Claims

1. A method of computer aided phenotyping of fibrosis-related conditions, the method comprising:

(a) receiving a bright light Whole Slide Imaging (WSI) digital image of a biological tissue sample, wherein the digital image indicates presence of collagens in the biological tissue sample;

(b) pre-processing the digital image, the pre-processing comprising performing color-based image segmentation to generate a collagen specific image,

(c) processing the collagen specific image to quantify a plurality of parameters, each parameter describing a feature of the collagens in the biological tissue sample that is expected to be different for different phenotypes of fibrosis,

wherein at least some of the features are selected from at least two of the group consisting of: (1) tissue level features that describe macroscopic characteristics of the collagens depicted in the digital image of the biological tissue sample; (2) morphometric level features that describe morphometric characteristics of the collagens depicted in the digital image of the biological tissue sample; and (3) texture level features that describe an organization of the collagens depicted in the digital image of the biological tissue sample,

wherein the depiction of collagens in the biological tissue sample results from a marker that is a collagen-specific stain used in a histopathology method, and

wherein at least some of the plurality of parameters are statistics associated with histograms corresponding to distributions of the associated parameters across at least some regions of the digital image, the statistics associated with histograms comprising skewness and kurtosis, and

(d) combining at least some of the plurality of parameters in (c) to obtain one or more composite scores that quantify a phenotype of fibrosis for the biological tissue sample.

2. The method of claim 1, wherein at least one of the features in (c) is a tissue level feature, at least another feature in the features of (c) is a morphometric level feature, and at least another feature in the features in (c) is a texture level feature.

3. The method of claim 1, wherein a first composite score of the one or more composite scores is specific to a feature type selected from the group consisting of tissue level, morphometric level, and texture level, and a second composite score of the one or more composite scores is specific to another feature type selected from the group consisting of tissue level, morphometric level, and texture level.

4. The method of claim 1, wherein the method is compatible with any modality of imaging that distinguishes between a presence and absence of collagens in the biological tissue sample.

5. The method of claim 1, wherein pixels of the digital image indicate presence and quantity of collagens in corresponding volumes of the biological tissue sample.

6. The method of claim 1, wherein at least some of the parameters describing a morphometric level feature or a texture level feature result from processing the histograms.

7. The method of claim 6, wherein cut-off values split the histograms into subsets of sample values, and at least some of the statistics are for a single subset of sample values.

8. The method of claim 1, wherein quantifying at least some of the plurality of parameters associated with histograms comprises processing the histograms to identify multiple modes of the histograms that are identified by deconvoluting the histogram.

9. The method of claim 8, wherein some modes of the histograms correspond to phenotypic signatures of the fibrosis-related conditions, wherein deconvoluting the histogram comprises filtering the histogram to determine whether the histogram exhibits a phenotypic signature and to quantify the exhibited phenotypic signature.

10. The method of claim 1, further comprising processing the digital image to distinguish between collagen classes in the biological tissue sample represented in the digital image.

11. The method of claim 10, wherein each of the plurality of parameters used to obtain at least one of the one or more composite scores in (d) corresponds to one class of collagen.

12. The method of claim 10, wherein collagen classes include one or more of fine collagen, assembled collagen, and tissue regions.

13. The method of claim 12, wherein each of the plurality of parameters used to obtain the at least one of the one or more composite scores in (d) corresponds to one collagen class.

14. The method of claim 11, wherein the collagen classes distinguish different stages of fibrosis.

15. The method of claim 1, wherein different features are selected to quantify different phenotypes of fibrosis.

16. The method of claim 1, wherein the plurality of parameters that are combined in (d) are selected from a list of candidate parameters using a calibration technique involving a calibration data set of calibration digital images taken from biological samples having known phenotypes of fibrosis.

17. The method of claim 1, wherein the method quantifies the severity of fibrosis of the biological tissue, progression of fibrosis for the subject, regression of fibrosis for the subject in response to a therapy, or type of fibrosis, on a continuous scale.

18. The method of claim 1, wherein the parameters that describe texture level features include at least one statistical parameter describing the distribution of one or more properties of a collagen image pixel intensity grey level co-occurrence matrix (GLCM) defined on a spatial dimension across a collagen image, the GLCM properties including at least one of the group consisting of: energy, homogeneity, contrast, correlation, inertia, entropy, skewness, and kurtosis.

19. The method of claim 18, wherein the texture level parameters are obtained by an image processing method configured to quantify perceived texture of the collagen image.

20. The method of claim 1, wherein the plurality of parameters that are combined in (d) are selected from a set of candidate parameters to reduce the dimension of the set of candidate parameters.

21. The method of claim 19, wherein the plurality of parameters that are combined in (d) are selected using artificial intelligence and machine learning.