has been described with particular reference to certain preferred embodiments thereof, variations and modifications of the present invention can be effected within the spirit and scope of the following claims.

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We claim

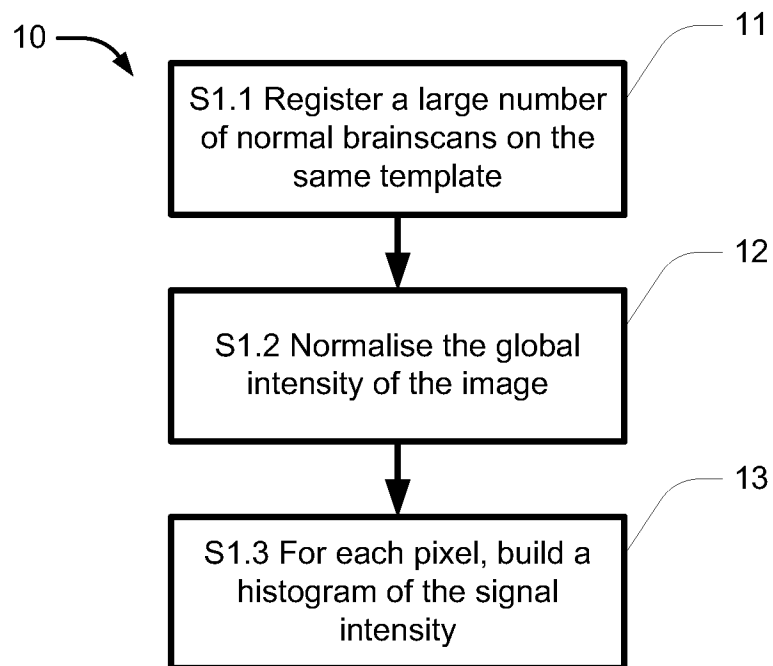
1. A method of detecting a subject outlier case for a subject image case, the method including the steps of:
 - (a) from a series of non outlier cases, generating a voxel by voxel basis in a template space;
 - 5 (b) testing a new subject image case by spatial normalization of the subject image case to the template;
 - (c) applying an comparison of the results of step (b) to determine a differential measure between the subject image case and the basis in the template space.
2. A method as claimed in claim 1 wherein said voxel by voxel basis comprises a model of
10 normal tissues of each voxel.
3. A method as claimed in claim 2 further comprising utilizing a probability density function method to quantify how different a voxel is from the model of normal tissue.
4. A method as claimed in any previous claim wherein said image comprises a medical scan image
- 15 5. A method as claimed in claim 4 wherein said image comprises an MRI image.
6. A method as claimed in any previous claim wherein the subject image case includes multiple images of the same object.
7. A method as claimed in claim 2 wherein said model includes forming a histogram of values for each voxel.
- 20 8. A method as claimed in claim 3 wherein said quantification includes thresholding the values of each voxel.
9. A method as claimed in claim 1 wherein said voxel by voxel basis includes a temporal component measuring scanning variations for said images.
10. A method as claimed in claim 1 wherein a model is built of outlier cases and a relative
25 distance measure between the subject image case and the model is also calculated.
11. A system for detecting a subject outlier case for a subject image case, the system including:
 - first processing means for generating a voxel by voxel basis in a template space for non
outliner cases;
 - 30 second processing means for testing the new subject image by spatial normalization of the subject image case to the template; and
 - comparison means for comparing the normalized subject image case to the basis in the template space.

