Classification of Benign and Malignant Vertebral Compression Fractures in Magnetic Resonance Images

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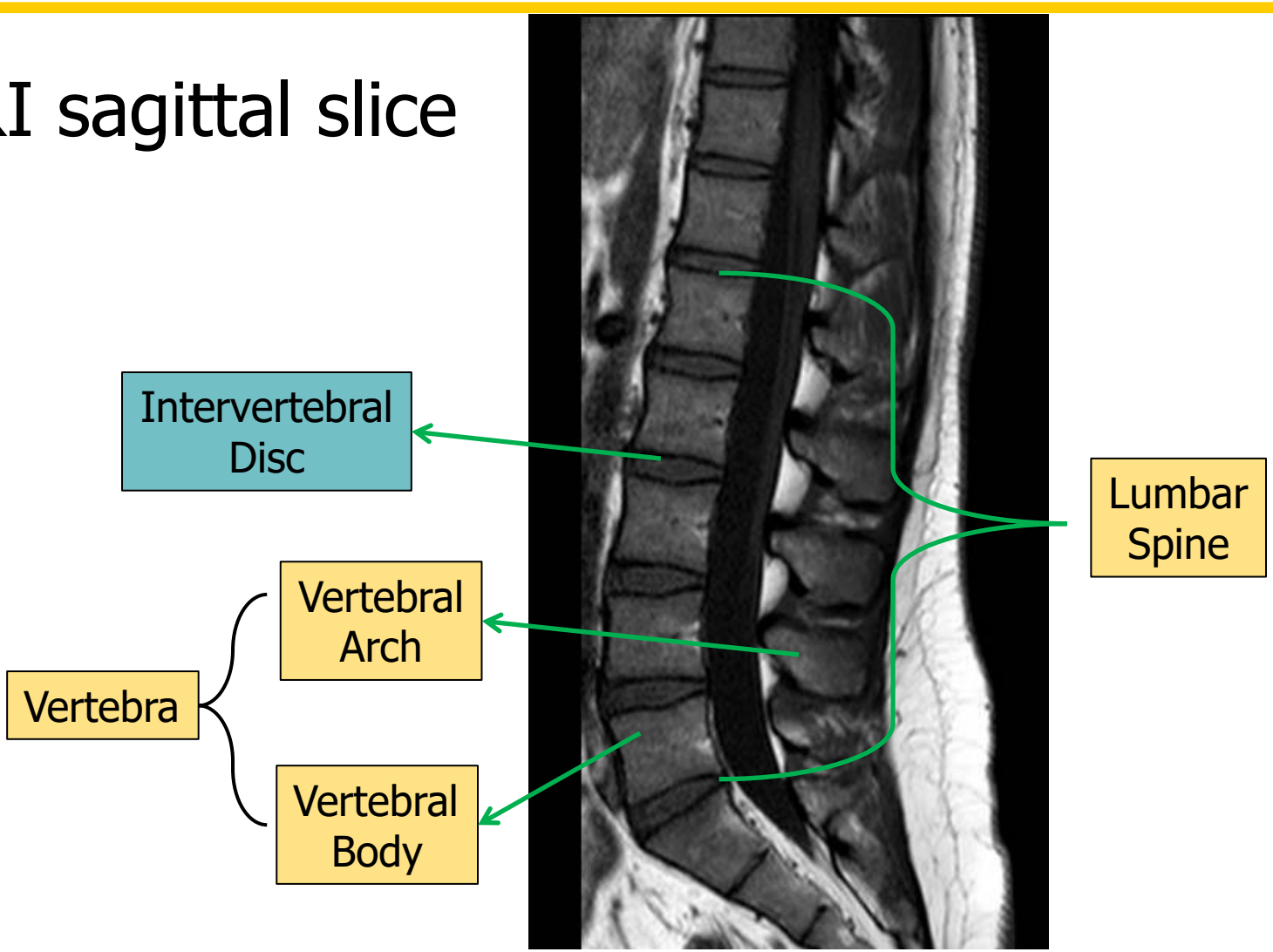
Anatomy of the spine

- MRI sagittal slice



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Vertebral compression fractures (VCFs)

