

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(10) International Publication Number
WO 2015/117875 A1

(43) International Publication Date
13 August 2015 (13.08.2015)

(51) International Patent Classification:
G06T 3/00 (2006.01)

(21) International Application Number:
PCT/EP2015/051745

(22) International Filing Date:
29 January 2015 (29.01.2015)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
14153744.9 4 February 2014 (04.02.2014) EP

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(81) Designated States (unless otherwise indicated, for every kind of national protection available): AE, AG, AL, AM,

AO, AT, AU, AZ, BA, BB, BG, BH, BN, BR, BW, BY, BZ, CA, CH, CL, CN, CO, CR, CU, CZ, DE, DK, DM, DO, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, GT, HN, HR, HU, ID, IL, IN, IR, IS, JP, KE, KG, KN, KP, KR, KZ, LA, LC, LK, LR, LS, LU, LY, MA, MD, ME, MG, MK, MN, MW, MX, MY, MZ, NA, NG, NI, NO, NZ, OM, PA, PE, PG, PH, PL, PT, QA, RO, RS, RU, RW, SA, SC, SD, SE, SG, SK, SL, SM, ST, SV, SY, TH, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, ZA, ZM, ZW.

(84) Designated States (unless otherwise indicated, for every kind of regional protection available): ARIPO (BW, GH, GM, KE, LR, LS, MW, NA, RW, SD, SL, ST, SZ, TZ, UG, ZM, ZW), Eurasian (AM, AZ, BY, KG, KZ, RU, TJ, TM), European (AL, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HR, HU, IE, IS, IT, LT, LU, LV, MC, MK, MT, NL, NO, PL, PT, RO, RS, SE, SI, SK, SM, TR), OAPI (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, KM, ML, MR, NE, SN, TD, TG).

Declarations under Rule 4.17:

— as to applicant's entitlement to apply for and be granted a patent (Rule 4.17(ii))

Published:

— with international search report (Art. 21(3))

(54) Title: METHOD FOR REGISTERING AND VISUALIZING AT LEAST TWO IMAGES

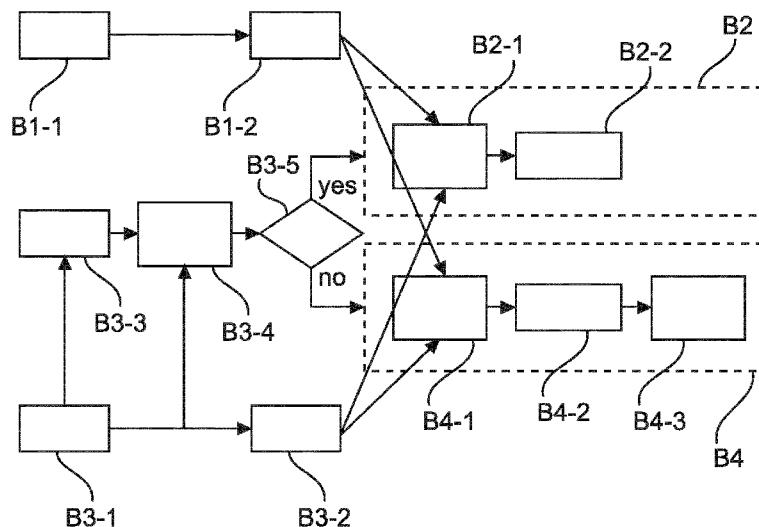


Fig. 3

(57) Abstract: The present invention relates to a method for registering and visualizing at least two images, the method comprising the steps of: - measuring (S1) a navigation speed used by a user during a scrollable and/or zoomable visualization of a first image of the at least two images and comparing the navigation speed with a navigation speed threshold value; - visualizing (S2) the first image by solving deformations of the first image using a first level of computational load, if the navigation speed is below the navigation speed threshold value; and visualizing (S3) the first image by solving deformations of the first image using a second level of computational load, if the navigation speed is above the navigation speed threshold value.

WO 2015/117875 A1

Method for registering and visualizing at least two images

FIELD OF THE INVENTION

The present invention relates to a method for registering and visualizing at least two images and to an imaging system for digital image registration and visualization.

5 BACKGROUND OF THE INVENTION

US 2013/0089249 A1 describes an image processing method in digital pathology. The described method for processing processes a first digital image, representing a sample in a region, and which image has been acquired from the sample by means of a 10 microscopic imaging system. The image is stored in a multi-resolution image data structure, retrieving a sub-region of the first digital image at a first resolution, executing a transform function on the retrieved sub-region, the transform function modifying a content of the sub-region according to at least one metric derived from a second resolution representation of the first digital image.

15 US 2008/013852 A1 describes a system, a method and a computer program product for improving quality of images. According to the described method, the pixels of the input image are used to generate two lists of pixels based on two different scale space values. Thereafter, the two pixel lists are processed to obtain an output image with improved quality.

US 2010/157079 A1 describes systems and methods to selectively combine images. An 20 apparatus includes a registration circuit configured to generate a set of motion vector data based on first image data corresponding to a first image and second image data corresponding to a second image.

US 2013016886 A1 describes a method for high-resolution digital imaging of adjacent slices of tissue samples. Values associated with image objects detected in each tile 25 are calculated. The tiles in adjacent images are co-registered. A first hyperspectral image is generated using a first image, and a second hyperspectral image is generated using a second image.

US2012/068928A1 describes a device and a method for examining and manipulating specimen slides in a digital pathology environment involves a set of operations.

