

WHAT IS CLAIMED IS: _____

1. A three-dimensional medical image analysis system for predicting ~~the~~a presence of a vertebral fracture in a subject, comprising:

a 3D image processor (101) for receiving and processing 3D image data of said subject, which has not been subjected to a segmentation of bone structures, producing two or more sets of 3D voxels, wherein each of the sets corresponds to the entire ~~said~~ 3D image, and wherein each of the sets consists of equal voxels of different dimensions;

a voxel classifier (104) for assigning for each of said voxels one or more class probabilities of a voxel to contain a fracture using a computational model; and

a fracture probability estimator (103) that uses the voxels classification output for estimating ~~the~~a probability of the presence of a vertebral fracture in said subject.

2. The system of claim 1 additionally comprising a spinal cord detector (102) for detection of the part of said image comprising the spinal cord, optionally

wherein the spinal cord detector (102) uses maximum signal intensities to locate the spinal cord in said image data, optionally

wherein the spinal cord detector (102) uses the anatomical prior information to locate the spinal cord along the x, y and z axes.

3. The system of claim 1, wherein said 3D image data is received via a computer network, or

~~wherein the 3D image processor (101);~~ wherein at least one set of 3D voxels is a set of isotropic voxels of 1mm^3 , optionally the voxel classifier (104) classifies each of said voxels in ~~the~~a context of the surrounding voxels, and classifies each of the voxels in ~~the~~a first set in the context of $30\text{-}40\text{ mm}^3$ of said voxels and each of the voxels in ~~the~~a second set in the context of $90\text{-}120\text{ mm}^3$ of said voxels, or

wherein the 3D image processor (101) produces ~~wherein~~ the first set of 3D voxels is a set of isotropic voxels of 1mm^3 , and the second set of 3D voxels is a set of isotropic voxels of 3mm^3 , or

wherein ~~the 3D image processor (101);~~ ~~wherein~~ at least one set of 3D voxels produced by the 3D image processor (101) is a set of anisotropic voxels, or

wherein the 3D image processor (101); outputs a set of 3D voxels that are normalized to mean and unit standard deviation of the intensity of said voxel.

4. The system of claim 1, wherein said voxel classifier (104) classifies each of said voxels in said ~~one~~ two or more sets of voxels in the context of the surrounding voxels, optionally the first set is classified

in the context of 35 mm³ of said voxels and the second set is classified in the context of 105 mm³ of said voxels, or

wherein the voxel classifier (104) classifies each voxel by assigning one or more class probabilities for each voxel, or

5 wherein the voxel classifier (104) classifies each voxel using a pre-trained classifier by assigning one or more class labels to said voxel, or

wherein the voxel classifier (104) calculates for each voxel a probability to be classified as background, normal, fracture class, or

wherein the voxel classifier (104) is utilizing a Convolutional Neural Network (CNN).

10 5. The system of claim 1, wherein the fracture probability estimator (103) comprises an image classifier (108) configured to receive an input from the voxel classifier (104), or

wherein the fracture probability estimator (103) comprises an image classifier (108) that is configured to classify said 3D image into having or not having a fracture and receives an input from the voxel classifier (104) for each voxel of said 3D image and provides an output of an aggregated
15 probability value for said 3D image, optionally wherein said image classifier (108) is configured to classify said 3D image based on the minimum threshold value of the number of voxels having assigned probability of the fracture class, or

wherein the fracture probability estimator (103) comprises a vertebra anatomical label assignor (106) present in said 3D image, or

20 wherein the fracture probability estimator (103) comprises a vertebrae locator (105), optionally wherein the vertebrae locator (105) produces centroid coordinates of each vertebra within said 3D image, or

wherein the fracture probability estimator (103) comprises vertebra classifier (107).

