CLAIMS

1. A computer implemented system (300) for determining an overall-classifier (332) of one or more source-histopathological-images (302),

in which the or each source-histopathological-image (302) has been obtained from one or more histopathological samples obtained from a subject, and in which the subject has, has been diagnosed as having, is suspected of having, is being treated for, has previously been treated for, and/or has previously had, cancer,

the system comprising:

a first tile generator configured to generate a plurality of first-tiles (306) from the one or more source-histopathological-images (302), in which each of the plurality of first-tiles (306) comprises a plurality of pixels that represents a region of the one or more source-histopathological-images having a first-area and a first-resolution;

a second tile generator configured to generate a plurality of second-tiles (307) from the one or more source-histopathological-images (302), in which each of the plurality of second-tiles (307) comprises a plurality of pixels that represents a region of the one or more source-histopathological-images having a second-area and a second-resolution, in which:

the first-area of the first-tiles (306) is larger than the second-area of the second-tiles (307); and

the second-resolution of the second-tiles (307) is higher than the first-resolution of the first-tiles (306);

a first machine-learning network (211; 311) configured to process the plurality of first-tiles (306) in order to determine a first-classifier (318) for the one or more source-histopathological-images (302), in which the first machine-learning network (311) comprises:

a first-neural-network (308) configured to process the plurality of first-tiles (306) in order to determine a tile-feature (310) for each of the plurality of first-tiles (306);

a pooling-function (312) configured to combine subsets of the tile-features to generate a bag-feature (314) for each of the subsets; and

a second-neural-network (316) configured to process the bag-features (314) in order to determine a first-classifier (318) for the one or more source-histopathological-images (302), in which the second-neural-network (316) is a classification network;

a second machine-learning network (215; 311) configured to process the plurality of second-tiles (307) in order to determine a second-classifier (319) for the one or more source-histopathological-images (302), in which the second machine-learning network (215; 311) comprises:

a first-neural-network (308) configured to process the plurality of second-tiles (307) in order to determine a tile-feature (310) for each of the plurality of second-tiles (307);

a pooling-function (312) configured to combine subsets of the tile-features to generate a bag-feature (314) for each of the subsets; and

a second-neural-network (316) configured to process the bag-features (314) in order to determine a second-classifier (319) for the one or more source-histopathological-images (302), in which the second-neural-network (316) is a classification network; and

a classifier combiner configured to combine the first-classifier (318) and the second-classifier (319) to determine the overall-classifier (332) for the one or more source-histopathological-images (302).

2. A computer implemented system (300) according to Claim 1, in which:

first-classifier (318) represents prognostic information related to the subject with which the one or more source-histopathological-images (302) are associated;

second-classifier (319) represents prognostic information related to the subject with which the one or more source-histopathological-images (302) are associated; and

the overall-classifier (318) represents prognostic information related to the subject with which the one or more source-histopathological-images (302) are associated.

3. A computer implemented system (300) according to Claim 2, in which the first-classifier (318), the second-classifier (319) and the overall-classifier (318) each represent:

cancer-specific survival within a defined period of time; and/or

the likelihood of recurrence of the cancer in the subject within a defined period of time.

4. A computer implemented system (300) according to Claim 1, in which the classifier combiner (230; 330) is configured to:

apply a thresholding function to the first-classifier (218; 318) in order to determine a thresholded-first-classifier;

apply a thresholding function to the second-classifier (219; 319) in order to determine a thresholded-second-classifier; and

combine the thresholded-first-classifier and the thresholded-second-classifier to determine the overall-classifier (232; 332).

5. A computer implemented system (300) according to Claim 1, in which:

the first machine-learning network (211; 311) is configured to process the plurality of first-tiles (206; 306) in order to determine a plurality of first-classifiers (218; 318) for the one or more source-histopathological-images (202; 302);

the second machine-learning network (215; 311) is configured to process the plurality of second-tiles (207; 307) in order to determine a plurality of second-classifiers (219; 319) for the one or more source-histopathological-images (202; 302); and

the classifier combiner (230; 330) is configured to:

apply a statistical function to the plurality of first-classifiers (218; 318) in order to determine a combined-first-classifier (340);

apply a statistical function to the plurality of second-classifiers (219; 319) in order to determine a combined-first-classifier (341);

combine the combined-first-classifier (340) and the combined-second-classifier (341) to determine the overall-classifier (232; 332).