By moving the scroll wheel quickly in either direction may be configured as an instruction to jump to a minimum or maximum magnification, or to progress by more than the next sequential increment, obviating the loading of intermediate magnification.

5 SUMMARY OF THE INVENTION

There may be a need to improve the digital image processing for fast or real-time complex image registration and visualization.

These needs are met by the subject-matter of the independent claims. Further exemplary embodiments are evident from the dependent claims and the following description.

10 An aspect of the invention relates to a method for registering and visualizing at least two images, the method comprising the steps of: measuring a navigation speed used by a user during a scrollable and/or zoomable visualization of a first image of the at least two images and comparing the navigation speed with a navigation speed threshold value; visualizing the first image by solving deformations of the first image using a first level of 15 computational load, if the navigation speed is below the navigation speed threshold value; and visualizing the first image by solving deformations of the first image using a second level of computational load, if the navigation speed is above the navigation speed threshold value.

20 A further aspect of the invention relates to an imaging system for digital image registration and visualization, the imaging system comprising: an image processor configured to compare a navigation speed with a navigation speed threshold value, wherein the navigation speed is used by a user during a scrollable and/or zoomable visualization of a first image of the at least two images; the image processor is further configured to, if the 25 navigation speed is below the navigation speed threshold value, visualize the first image by solving deformations of the first image using a first level of computational load; the image processor is further configured to, if the navigation speed is above the navigation speed threshold value, visualize the first image by solving deformations of the first image using a second level of computational load; and a display adapted to display the at least two images.

30 The present invention allows performing real-time or fast complex image registration and visualization. Two images are used for registration. An algorithm that identifies the coarse transformation between both images is performed. An algorithm that identifies the fine transformation between both images is conducted. An algorithm that indicates the amount of change between successive images is performed which is used to trigger the transition from coarse to fine and vice versa.

The present invention advantageously provides a method for registering two big size images such as digital pathology images, so that registration happens as quickly as possible in order to reduce the feedback time to the user. The method is based on a coarse registration and visualization followed by a fine registration and visualization.

5 An image of the sample region of interest (ROI) and/or of the remaining sample is generated after the isolation of the sample ROI. This image may be generated with the same image generating unit that also generated the image of the whole sample, or with a separate device. The image of the sample ROI (or of the remainder of the sample) can be compared to the image of the whole sample and particularly to the selected image ROI, thus
10 allowing for a verification if the actual sample ROI corresponds to the desired region of interest or not.

According to an exemplary embodiment of the invention, the step of solving deformations of the first image comprises an image translation of the first image, an image rotation of the first image, a scale variation of the first image, a further linear deformation of
15 the first image or a non-linear deformation of the first image.

According to an exemplary embodiment of the invention, the navigation speed used by the user during the scrollable and/or zoomable visualization of the first image is obtained from a user interface device.

20 In case of registration of two digital images, the navigation speed can be advantageously determined by the amount of time since the last update request of the user. In case the user is constantly panning and/or zooming, the fine transformation is omitted. In case the user does not change his viewpoint, e.g. no panning and/or zooming, the fine transformation is performed.

According to an exemplary embodiment of the invention, the navigation speed
25 used by the user during the scrollable and/or zoomable visualization of the first image is measured using a SIFT feature matching.

According to an exemplary embodiment of the invention, the method further comprises the step of performing a local registration of the at least two images.

30 According to an exemplary embodiment of the invention, if the navigation speed is above the navigation speed threshold value, the solving of deformations of the first image comprises applying translational and rotational transformations; and, if the navigation speed is below the navigation speed threshold value, the solving of deformations of the first image comprises applying non-linear refinements.

According to an exemplary embodiment of the invention, if the navigation speed is above the navigation speed threshold value, the solving of deformations of the first image comprises applying transformations with a first resolution level; and, if the navigation speed is below the navigation speed threshold value, the solving of deformations of the first 5 image comprises applying transformations with a second resolution level, wherein the first resolution level is lower than the second resolution level.

The invention further relates to digital image analysis as used for molecular diagnostics, molecular pathology, in particular for oncology applications, biological sample analysis, chemical sample analysis, food analysis, and/or forensic analysis. Molecular 10 diagnostics may for example be accomplished with the help of magnetic beads or fluorescent particles that are directly or indirectly attached to target molecules.

A more complete appreciation of the invention and the attendant advantages 15 thereof will be more clearly understood by reference to the following schematic drawings, which are not to scale, wherein:

Fig. 1 shows schematically the examination of a sample according to the present invention;

Fig. 2 shows an illustration of image registration of two 20 immunohistochemistry stained slides for explaining the invention;

Fig. 3 shows an overview of building blocks according to an exemplary embodiment of the invention; and

Fig. 4 shows a schematic flowchart diagram of a method for registering and visualizing at least two images according to an exemplary embodiment of the invention.

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DETAILED DESCRIPTION OF EMBODIMENTS

The illustration in the drawings is schematically and not to scale. In different drawings, similar or identical elements are provided with the same reference numerals.

The term "navigate" as used in the present patent application refers to any movement, 30 including scrolling, panning, zooming or tilting, of the user's view across what is apparently a larger image that is not wholly seen. In other words to scroll according to the present patent application means to change one's view of data on a computer's display. The scrolling may take place in discrete increments, perhaps one or a few parts of the image at a time or continuously.