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- Partial collapse of vertebral bodies
- Traumatic VCFs raise no doubt about their etiology
- But a recent vertebral collapse without history of significant trauma creates difficulty in defining the cause of the VCF

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Medical diagnosis

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- Young patient with a VCF
- History of significant acute trauma
- Usually easy diagnosis

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Medical diagnosis

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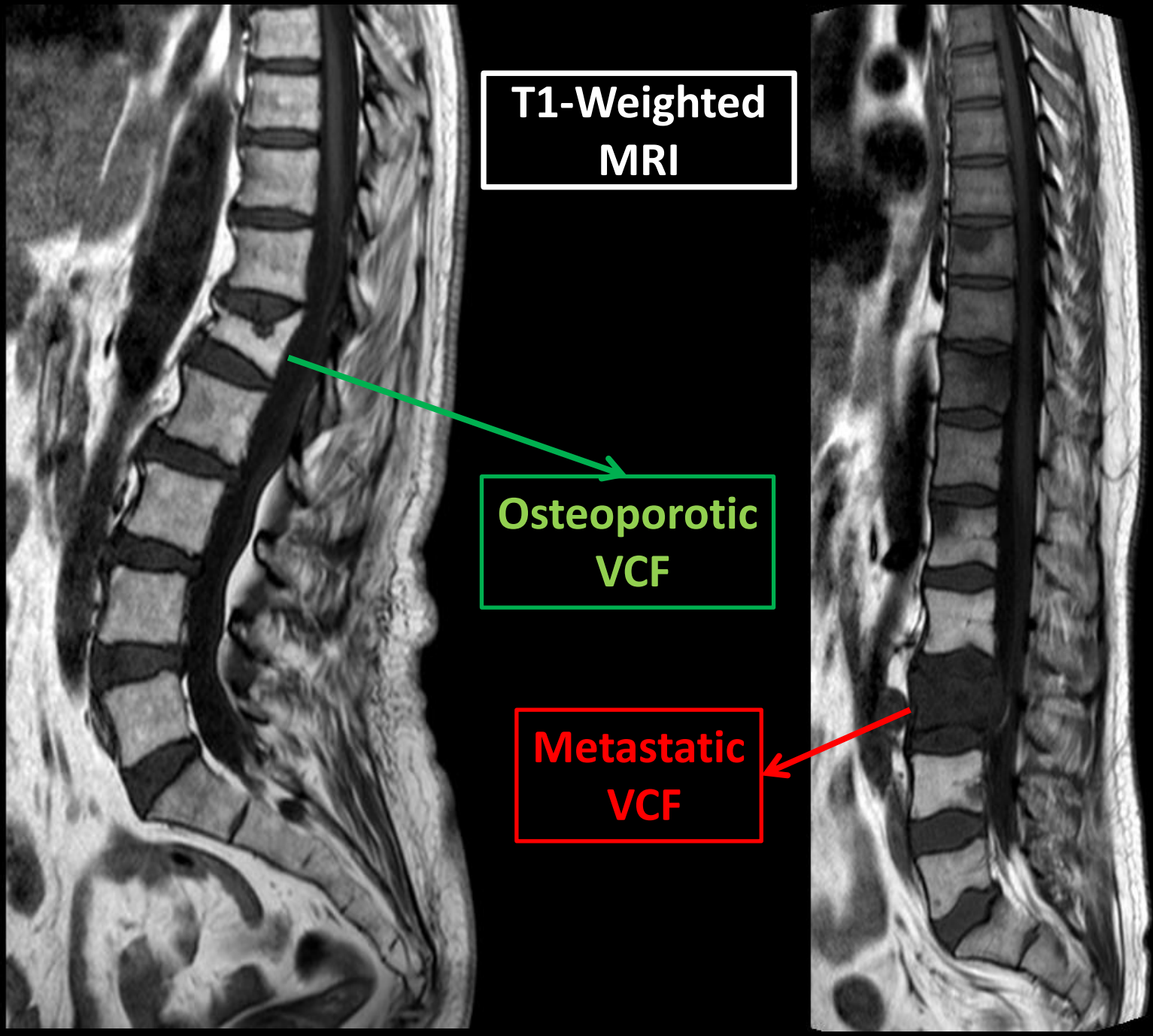
- Elderly patient with VCF
- No history of significant acute trauma
- Diagnosis ?