6. A computer implemented system (300) according to Claim 1, in which the classifier combiner (330) is configured to perform a logical combination of the first-classifier (218; 318)

and the second-classifier (219; 319) to determine the overall-classifier (232; 332) for the one or more source-histopathological-images (202; 302).

7. A computer implemented system (300) according to Claim 1, further comprising:

a loss-function (126) configured to:

compare the classifier (118; 318) that is determined by the second-neural-network (116; 316) with a ground-truth that is represented by truth-data (120; 320), and

set trainable parameters for the first-neural-network (108; 308), the pooling-function (112; 312), and the second-neural-network (116; 316) based on the result of the comparison.

8. A computer implemented system (300) according to any preceding claim, further comprising:

a segmentation block (122) that is configured to apply an image segmentation method to a whole-slide-image-histopathological image (124; 324) in order to provide a source-histopathological-image (102; 302).

9. A computer implemented system (300) according to Claim 1, in which the first tile generator (204) and the second tile generator (205) are configured to generate their respective tiles independently of one another.

10. A computer implemented system (300) according to Claim 1, in which:

the first and second machine-learning networks (211; 311) have been trained using training-histopathological-images and associated ground-truths, and

the or each training-histopathological-image (302) has been obtained from one or more histopathological samples obtained from one or more subjects, and in which the or each subject has, has been diagnosed as having, is suspected of having, is being treated for, has previously been treated for, and/or has previously had, cancer.

11. A computer implemented method of determining an overall-classifier (332) for one or more source-histopathological-images (302),

in which the or each source-histopathological-image (302) has been obtained from one or more histopathological samples obtained from a subject, and in which the subject has,

has been diagnosed as having, is suspected of having, is being treated for, has previously been treated for, and/or has previously had, cancer,

the method comprising:

generating a plurality of first-tiles (306) from the one or more source-histopathological-images (302), in which each of the plurality of first-tiles (306) comprises a plurality of pixels that represents a region of the one or more source-histopathological-images having a first-area and a first-resolution;

generating a plurality of second-tiles (307) from the one or more source-histopathological-images (302), in which each of the plurality of second-tiles (307) comprises a plurality of pixels that represents a region of the one or more source-histopathological-images having a second-area and a second-resolution, in which:

the first-area of the first-tiles (306) is larger than the second-area of the second-tiles (307); and

the second-resolution of the second-tiles (307) is higher than the first-resolution of the first-tiles (306);

applying a first machine-learning network (211; 311) to the plurality of first-tiles (306) in order to determine a first-classifier (318) for the one or more source-histopathological-images (302), in which applying the first machine-learning network (211; 311) comprises:

applying a first-neural-network (308) to the plurality of first-tiles (306) in order to determine a tile-feature (310) for each of the plurality of first-tiles (306);

combining subsets of the tile-features to generate a bag-feature (314) for each of the subsets; and

applying a second-neural-network (316) to the bag-features (314) in order to determine a first-classifier (318) for the one or more source-histopathological-images (302), in which the second-neural-network (316) is a classification network;

applying a second machine-learning network (215; 311) to the plurality of second-tiles (307) in order to determine a second-classifier (319) for the one or more source-histopathological-images (302), in which applying the second machine-learning network (311) comprises:

applying a first-neural-network (308) to the plurality of second-tiles (307) in order to determine a tile-feature (310) for each of the plurality of second-tiles (307);

combining subsets of the tile-features to generate a bag-feature (314) for each of the subsets; and

applying a second-neural-network (316) to the bag-features (314) in order to determine a second-classifier (319) for the one or more source-histopathological-images (302), in which the second-neural-network (316) is a classification network; and

combining the first-classifier (318) and the second-classifier (319) to determine the overall-classifier (332) for the one or more source-histopathological-images (302).

12. A computer implemented method of processing one or more histopathological images according to Claim 11,

in which the method is a method of producing a diagnostic and/or prognostic determination for a subject that has, has been diagnosed as having, is suspected of having, is being treated for, has previously been treated for, and/or has previously had, cancer,

in which the method comprises receiving one or more source-histopathological-images (102; 202; 302) obtained from one or more histopathological samples (typically, *ex vivo* histopathological samples) obtained from the subject, and in which the method comprises:

determining the overall-classifier (232; 332) for the one or more source-histopathological-images (202; 302) according to a method according to Claim 9, and

attributing a diagnostic and/or prognostic evaluation to the classifier (118) and/or overall-classifier (232; 332).

