

Claims

1. A computerized method for determining a stage of fibrosis in a liver, the method comprising performing:

- 5 operation (1a) of receiving input image data relating to the liver, the input image data comprising a first image in a Two-Photon Excitation Fluorescence (TPEF) channel and a second image in a Second Harmonic Generation (SHG) channel, wherein the first and second images relate to a tissue structure in the liver and information relating to collagen content in the liver;
- 10 operation (1b) of identifying a plurality of morphological features of the liver from the first and second images of the input image data relating to the liver, said morphological features comprising collagen areas, operation (1b) further comprising:
- segmenting a plurality of image pixels in the first image into
- 15 different groups of image pixels based on intensities of the plurality of image pixels;
- forming a mask by assigning a weight to each group of image pixels in the first image based on a probability of collagen aggregation in areas comprising the each group of image pixels, wherein each mask
- 20 pixel comprises one of the assigned weights;
- applying the mask to the second image to form an enhanced second image with enhanced collagen areas; and
- segmenting the enhanced second image with the enhanced collagen areas to identify the collagen areas in the second image and to
- 25 thereby perform said identifying of the plurality of morphological features comprising the identified collagen areas;
- operation (1c) of generating a plurality of measurements based on the identified plurality of morphological features; and
- operation (1d) of automatically determining the stage of fibrosis in the
- 30 liver based on the generated plurality of measurements.

2. A method according to claim 1, wherein the plurality of morphological features further comprises one or more of the following groups:

group (i) comprising portal tracts and central veins; and

group (ii) comprising one or more of hepatocytes, bile duct cells, and
5 inflammatory cells.

3. A method according to claim 2, wherein the identified plurality of morphological features comprises the portal tracts and the central veins, and wherein the generated plurality of measurements comprises a measurement
10 based alone on the identified portal tracts and the identified central veins, and the collagen areas are portal tracts.

4. A method according to claim 3 wherein the measurement based alone on the identified portal tracts and at least one of the identified central veins is a portal
15 tract bridging index indicating a percentage of the identified portal tracts which have bridged to other identified portal tracts or the identified central veins.

5. A method according to claim 2, wherein the identified plurality of morphological features comprises the hepatocytes and the bile duct cells, and
20 wherein the plurality of measurements further comprises measurements relating to one or more of the following:

a total amount of collagen in the identified collagen areas;

an amount of collagen not indicative of fibrosis in the identified collagen
areas;

25 an amount of bile duct cell proliferation generated based on the identified bile duct cells; and

an amount of dying hepatocytes generated based on the identified bile duct cells and the identified hepatocytes.

30 6. A method according to claim 2, wherein operation (1b) further comprises:
segmenting bile duct cells in the first image of the input image data of the liver;

segmenting hepatocytes in the first image of the input image data of the liver; and

identifying segmented hepatocytes surrounded by the segmented bile duct cells as dying hepatocytes.

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7. A method according to claim 1, wherein the plurality of measurements further comprises measurements relating to one or more of the following:

an amount of collagen indicative of fibrosis in the identified collagen areas; and

10 an amount of collagen in portal tracts identified in the plurality of morphological features.

8. A method according to claim 1, wherein the different groups of image pixels in the first image comprise a group of image pixels representing sinusoidals and
15 bile duct canaliculi in the liver and the weight assigned to said group of image pixels representing the sinusoidals and bile duct canaliculi in the liver is higher as compared to the weights assigned to other ones of the different groups of image pixels.

20 9. A method according to claim 1, wherein after said identifying of the collagen areas in the second image and before operation (1c), the method further comprises:

identifying boundary pixels of lumens in the first image;

25 locating boundary pixels of lumens in the second image using the identified boundary pixels of lumens in the first image;

locating image pixels in the second image which belong to the identified collagen areas and which are neighbouring the located boundary pixels of lumens in the second image; and

30 dividing the identified collagen areas by classifying said located image pixels in the second image as belonging to the collagen areas not indicative of fibrosis and any remaining pixels in the identified collagen areas as belonging to the collagen areas indicative of fibrosis, such that the identified collagen areas

are divided into collagen areas indicative of fibrosis and collagen areas not indicative of fibrosis.

10. A method according to claim 9, wherein said identifying of boundary pixels
5 of lumens in the first image comprises:
- identifying a group of image pixels representing lumens in the first image;
 - forming an initial mask from the first image by setting the group of image pixels representing lumens in the first image as foreground pixels and remaining pixels in the first image as background pixels;
 - 10 forming a new mask by converting foreground pixels in the initial mask corresponding to image pixels along object boundaries in the first image to background pixels; and
 - subtracting the new mask pixel-by-pixel from the initial mask to form a difference mask indicating locations of the boundary pixels of lumens in the first
15 image.

11. A method according to claim 10, wherein after said forming of the initial mask and before said forming of the new mask, the method further comprises filling holes in areas formed by the foreground pixels in the initial mask.