VCFs without history of significant trauma

- VCFs are the most common type of osteoporotic fractures
- The elderly have a high incidence of VCFs related to metastatic cancer affecting bone
- MRI is the most commonly used imaging method for spinal diseases and early detection of fractures


T1-Weighted MRI
Osteoporotic VCF
Metastatic VCF

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Clinical classification of VCFs

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- Osteoporotic VCFs
  - classified as Benign VCFs
- Metastatic VCFs
  - classified as Malignant VCFs

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Benign VCFs in T1-weighted MRI

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- Partial preservation of normal fatty bone-marrow signal in the vertebral body
- Spatially limited loss of T1 signal intensity
- Degeneration of normally rectangular shapes of vertebrae into concave and rough shapes with indentations
- Rougher contours than malignant VCFs and normal vertebrae

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Malignant VCFs in T1-weighted MRI

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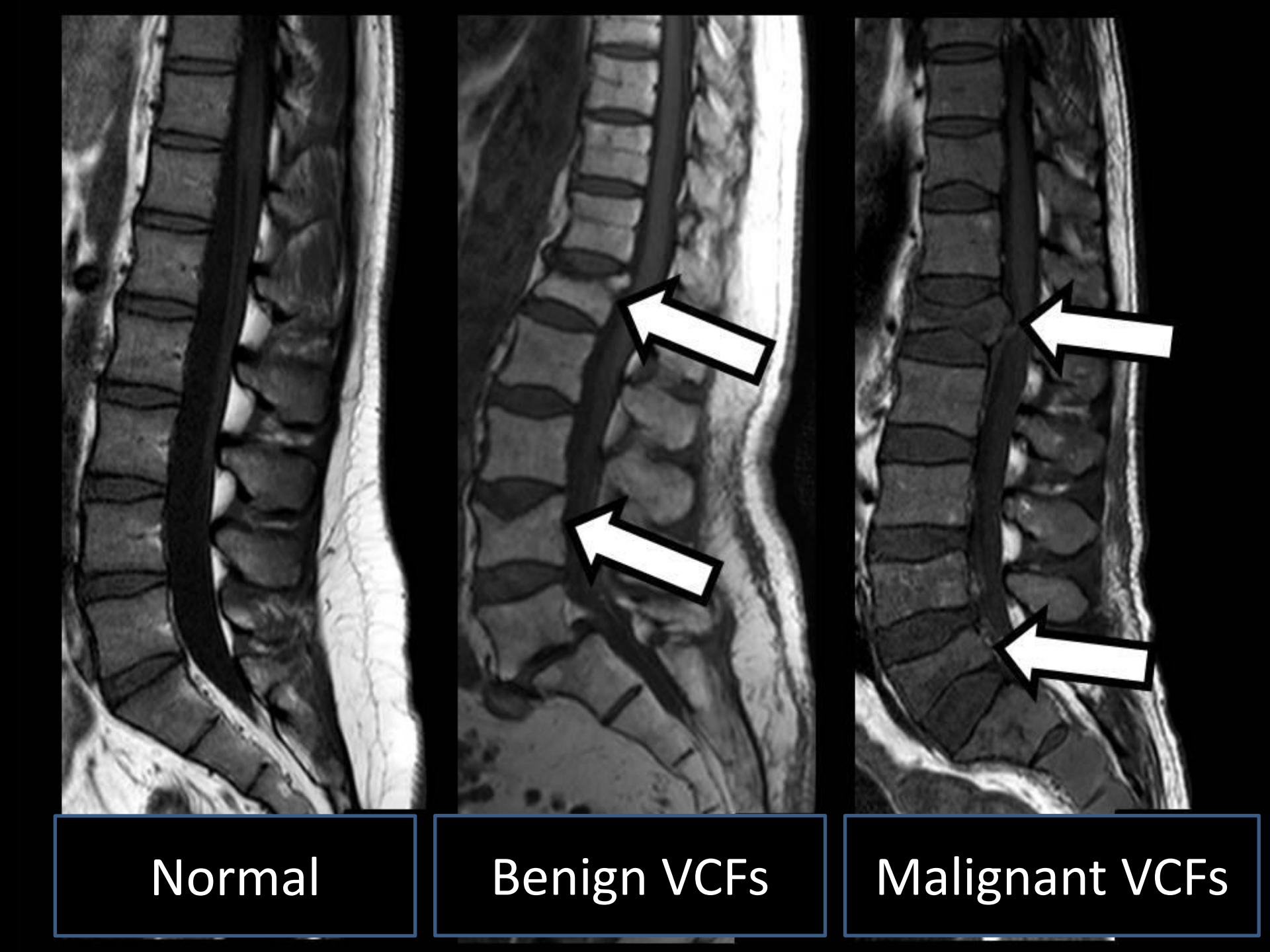
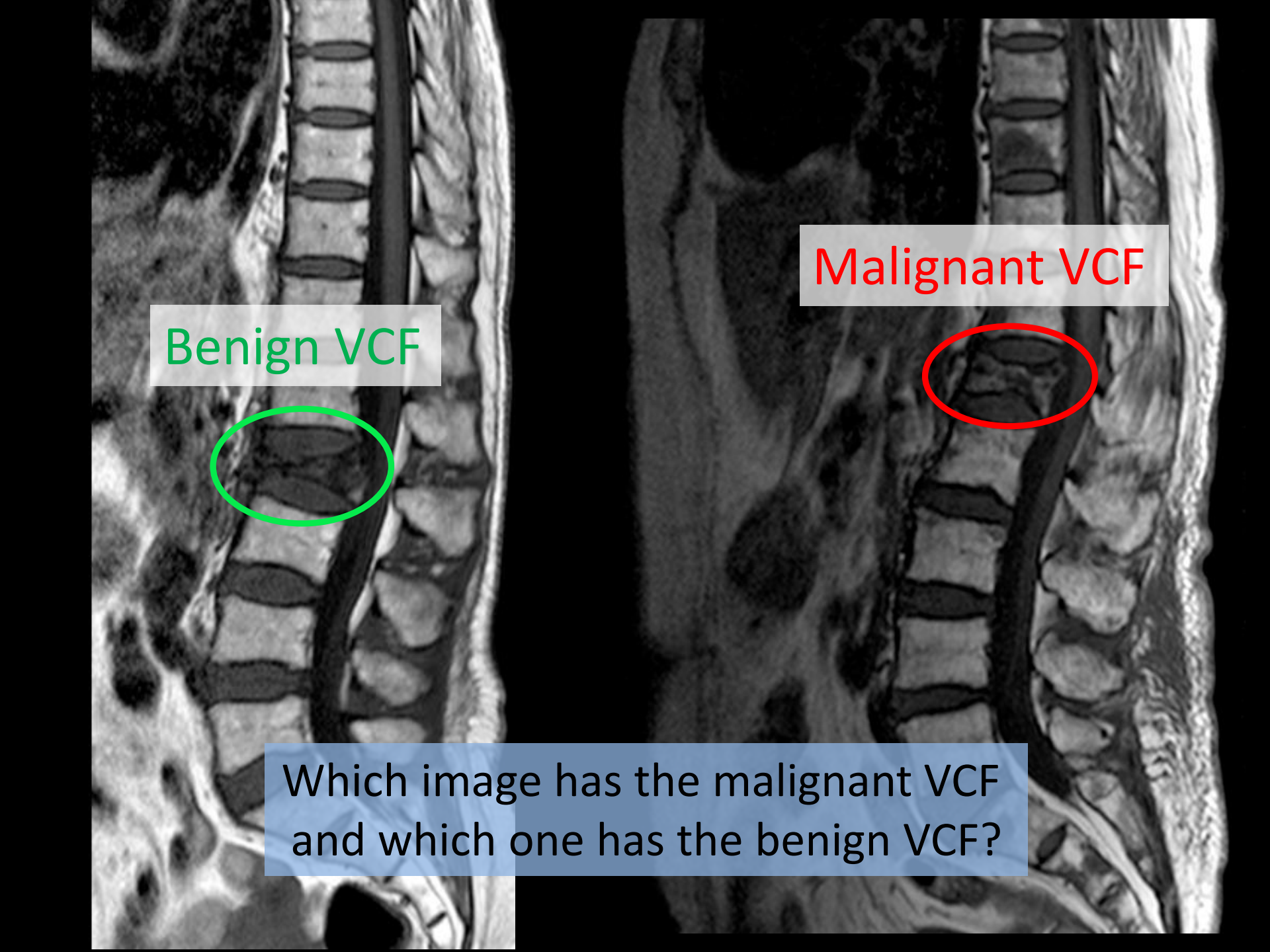
- Reduction of T1 signal intensity or nodular abnormality all over the affected vertebra
- Could result in a posterior convexity without substantial concavities
- May also cause the contours of vertebrae to be relatively smoothened due to convexity