Generally, identical parts, units, entities or steps are provided with the same reference symbols in the figures.

Pathology diagnostic investigation of patient material (tissue and cells) is the basis of many treatment decisions, in particular in oncology. Standard, thin slices from a 5 biopsy are presented on microscope slides and stained according to certain protocols to visualize the morphology of the tissue. More recently in situ staining for disease-specific biomarkers is being developed for companion diagnostics of targeted drugs. Assessment may be done with a bright field microscope. Slides need to be stored after investigation for a long period as back-up in case the diagnosis needs to be re-assessed.

10 Digital pathology is a new technology in which the microscope is replaced by a digital scanner which scans the stained tissue sections automatically and stores the images in digital format with sufficient resolution and color rendering that the pathologist can do the same diagnosis from the digital image as he/she would do directly at the microscope. The latter means that the digital image can replace the physical slide. Digital images may be 15 stored instead of the slides.

Next to the above forms of analysis, tissue and cell biopsies may also be investigated with molecular methods (abbreviated as "molecular diagnostics" or "MDx"), like q-PCR and sequencing. This so-called molecular pathology is increasing in importance with the advent of new molecular biomarkers. Often the pathologist decides based on the 20 morphological information to run a molecular test to identify the biological characteristics of the cancer tissue for the right therapy choice. Since many molecular biomarkers cannot be quantified in situ on tissue – or at least not with the required precision – a separate molecular diagnostics test, like PCR or sequencing is carried out on a sample which is taken from the biopsy, in general from a coupe that has already been taken from the biopsy. This tissue 25 section is processed by cell lysis before the measurement of DNA or mRNA markers. As a consequence the spatial information is lost.

Tumor tissues generally consist of different cell types, not only cancer cells, and even the cancer cells can differ a great deal in molecular constitution in different areas of the tumor. The result of a molecular analysis will therefore depend on the exact composition 30 of the tissue section which is used as sample for the molecular test. The more diluted the cancer cells are, the more insensitive and inconclusive the test result will be. In addition, heterogeneity within the cancer cell population will also cause noise in the MDx assays, reducing sensitivity and specificity as well as reproducibility. Reproducibility is in general a main issue, simply because each sample is unique.

With digital pathology there is currently no possibility to run a molecular test on a subsection of a biopsy coupe. Tests on full coupes have suboptimal precision and sensitivity due to dilution of the target cells with benign cells of different origin (e.g. endothelial, fibroblast and immune cells) and cancer cell heterogeneity.

5 Manual selection often lacks accuracy and is therefore likely to create contamination, especially for PCR which amplifies even very low concentrations of contamination.

10 Obtaining a pure fraction of cells of interest can be time consuming and requires a high definition with removal. The aforementioned approach allows relaxing the requirements for selection and balance that with additional parameters that take into account 15 how easy or reliable sections can be removed and control the total size of the selection. For a convenient selection larger, continuous sections are preferred.

15 The image analysis can provide tabular parameters, like the number and fractions of each identified cell type in the finally dissected tissue. The shape of the area can be limited by design criteria including parameters, like total area, allowable curvatures and 20 connectivity. Based on an algorithm an optimum can be determined given a certain selection algorithm which can be specific for each MDx assay.

20 In an exemplary embodiment of this approach, a tissue slide may be stained according to a certain clinical indication with a HER2 immuno-histochemistry or immunofluorescent stain, or a combination of staining assays.

25 The slide may then be scanned by a digital scanner, and the resulting image may be analyzed by a computer program to identify and indicate areas of common features. Those areas may be presented to the pathologist for confirmation and adaptation if necessary or otherwise desirable. From those areas a region of interest, called "sample ROI", may be defined by a software program that represents the part of the sample that is selected for MDx testing.

30 Typical parameters are annotated to that sample ROI, like the average expression of HER2 in the given example, and the statistical distribution of the expression over the cells. The coordinates of that selected sample ROI may be transmitted to a sample isolation unit that takes care of the physical selection of the sample for MDx. The selected "sample ROI" may be transferred to a transfer device or directly a disposable that is used for MDx testing.

The MDx testing may comprise sample preparation and molecular analysis, like qRT-PCR, qrt-PCR, sequencing or next gen sequencing, or micro-array hybridization, or

a combination of these. The results of that analysis may finally be related to the information from the tissue selection algorithm and optionally be interpreted and presented to the pathologist together with the digital image of the tissue in which the sample ROI that was selected for MDx is indicated as well.

5 Figure 1 schematically shows the examination of a sample according to the present invention.

The examination starts at a sample preparation unit 100 in which a slice 11 of body tissue is prepared on a microscope slide 10 serving as a carrier. Typically, tissue samples are obtained by cutting a thin section of about 4-8 microns from a paraffin-10 embedded biopsy. The so-called coupes are placed on the microscope glass slide 10 on a water film to relax from the micro-tomining strain and are then left to dry.

Moreover, the sample 11 may optionally be stained by an appropriate stain 12, e.g. by Hematoxylin-Eosin (H&E) or IHC. There are a number of staining protocols available for different applications. Staining protocols can be carried out on the bench manually by 15 dipping the slide with the coupe in different solutions containing the reagents, but can also be performed in an automated fashion.

One or more markers M may be printed on or engraved in the microscope slide 10 that can later serve as reference points for relating image coordinates to actual coordinates on the slide 10. Moreover, the slide 10 with the sample 11 is preferably covered 20 with a cover slip (not shown) in order to allow for a high image quality during later scanning and to guarantee preservation of the sample over long storage time.