6. The system of claim 4, wherein the voxel classifier (104) is utilizing a CNN comprising a set of
25 neural network layers, wherein ~~the~~ a sequence of the neural network layers comprises:

for each set of voxels, one or more convolutional layers configured to receive an input derived from said set of voxels in the context of the surrounding voxels to generate two or more convolved outputs;

one or more fully connected layers for aggregating said two or more convolved outputs; and

30 a classification layer receiving an input from said one or more fully connected layers to perform final classification,

optionally wherein the final classification is assigning a probability to each of the voxels to be classified as normal, fracture or background.

7. The system of claim 1, wherein the voxel classifier (104) is pre-trained using a set of annotated input 3D images divided into voxels, wherein an intensity noise signal is added to each 3D voxel along x, y and z axis, or

the voxel classifier (104) is utilizing a CNN pre-trained using a set of annotated input 3D images using a sampling ratio to favor foreground, or

wherein the voxel classifier (104) is utilizing a CNN is pre-trained using a set of annotated input 3D images using a sampling ratio of background:normal:fracture of 1:3:3.

8. The system of claim 1, wherein said 3D image data comprises image intensities, said image intensities having a dynamic signal range, or

wherein said 3D image data is received and stored in a database system.

9. ~~Medical~~ A medical imaging workstation comprising:

an imaging apparatus for generating at least one 3D image (1401) of a subject and

a system for predicting ~~the~~ a presence of a vertebral fracture in said subject in at least one generated image according to any one of claims 1-8.

10. A three-dimensional medical image analysis method of predicting ~~the~~ a presence of a vertebral fracture in an individual, said method comprising ~~the~~ steps of:

receiving a 3D imaging data (201) comprising imaging information of ~~the~~ a spinal cord;

processing said image and producing two or more sets of 3D voxels, wherein each of the sets corresponds to ~~the~~ an entire ~~said~~ 3D image, and wherein each of the sets consists of equal voxels of different dimensions (202);

computing for each voxel class probability of a voxel to contain fracture using a computational model (204);

identifying if any of said voxels are classified as containing a fracture (205); and

predicting the presence of a vertebral fracture (206) in said individual based on ~~the~~ an identification of said voxels classified as containing a fracture.

11. The method of claim 10 additionally comprising a step of locating within said image the spinal cord and generating spine-cropped output images for each set of voxels including the spinal cord (203) and outputting sets of voxels including the spinal cord, optionally

wherein the step of locating within said image the spinal cord (203) is based on maximum signal intensities to roughly locate the spinal cord in said image data, or

wherein the step of locating within said image the spinal cord (203) uses the anatomical prior information to coarsely locate the spinal cord along the x, y and z axes.

12. The method of claim 10, wherein said 3D imaging information is received via a computer network.

5 13. The method of claim 10, wherein said classification is performed using a model trained using a training data set generated using a method comprising following steps:

- i. inputting via ~~a~~the user interface ~~the~~ centroid coordinates for each vertebra in a ~~the~~ training image;
- ii. inputting via ~~a~~the user interface a vertebra fracture label;
- 10 iii. fitting a Gaussian centroid likelihood function around selected centroid coordinates;
- iv. producing a dataset of pairs of signal intensity and label for each of said images in the training data set.

14. The method of claim 10, wherein said computational model is trained on a set of pre-annotated images, or

15 wherein said computation model is trained on a set of pre-annotated images that have been divided into two or more sets of voxels.

15. The method of claim 10, wherein processing and dividing said image into two or more sets of voxels (202) includes adding an intensity noise signal to each produced 3D voxel along x, y and z axis.

20 16. The method of claim 10, wherein at least one of said sets of 3D voxels is a set of isotropic voxels of 1 mm³, or

wherein at least one of said sets of 3D voxels is a set of isotropic voxels.

17. The method of claim 10, wherein processing and dividing said image into a set of voxels (202) additionally comprises a step of normalization to mean and unit standard deviation of ~~the~~ intensity of
25 said voxels, or

wherein processing and dividing said image into a set of voxels (202) additionally comprises a step of adding intensity noise to each produced 3D voxel along x, y and z axis.