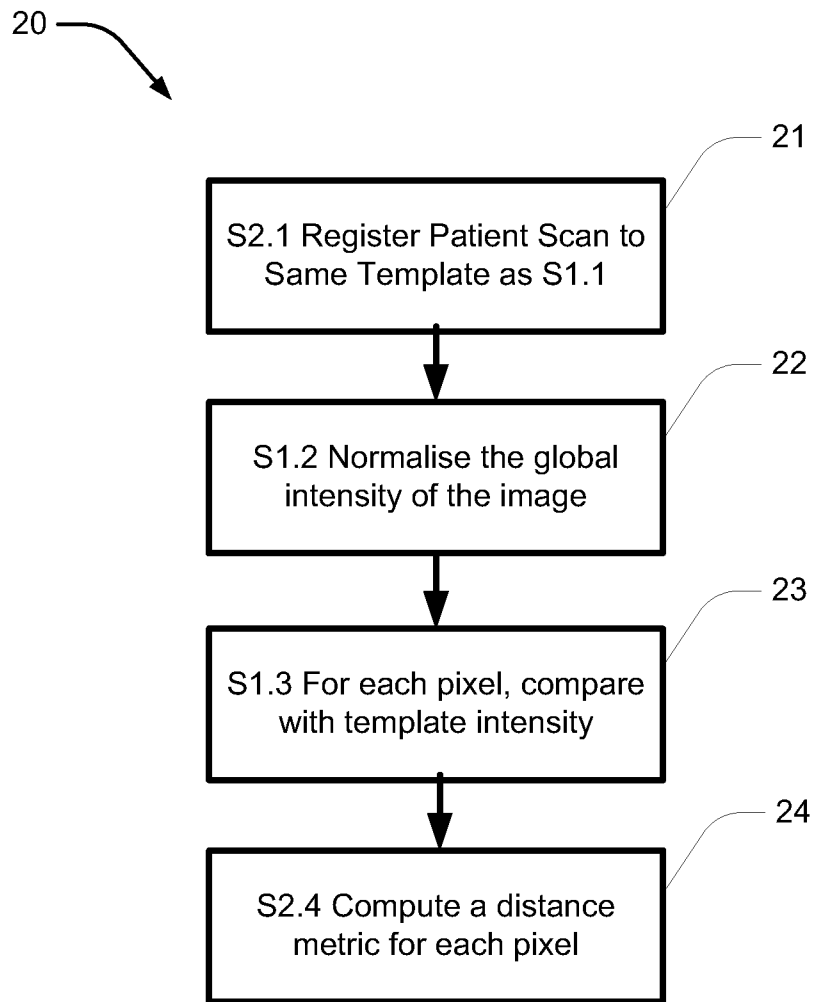
- 9 -

12. A system as claimed in claim 11 wherein said voxel by voxel basis comprises a model of normal tissues of each voxel.

13. A system as claimed in claim 11 wherein said comparison means utilizes a model to quantify how different a voxel is from the model of normal tissue.

5 14. A system as claimed in claim 11 wherein said subject image case includes multiple images of the same object.