After the preparation step, the slide 10 with the sample 11 is transferred to an image generating unit 200, which may particularly be a digital scanning microscope.

A digital image I of the sample is generated by the microscope 200. The 25 microscope is connected to an imaging system 300, which uses the microscope 200 as a video image source and comprises a display 301 and an image processor 302 for digital image processing of the video image source data.

The imaging system 300 may comprise a user interface device, for instance, a mouse or a keyboard, and the imaging system 300 may be configured to provide a scrollable 30 and/or zoomable visualization of a first image and/or the second image. The scrollable and/or zoomable visualization may be performed according to input commands by using the user interface device. A user may vary and control the navigation speed used during the scrollable and/or zoomable visualization of a first image and/or the second image. The imaging system 300 may be configured to provide a visualization of a first image and/or the second image

based on various image transformations as used in digital image processing. By means of the image processor 302, algorithms to perform image processing on digital images are used. The algorithms may be applied to the input data and can avoid problems such as the build-up of noise and signal distortion during processing.

5 Different computational load capacity may be used for the image transformations by the image processor 302, also a maximum threshold of capacity to be used may be defined by the imaging system 300, which is advantageous in case there are multiple users of the same processing unit.

10 Figure 2 shows an illustration of image registration of two immunohistochemistry stained slides. In the upper-left part of Figure 2, an illustration of misalignment error between both slides is shown. In the lower-left part of Figure 2, an illustration of registration result of complete image is presented. On the right part of Figure 2, simultaneous visualization of matching field-of-views in both slides is presented.

15 Besides analysis of histopathological images, also molecular methods, for instance PCR or sequencing, are used to identify biological characteristics of the (tumor) tissue. Polymerase chain reaction (PCR) is a biochemical technology in molecular biology to amplify a single or a few copies of a piece of DNA across several orders of magnitude, generating thousands to millions of copies of a particular DNA sequence.

20 In molecular methods, a portion of the tissue is selected for further molecular analysis. As the molecular analysis heavily depends on the exact composition of the selected tissue region, the accuracy of the selection of the Region-of-Interest (ROI) is important. Currently, the ROI is manually selected from the H&E stained sample.

25 If MDx is selected as next step, one or more consecutive samples are used. One of the reasons for using a new sample is the fact that the H&E sample is sealed between glass plates. Other reasons are the wish for keeping the H&E sample intact for future reference and long term storage (legal reasons) and incompatibility of the H&E stain with MDx.

30 Typically, the medical specialist will place the second sample (without cover slip) under a microscope and browse the sample to find the tissue part that matches the earlier detected ROI. Depending on the differences in appearance between the H&E sample and the second sample, the retrieval of the ROI in the second sample can be cumbersome. Because of the importance of the correctness of the ROI selection step, means to assist the operator in this step are valuable.

Image analysis algorithms can be developed to match the image data of the selected ROI in the H&E sample against the live video stream of the second sample obtained with the microscope. This process of image matching requires computation time and consequently introduces delay in the image pipeline. Besides image matching, also the 5 visualization of the image matching result will consume computation time, and therefore will add to the delay. As long as the total delay remains small, e.g. above 10Hz, the delay introduced in the video stream is acceptable. A more complex transformation between samples typically results in longer computation times. Differences in transformation between samples can be large, consisting of simple translation and rotation, but also possible small 10 variation in scale and non-linear local deformations caused by tissue stretching, tears, and folds.

Figure 3 shows an overview of building blocks according to an exemplary embodiment of the invention.

Figure 3 shows the algorithmic structure according to the present invention.

15 Inputs of the algorithm are an image of tissue sample 1 (“reference image”) and an image of tissue sample 2 (“target image”). The image content of target image at time t is compared with the target image captured previously and that has been stored in the image buffer. In one embodiment of the present invention, the difference image is computed on a subset of the pixels in the image.

20 In case of motion or motion above a predefined threshold value or change of magnification, the target image at time t and the target image at time t-1 substantially differ, leading to a complex matching the image with the (complete) reference image leaving insufficient time for non-linear refinement (both estimation of the non-linear deformation as well as visualization). Therefore, we estimate the rigid transformation parameters that 25 describe the simple transformation between the reference image and the target image in terms of only translation {Tx,Ty} and rotation {R} and scale. Initially it is our intention to compensate the registration for change in translation only. However, the estimation of the transformation parameters is likely to become unstable or inaccurate if rotation is ignored.

30 In case of no motion or only limited computation time is lost in motion estimation, leaving time to estimate the more accurate non-linear transformation parameters that describe the transformation between both images. The visualization of the target image is updated with translation and rotation. In a next step, also the transformation is further refined in the illustration with its non-linearity component.

In case of small motion, wherein small motion refers to motion below a predefined threshold value, displacement can be estimated with relatively simple / efficient motion estimation methods (e.g. based on projected intensities plus 1D correlations). Besides, it is possible to reuse results for the part that is still observed in the field of view. This again 5 leaves room for estimation and visualization of more detailed transformations.

The navigation speed threshold value or motion threshold value may be predefined, for instance, between a range of 0 and 5 images per second, or may be defined in terms of the screen height or the screen width per second, for instance between a range of 0 and 5 screen height or width, respectively, per second. The navigation speed threshold value 10 can be dynamically set, i.e. the threshold value may not represent a fixed value. The navigation speed threshold value may be based on available computational resources.