Normal
Benign VCFs
Malignant VCFs

Benign vs Malignant VCFs

- Both tend to create concavities in the vertebral plateaus
- Could cause doubt in the diagnosis
- Correct classification is critical for planning treatment


Benign VCF
Malignant VCF
Which image has the malignant VCF
and which one has the benign VCF?

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Objectives

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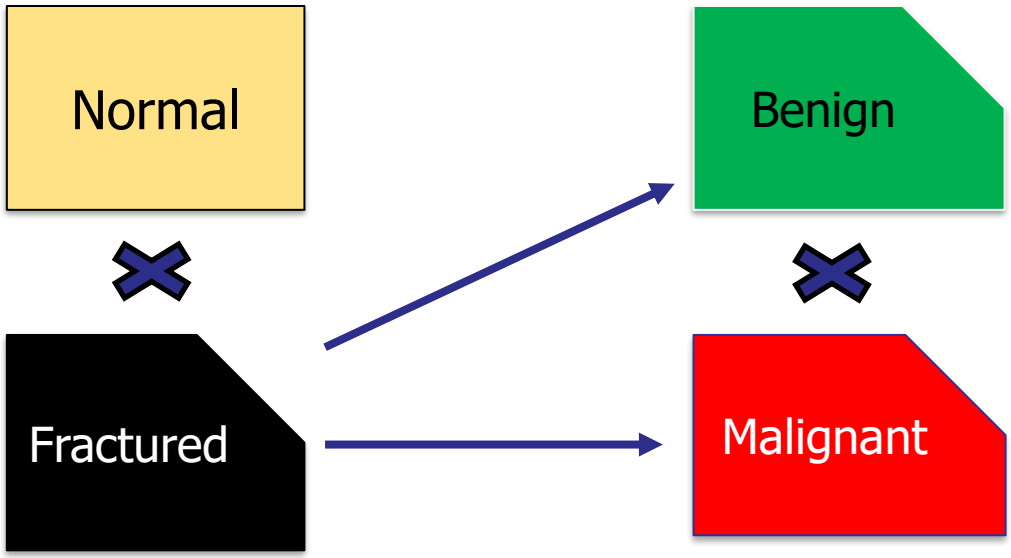
- Study the characteristics of VCFs in MRI
- Develop image processing techniques to extract features
- Classify VCFs



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Study steps

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- Selection of cases and images
- Manual segmentation of vertebral bodies
- Extraction of features of vertebral bodies
- Classification, validation, and statistical analysis

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Database

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- University Hospital of Ribeirão Preto Medical School – University of São Paulo
- Cases and images collected from the Radiology Information System (RIS)
- Cases from September 2010 to March 2014
- Philips 1.5T MRI System – T1-weighted MRI

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Database

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- Lumbar vertebral bodies (L1 to L5)
- Median sagittal slice
- TIFF images with 8-bits/pixel
- 153 exams analyzed, 63 selected
- 38 women, 25 men
- Mean age: 62 years

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Database

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- 63 selected exams:
  - At least one VCF per patient
  - The nonfractured vertebral bodies of patients without malignant fractures are considered to be normal

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Excluded cases

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- Vertebral fractures secondary to trauma
- Infection and avascular necrosis
- Severe degenerative scoliosis
- Previous surgeries, radiotherapy, and chemotherapy