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12. A method according to claim 9, wherein said locating of image pixels in the second image which belong to the identified collagen areas and which are neighbouring the located boundary pixels of lumens is performed using a region growing method with the located boundary pixels of lumens as starting pixels,
25 wherein the region growing method comprises iteratively locating image pixels in the second image until a number of most recently located image pixels is less than a number of image pixels located in a first iteration.

13. A method according to claim 1, wherein operation (1b) further comprises:
- 30 identifying lumens in the first image;
 - locating groups of clustered lumens from the identified lumens;

determining if each of the identified lumens belongs to a group of clustered lumens; and

identifying each group of clustered lumens as a portal tract and each lumen not belonging to any group of clustered lumens as a central vein.

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14. A method according to claim 13, wherein after said identifying of lumens in the first image and before said locating of groups of clustered lumens from the identified lumens, the method further comprises excluding lumens with irregular shapes from the identified lumens.

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15. A method according to claim 13, wherein said locating of groups of clustered lumens from the identified lumens comprises:

generating a set of lines connecting each identified lumen to its natural neighbouring identified lumens;

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extracting spatial texture features of each identified lumen based on the generated set of lines connected to the each identified lumen; and

clustering the identified lumens based on the extracted spatial texture features to thereby perform said locating of the groups of clustered lumens from the identified lumens.

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16. A method according to claim 15, further comprising identifying portal tract regions and central vein regions based on the following:

forming a plurality of polygons by generating a polygon for each identified lumen, the polygon enclosing intermediate identified lumens closer to the identified lumen than to other identified lumens; and

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for each polygon, identifying a region in the polygon as a portal tract region if the polygon is generated for an identified lumen belonging to a group of clustered lumens and as a central vein region if the polygon is generated for an identified lumen not belonging to any group of clustered lumens.

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17. A method according to claim 1, wherein the stage of liver fibrosis is determined using supervised machine learning algorithms or unsupervised clustering algorithms.

5 18. A method according to claim 1, wherein the first and second images of the input image data relating to the liver comprise three-dimensional image data.

19. A method according to claim 1, wherein the first and second images of the input image data relating to the liver are acquired without staining the liver.

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20. A method according to claim 1, further comprising capturing the first and second images of the input image data relating to the liver using a second harmonic generation based imaging system.

15 21. A computer system having a data storage device and a processor,
the data storage device storing instructions operable by the processor to cause the processor to determine a stage of fibrosis in a liver based on input image data relating to the liver, the input image data comprising a first image in a Two-Photon Excitation Fluorescence (TPEF) channel and a second image in
20 a Second Harmonic Generation (SHG) channel, wherein the first and second images relate to a tissue structure in the liver and information relating to collagen content in the liver, the processor determining the stage of fibrosis by:

identifying a plurality of morphological features of the liver from the first and second images of the input image data relating to the liver, said
25 morphological features comprising collagen areas, said identifying comprising:

segmenting a plurality of image pixels in the first image into different groups of image pixels based on intensities of the plurality of image pixels;

30 forming a mask by assigning a weight to each group of image pixels in the first image based on a probability of collagen aggregation in areas comprising the each group of image pixels, wherein each mask pixel comprises one of the assigned weights;

applying the mask to the second image to form an enhanced second image with enhanced collagen areas; and

segmenting the enhanced second image with the enhanced collagen areas to identify the collagen areas in the second image and to
5 thereby perform said identifying of the plurality of morphological features comprising the identified collagen areas;

generating a plurality of measurements based on the identified plurality of morphological features; and

10 automatically determining the stage of fibrosis in the liver based on the generated plurality of measurements.

22. A non-transitory computer program product storing instructions operable by a processor of a computer system to cause the processor to determine a stage of fibrosis in a liver based on input image data relating to the liver, the input
15 image data comprising a first image in a Two-Photon Excitation Fluorescence (TPEF) channel and a second image in a Second Harmonic Generation (SHG) channel, wherein the first and second images relate to a tissue structure in the liver and information relating to collagen content in the liver,

the instructions being operable to cause the processor to determine the
20 stage of fibrosis by:

identifying a plurality of morphological features of the liver from the first and second images of the input image data relating to the liver, said morphological features comprising collagen areas;, said identifying comprising:

25 segmenting a plurality of image pixels in the first image into different groups of image pixels based on intensities of the plurality of image pixels;

forming a mask by assigning a weight to each group of image pixels in the first image based on a probability of collagen aggregation in areas comprising the each group of image pixels, wherein each mask
30 pixel comprises one of the assigned weights;

applying the mask to the second image to form an enhanced second image with enhanced collagen areas; and

segmenting the enhanced second image with the enhanced collagen areas to identify the collagen areas in the second image and to thereby perform said identifying of the plurality of morphological features comprising the identified collagen areas;

- 5 generating a plurality of measurements based on the identified plurality of morphological features; and
automatically determining the stage of fibrosis in the liver based on the generated plurality of measurements.