Building block B1-1 represents a reference image t ; building block B1-2 symbolizes a feature extraction subroutine. Building block B2-1 corresponds to an estimate rigid feature transformation, building block B2-2 signifies a registration $\{Tx, Ty, R\}$ and scale. 15 Building block B3-1 represents a target image t , building block B3-2 symbolizes a feature extraction. Building block B3-3 corresponds to an image buffer, building block B3-4 signifies a computed SIFT based motion estimation or any other motion estimation. Building block B3-5 is a symbol of a query regarding whether motion is present or whether a navigation speed threshold is surpassed.

20 Building block B4-1 represents an estimate of a non-linear transformation, building block B4-2 symbolizes a registration in the form of $\{Tx, Ty, R\}$ and scale. Building block B4-3 corresponds to a registration in the form of $\{Tx, Ty, \text{non-linear}\}$.

Figure 4 shows a schematic flowchart diagram of a method for registering and visualizing at least two images according to an exemplary embodiment of the invention.

25 The method for registering and visualizing at least two images comprises the following steps.

As a first step of the method, measuring S1 a navigation speed used by a user during a scrollable and/or zoomable visualization of a first image of the at least two images and comparing the navigation speed with a navigation speed threshold value is performed.

30 As a second step of the method, visualizing S2 the first image by solving deformations of the first image using a first level of computational load is conducted, if the navigation speed is above the navigation speed threshold value.

As a third step of the method, visualizing S3 the first image by solving deformations of the first image using a second level of computational load is performed, if the navigation speed is below the navigation speed threshold value.

5 In an exemplary embodiment of the present invention, a live registration of a camera-feed, using a digital scan as a reference is conducted by the method for registering and visualizing at least two images.

In another exemplary embodiment of the present invention, an image registration of two or more digital scans is conducted by the method for registering and visualizing at least two images.

10 In case of two or more digital scans, displacement information is sometimes directly available from the user interaction device (e.g. mouse, keyboard, or other devices used for navigation in the digital environment). Although this case doesn't require computation time for motion estimation, the difference between coarse visualization (only {Tx,Ty,R}) and refined visualization is still desirable to save on computational load of the 15 server.

In order to perform a registration between two images, which may be high-resolution images, a subset of the following steps is performed:

A calculation of features is performed by means of SIFT, which is an algorithm in computer vision to detect and describe local features in images.

20 A calculation of the transformation, for instance is performed based on SIFT feature matching or based on correlation of projected intensities, which may be applicable for relatively small displacements, e.g. displacements below the threshold value.

A calculation of the local deformation is conducted, for instance, by matching local edge structures.

25 Transforming the image is performed only using the translation and the rotation. This may be performed by even scale.

As a further step, local deforming of one of the at least two images could be conducted.

30 Depending on the amount of time and/or computational load to be processed available which may be restricted by the viewing or loading delay of the requested viewport or the frame rate for which user experience is still pleasant, different strategies using the above mentioned steps are applicable. These steps may be mixed or simultaneously processed.

In another exemplary embodiment of the present invention, for large displacements, a coarse overview is presented rather than also applying local deformations.

Therefore, a calculation of the local deformation and a local deforming of one of the at least two images can be ignored resulting in a coarse but acceptable registration, an acceptable high frame rate with limited delay.

5 In another exemplary embodiment of the present invention, in the case of small displacements, e.g. below a displacement threshold value, time or computational load can be saved, for instance by using a more efficient algorithm for motion estimation, for instance, based on correlation of projected intensities or by reusing information from the overlapping area with the previous frame. Then, the saved time can be used to compute local deformation and for visualization of local deformation.

10 In another exemplary embodiment of the present invention, actively panning and zooming is applied: In case the user is actively panning and zooming, compensation is performed for the translation and the rotation. While being active with panning and zooming, non-linear and/or fine details of the registration are not necessary and may be omitted.

15 In another exemplary embodiment of the present invention, no panning and/or zooming occurs, e.g. the user is not panning and/or zooming, the image is displayed using translation and rotation. Then, the calculation of the local deformation is started. Once, the local deformed image is available, the viewport is updated.

20 In another exemplary embodiment of the present invention, a computer program or a computer program element is provided that is characterized by being adapted to execute the method steps of the method according to one of the preceding embodiments, on an appropriate system.

The computer program element might therefore be stored on a computer unit, which might also be part of an embodiment of the present invention. This computing unit may be adapted to perform or induce a performing of the steps of the method described above.

25 Moreover, it may be adapted to operate the components of the above described apparatus. The computing unit can be adapted to operate automatically and/or to execute the orders of a user. A computer program may be loaded into a working memory of a data processor. The data processor may thus be equipped to carry out the method of the invention.

30 This exemplary embodiment of the invention covers both, a computer program that right from the beginning uses the invention and a computer program that by means of an up-date turns an existing program into a program that uses the invention.

Further on, the computer program element might be able to provide all necessary steps to fulfil the procedure of an exemplary embodiment of the method as described above.

According to a further exemplary embodiment of the present invention, a computer readable medium, such as a CD-ROM, is presented wherein the computer readable medium has a computer program element stored on it, which computer program element is described by the preceding section.

5 A computer program may be stored and/or distributed on a suitable medium, such as an optical storage medium or a solid state medium supplied together with or as part of other hardware, but may also be distributed in other forms, such as via the internet or other wired or wireless telecommunication systems.