18. The method of claim 10, wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) comprises classification of each voxel by
30 assigning a probability of one or more classes per voxel, ~~or~~.

19. The method of claim 10, wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) includes classification each of said voxels in said ~~one~~two or more sets of voxels in ~~the~~ context of ~~the~~ surrounding voxels.

20. The method of claim 19, wherein classification of each of said voxels is performed in the context of the surrounding voxels, and classifies each of the voxels in ~~the a~~ first set in ~~the a~~ context of 30-40 mm³ of said voxels and each of the voxels in ~~the a~~ second set in ~~the a~~ context of 90-120 mm³ of said voxels, optionally

5 wherein the first set is classified in ~~the a~~ context of 35 mm³ of said voxels and the second set is classified in ~~the a~~ context of 105 mm³ of said voxels.

21. The method of claim 19, wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) uses a classifier to classify each voxel in the context of surrounding voxels using ~~a pre-trained~~ ~~the~~ classifier by assigning one or more class labels to
10 said voxels, or

 wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) produces an output probability to be classified as background, normal, or fracture class for each voxel in the image.

22. The method of claim 10, wherein the step of predicting the ~~risk~~ ~~presence~~ of a vertebral fracture
15 (206) includes classification of said 3D image into having or not having a fracture, and wherein said step receives an input classification value from the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) for each voxel of said 3D image, and wherein said step provides an output of an aggregated probability value for said 3D image, or

 wherein the step of predicting the ~~risk~~ ~~presence~~ of a vertebral fracture (206) includes
20 classification of said 3D image based on the minimum threshold value of the number of voxels having assigned probability of ~~the~~ fracture class.

23. The method of claim 10 additionally comprising a step of locating the vertebrae in the image and a step of assigning anatomic labels to ~~the~~ vertebra ~~present~~ in the 3D image, optionally wherein said step of locating the vertebrae produces centroid coordinates of each vertebra within said 3D image, ~~or~~

25 ~~additionally comprising a step of assigning labels to vertebra present in the 3D image, or~~

 additionally comprising a step of vertebra classification by assigning a probability of said vertebrae having a fracture.

24. The method of claim 10, wherein the step of computing for each voxel class probability of a voxel
30 to contain fracture using a computational model (204) is utilizing a Convolutional Neural Network (CNN).

25. The method of claim 19, wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) is utilizing a Convolutional Neural Network (CNN) comprising a set of neural network layers, wherein the set of neural network layers comprises:

for each set of voxels, first one or more convolutional layers configured to receive an input derived from said set of voxels in the context of the surrounding voxels to generate two or more convolved outputs;

an aggregation layer for aggregating ~~the~~ output from said ~~one~~ two or more convolved outputs for each of the sets of voxels;

second one or more convolutional layers receiving an input from said aggregated output from first and the second convolved outputs;

one or more fully connected layers for aggregating said two or more convolved outputs; and
a classification layer receiving an input from said one or more fully connected layers to perform final classification.

26. The method of claim 25, wherein the final classification is performed by assigning a probability to each of the voxels to be classified as normal, fracture or background.

27. The method of claim 10, wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) is utilizing a Convolutional Neural Network (CNN) that is pre-trained using a set of annotated input 3D images using ~~sampling ratio~~ a sampling ratio to favor foreground, or

wherein the step of computing for each voxel class probability of a voxel to contain fracture using a computational model (204) is utilizing a Convolutional Neural Network (CNN) that is pre-trained using a set of annotated input 3D images using a sampling ratio of background:normal:fracture of 1:3:3.

28 The method of claim 10, wherein said 3D image data comprises image intensities, said image intensities having a dynamic signal range.

29. A computer program comprising code means for performing the steps of the method of any one of claims 10-28, wherein said computer program execution is carried on a computer.

30. A non-transitory computer-readable medium storing thereon executable instructions, that when executed by a computer, cause the computer to execute the method of any one of claims 10-28 for predicting ~~the~~ a risk of a vertebral fracture in an individual.