1/4**Fig. 1**

2/4**FIG. 2**

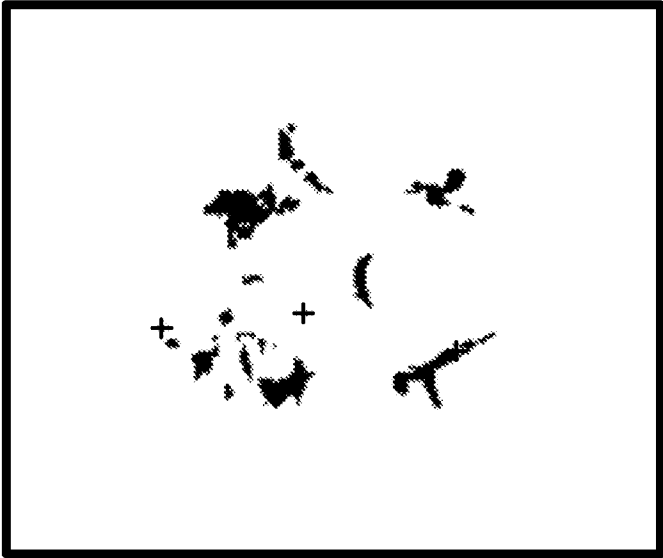


Fig. 5

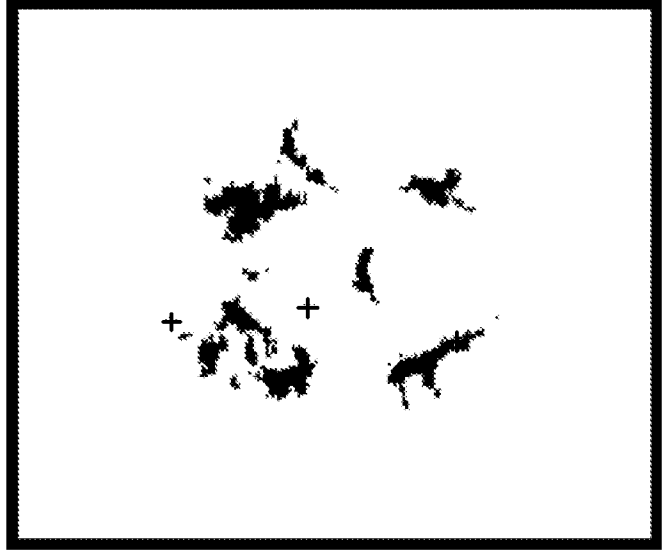


Fig. 4

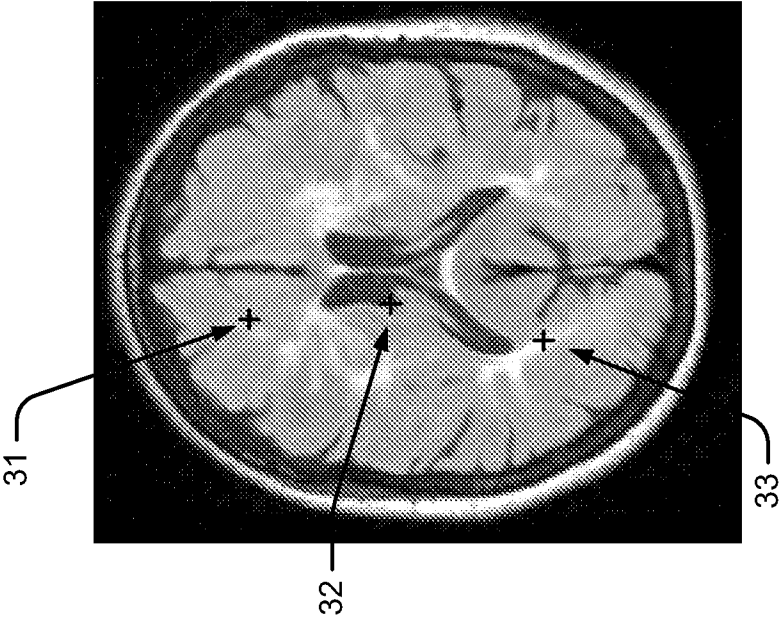


Fig. 3

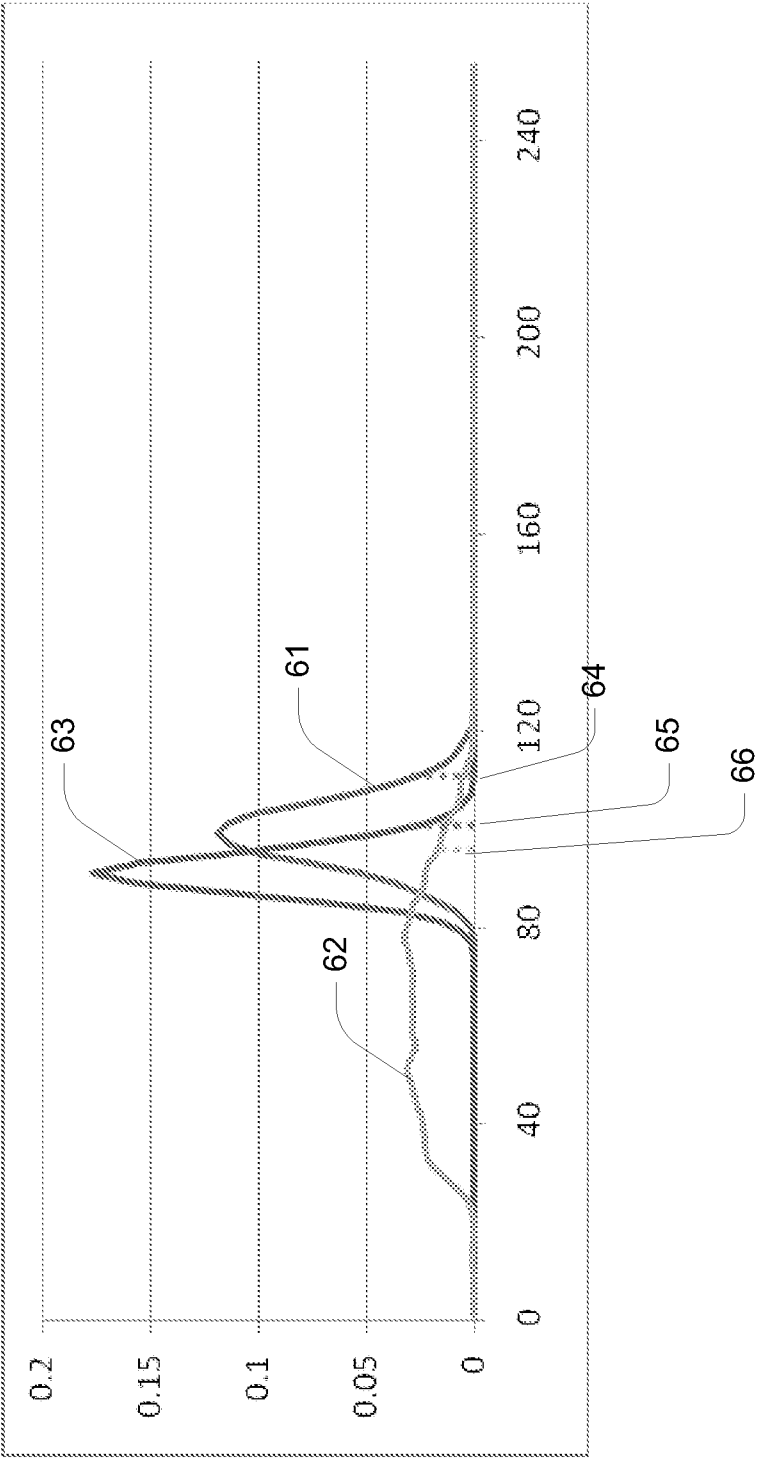


Fig. 6

INTERNATIONAL SEARCH REPORT

International application No.

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A. CLASSIFICATION OF SUBJECT MATTER		
Int. Cl.		
<i>A61B 5/00</i> (2006.01) <i>G06T 7/40</i> (2006.01)		
According to International Patent Classification (IPC) or to both national classification and IPC		
B. FIELDS SEARCHED		
Minimum documentation searched (classification system followed by classification symbols)		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used) WPI and A61B6-, A61B5- and EPODOC and A61B6-, A61B5-, G06F19- and keywords and phrases such as gray matter, grey matter, white matter, brain, CSF, cerebral, image, pixel, voxel, pel, normalization, normalisation, scaling, standard, nominal, abnormal, lesion, diseased, damaged, pathological, parametric, a priori, a posteriori, maximum a posteriori, expectation maximization, classification and the like.		
C. DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2005/0085705 A1 (RAO et al.) 21 April 2005 Abstract, Figs. 3-5; paragraphs [0021]-[0023], [0025]-[0029], [0032], [0033]; elements (50), (52), (58).	1-14
X	US 2005/0273007 A1 (BURBAR) 08 December 2005 Abstract, paragraphs [0009]-[0013], [0016], [0019], [0020], [0035]-[0056], [0058], [0059] Figs. 2A, 2B, Figs. 3-7.	1-14