However, the computer program may also be presented over a network like the
10 World Wide Web and can be downloaded into the working memory of a data processor from such a network.

According to a further exemplary embodiment of the present invention, a medium for making a computer program element available for downloading is provided, which computer program element is arranged to perform a method according to one of the
15 previously described embodiments of the invention.

It has to be noted that embodiments of the invention are described with reference to different subject matters. In particular, some embodiments are described with reference to method type claims whereas other embodiments are described with reference to the device type claims.

20 However, a person skilled in the art will gather from the above and the following description that, unless otherwise notified, in addition to any combination of features belonging to one type of subject matter also any combination between features relating to different subject matters is considered to be disclosed with this application. However, all features can be combined providing synergetic effects that are more than the
25 simple summation of the features.

While the invention has been illustrated and described in detail in the drawings and foregoing description, such illustration and description are to be considered illustrative or exemplary and not restrictive; the invention is not limited to the disclosed embodiments. Other variations to the disclosed embodiments can be understood and effected by those
30 skilled in the art and practising the claimed invention, from a study of the drawings, the disclosure, and the appended claims.

In the claims, the word “comprising” does not exclude other elements or steps, and the indefinite article “a” or “an” does not exclude a plurality. A single processor or controller or other unit may fulfil the functions of several items recited in the claims. The mere fact that

certain measures are recited in mutually different dependent claims does not indicate that a combination of these measures cannot be used to advantage. Any reference signs in the claims should not be construed as limiting the scope.

CLAIMS:

1. Method for registering and visualizing at least two images, the method comprising the steps of:

- measuring (S1) a navigation speed used by a user during a scrollable and/or zoomable visualization of a first image out of the at least two images and comparing the

5 navigation speed with a navigation speed threshold value;

- visualizing (S2) the first image by solving deformations of the first image using a first level of computational load, if the navigation speed is below the navigation speed threshold value; and

- visualizing (S3) the first image by solving deformations of the first image

10 using a second level of computational load, if the navigation speed is above the navigation speed threshold value,

wherein the method further comprises the step of performing a local registration of the at least two images.

15 2. The method according to claim 1,

wherein the step of solving deformations of the first image comprises an image translation of the first image, an image rotation of the first image, a scale variation of the first image, a further linear deformation of the first image or a non-linear deformation of the first image.

20 3. The method according to claim 1 or 2,

wherein the navigation speed used by the user during the scrollable and/or zoomable visualization of the first image is obtained from a user interface device.

4. The method according to any of the preceding claims 1 to 2,

25 wherein the navigation speed used by the user during the scrollable and/or zoomable visualization of the first image is measured using a scale-invariant feature transform feature matching.

5. The method according to any of the preceding claims 1 to 4, wherein, if the navigation speed is above the navigation speed threshold value, the solving of deformations of the first image comprises applying translational and rotational transformations; and, if the navigation speed is below the navigation speed threshold value,

5 the solving of deformations of the first image comprises applying non-linear refinements.

6. The method according to any of the preceding claims 1 to 5,

wherein, if the navigation speed is above the navigation speed threshold value, the solving of deformations of the first image comprises applying transformations with a first resolution 10 level; and, if the navigation speed is below the navigation speed threshold value, the solving of deformations of the first image comprises applying transformations with a second resolution level, wherein the first resolution level is lower than the second resolution level.

7. A computer program, which, when executed by a processor performs

15 the steps of the method according to one of the preceding claims 1 to 6.

8. A computer-readable medium, on which a computer program according to claim 7 is stored.

20 9. A processor, which is configured to execute the method according to one of the preceding claims 1 to 76.

10. An imaging system (300) for digital image registration and visualization, the imaging system comprising:

25 - an image processor (302) configured to compare a navigation speed with a navigation speed threshold value, wherein the navigation speed is used by a user during a scrollable and/or zoomable visualization of a first image of at least two images;
- the image processor is further configured to, if the navigation speed is below the navigation speed threshold value, visualize the first image by solving deformations of the first image 30 using a first level of computational load;
- the image processor is further configured to, if the navigation speed is above the navigation speed threshold value, visualize the first image by solving deformations of the first image using a second level of computational load;
- the image processor is further configured to perform a local registration of the at least two

images; and

- a display (301) adapted to display the at least two images.