13. A computer implemented method of processing one or more histopathological images according to Claim 12, in which the subject is a human.

14. A computer implemented method of processing one or more histopathological images according to Claim 12 or 13, in which the or each histopathological sample obtained from the subject is, or are, obtained from the part of the subject's body that has, is suspected of having, is being treated for, has been treated for, and/or has previously had, cancer.

15. A system according to any of Claims 1 to 10, or a method according to any of Claims 11 to 14, in which the cancer is selected from the group consisting of carcinoma, sarcoma, myeloma, leukemia, lymphoma and a mixed type of cancer.

16. A system or method according to Claim 15, in which the cancer is a colorectal cancer, or lung cancer.

17. A method according to any of Claims 12 to 16, in which the method comprises assessing a plurality of source-histopathological-images (102; 202; 302) obtained from a plurality of histopathological samples obtained from the subject in order to determine a plurality of classifiers and/or overall-classifiers, and:

optionally attributing the diagnostic and/or prognostic evaluation to the plurality of classifiers and/or overall-classifiers.

18. A method according to any of Claims 12 to 17, in which the method comprises assessing one or more further diagnostic and/or prognostic markers for the cancer, and

in which the step of attributing a diagnostic and/or prognostic evaluation to the classifier and/or overall-classifier includes an assessment of the or each of the results of the assessment of the or each further diagnostic and/or prognostic markers.

19. A method according to any of Claims 12 to 18, in which the method further comprises making a treatment decision for the subject on the basis of the diagnostic and/or prognostic evaluation,

optionally in which the treatment decision is in respect of a diagnosed or prognosed cancer condition, for example a cancer selected from the group consisting of carcinoma, sarcoma, myeloma, leukemia, lymphoma and a mixed type of cancer, and optionally in which the cancer is a colorectal cancer or lung cancer.

20. Use of a therapeutic agent in the manufacture of a therapy for of treatment of a diagnosed or prognosed pathological condition in a subject in need thereof, in which the diagnostic and/or prognostic evaluation has been attributed to the subject by a method according to any of Claims 12 to 19;

in which the treatment for the diagnosed or prognosed pathological condition is for the treatment of cancer, for example a cancer selected from the group consisting of carcinoma, sarcoma, myeloma, leukemia, lymphoma and a mixed type of cancer, and optionally in which the cancer is a colorectal cancer or lung cancer.

21. Use according to Claim 20, in which the subject is a human.

22. Use according to Claim 20 or 21, in which the subject:

(a) has, has been diagnosed as having, is suspected of having, is being treated for, has previously been treated for, and/or has previously had, cancer; and/or

(b) in which a diagnostic and/or prognostic evaluation of a cancer condition has been attributed to the subject by a method according to any of Claims 12 to 19.

23. Use according to Claim 22, in which the pathological condition is a cancer selected from the group consisting of carcinoma, sarcoma, myeloma, leukemia, lymphoma and a mixed type of cancer, and optionally in which the cancer is a colorectal cancer or lung cancer.

24. Use according to any of Claims 20 to 23, in which the treatment comprises adapting one or more parameters of the therapy in view of the diagnostic and/or prognostic evaluation that has been attributed to the subject by a method according to any of Claims 12 to 19, and optionally

in which the one or more parameters of the therapy are selected from the group consisting of the nature of the therapy, the timing of the therapy, period of the therapy, the dosage of the therapy, the route of administration of the therapy, and the site(s) in the body that is targeted by the therapy.

25. A method according to Claim 19 or use according to any of Claims 20 to 24, in which the diagnostic and/or prognostic evaluation of the subject includes the assessment of the effect on the subject of an earlier, or ongoing, treatment by therapy,

for example, in order to monitor the progress and/or effect of such treatment, and further optionally

in which the method includes the step of making a further treatment decision, such as the cessation, continuation, repetition or modification an earlier, or ongoing, treatment and/or the implementation of a different treatment modality, and optionally,

implementing that further treatment decision in respect of the subject; in which:

the diagnostic and/or prognostic evaluation, the treatment and/or the treatment decision is in respect of a cancer condition, for example a cancer selected from the group consisting of carcinoma, sarcoma, myeloma, leukemia, lymphoma and a mixed type of cancer, and optionally in which the cancer is a colorectal cancer.