X	US 2003/0229278 A1 (SINHA) 11 December 2003 Fig. 3, element (310); Fig. 6, element (620); paragraphs [0012], [0013], [0027], [0052], [0059]-[0061], Figs. 7 and 8; [0031]-[0038], elements (670), (710), Figs. 6-8; [0049]-[0061].	1-5, 10-13
☒ Further documents are listed in the continuation of Box C ☒ See patent family annex		
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Date of the actual completion of the international search 11 May 2011		Date of mailing of the international search report 16 MAY 2011
Name and mailing address of the ISA/AU AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. +61 2 6283 7999		Authorized officer VIARA VAN RAAD AUSTRALIAN PATENT OFFICE (ISO 9001 Quality Certified Service) Telephone No : +61 2 6222 3643

INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU2011/000273

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 2009/133383 A1 (BAE SYSTEMS PLC) 05 November 2009 Abstract, page 8, ln. 21-page 9, ln. 9;; page 11, ln. 10-page 15, ln. 20; page 2, ln. 14-page 15, ln. 24;	1-14

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No.

PCT/AU2011/000273

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report				Patent Family Member			
US	2005085705	US	2005107682	US	2005267357		
US	2005273007	EP	1771113	US	7873405	WO	2005117707
US	2003229278	NONE					
WO	2009133383	AU	2009241650	EP	2113866	EP	2291794
		US	2011096999				
Due to data integration issues this family listing may not include 10 digit Australian applications filed since May 2001.							
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