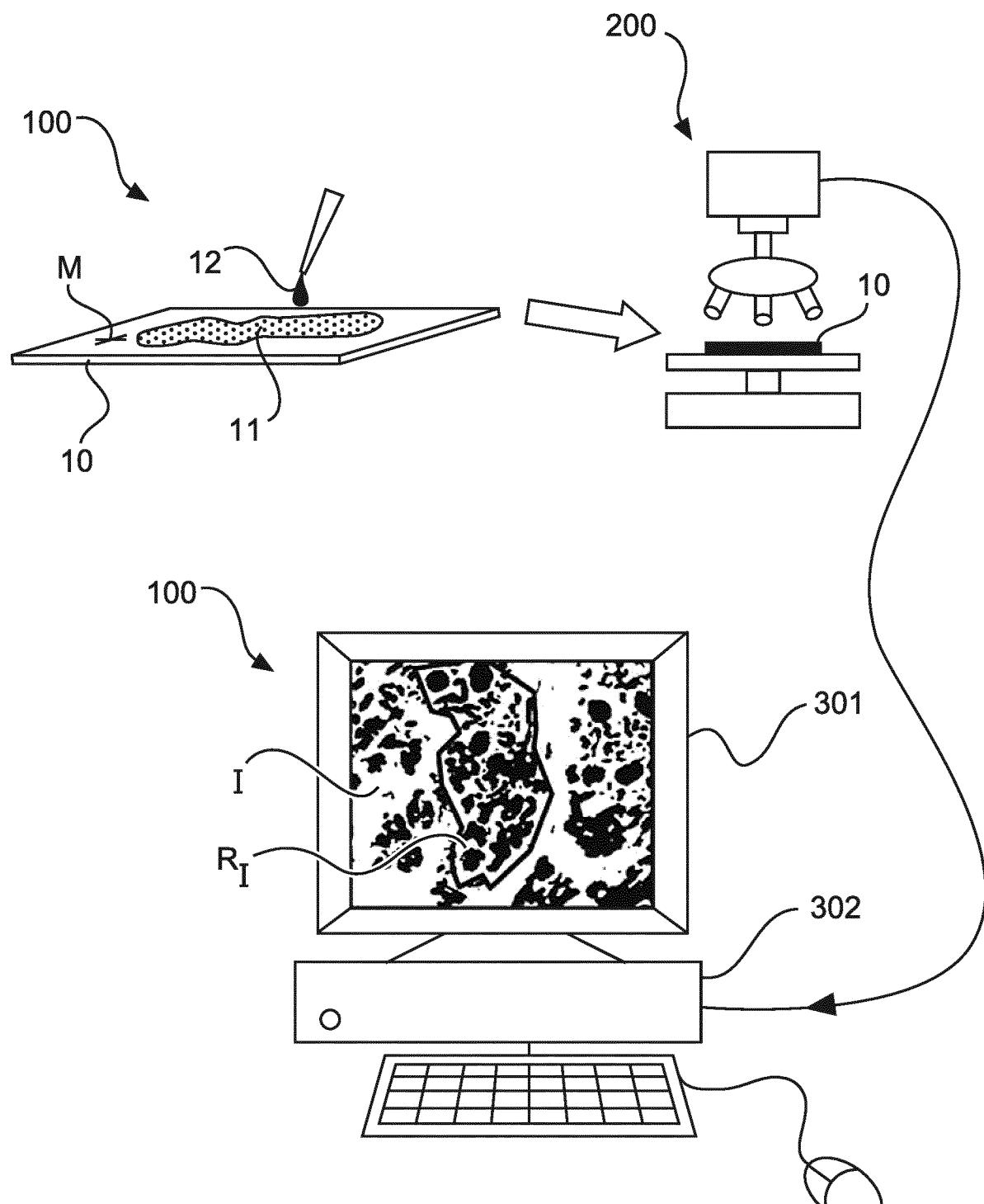


Fig. 1

2/3

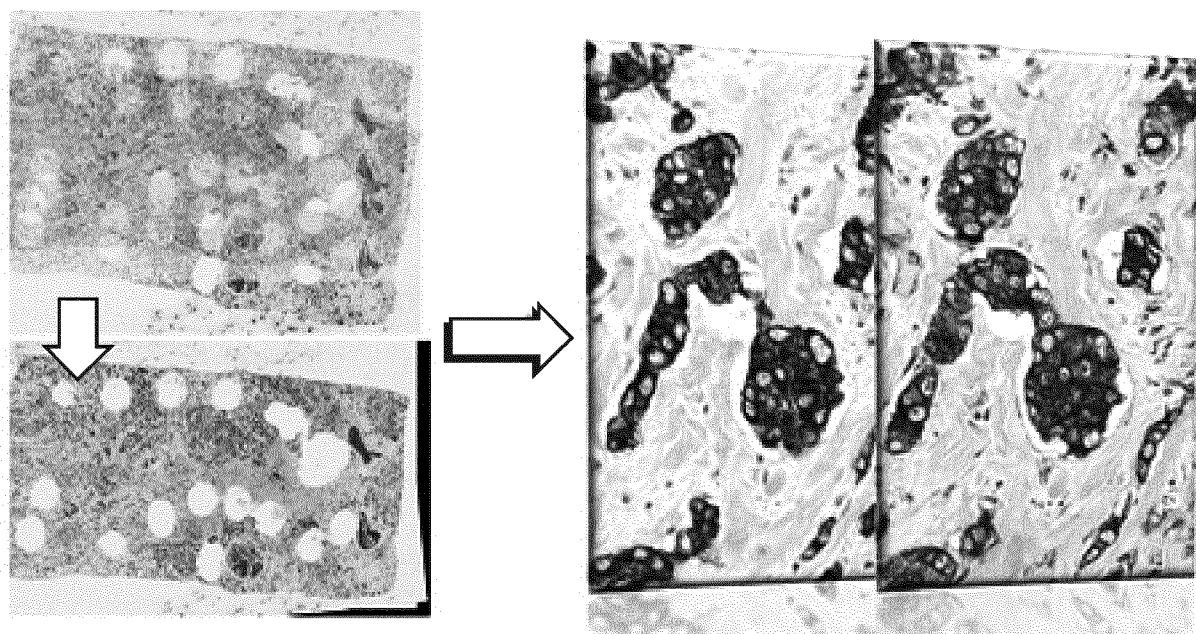
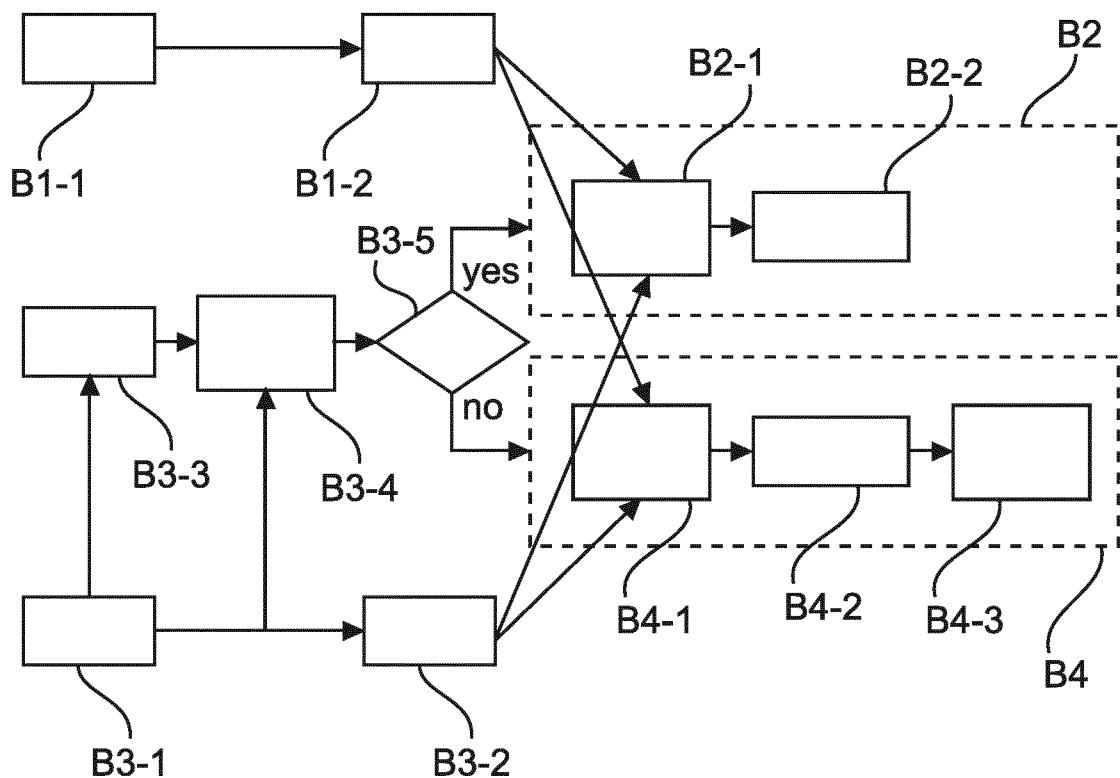
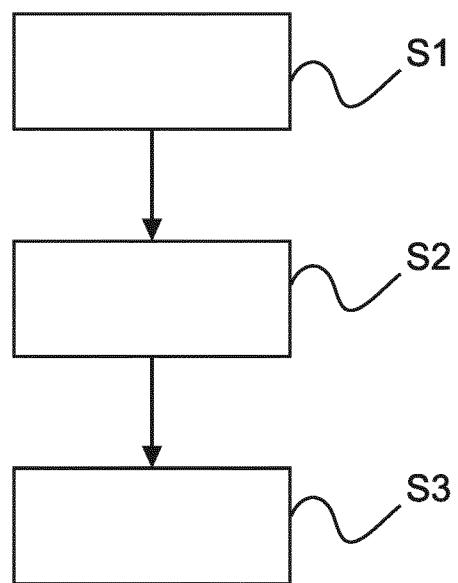


Fig. 2

3/3

**Fig. 3****Fig. 4**

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/051745

A. CLASSIFICATION OF SUBJECT MATTER
INV. G06T3/00
ADD.

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)
G06T

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)

EPO-Internal, WPI Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 2012/068928 A1 (BRUSS ANDREW [US] ET AL) 22 March 2012 (2012-03-22) abstract paragraph [0002] ----- paragraph [0051] - paragraph [0058] paragraph [0066] - paragraph [0067] paragraph [0095] - paragraph [0096] figure 1 ----- US 2006/264746 A1 (FRISA JANICE [US] ET AL) 23 November 2006 (2006-11-23) abstract paragraph [0012] - paragraph [0017] ----- -/--	1-10
A		1-10

Further documents are listed in the continuation of Box C.

See patent family annex.

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

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

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

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

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
7 May 2015	15/05/2015
Name and mailing address of the ISA/ European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Fax: (+31-70) 340-3046	Authorized officer Luca, Mihai Bogdan

INTERNATIONAL SEARCH REPORT

International application No
PCT/EP2015/051745

C(Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>ROJO MARCIAL GARCÍA ET AL: "Critical comparison of 31 commercially available digital slide systems in pathology", INTERNATIONAL JOURNAL OF SURGICAL PATHOLOGY, CHURCHILL LIVINGSTONE, NAPERVILLE, IL, US, vol. 14, no. 4, 1 October 2006 (2006-10-01), pages 285-305, XP002664839, ISSN: 1066-8969, DOI: 10.1177/1066896906292274 the whole document</p> <p>-----</p> <p>EP 2 639 765 A2 (SONY CORP [JP]) 18 September 2013 (2013-09-18) abstract claims 1-11</p> <p>-----</p>	1-10
A		1-10

INTERNATIONAL SEARCH REPORT

Information on patent family members

International application No

PCT/EP2015/051745

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