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Database

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	L5	L4	L3	L2	L1	Total
Benign VCFs	6	7	9	10	21	53
Malignant VCFs	9	11	10	10	9	49
Normal	26	24	23	22	11	106
Total	41	42	42	42	41	208

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Examples of vertebral bodies

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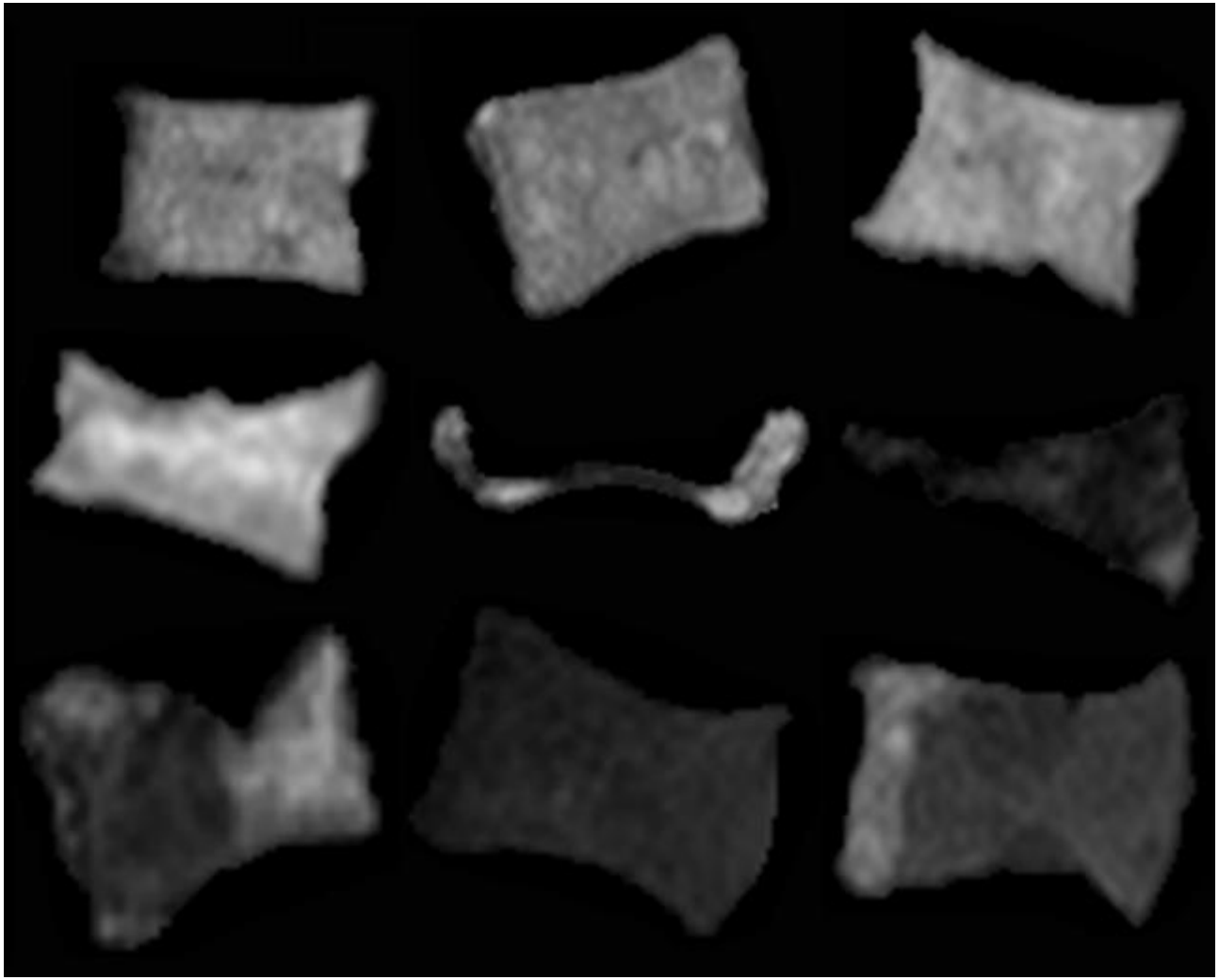
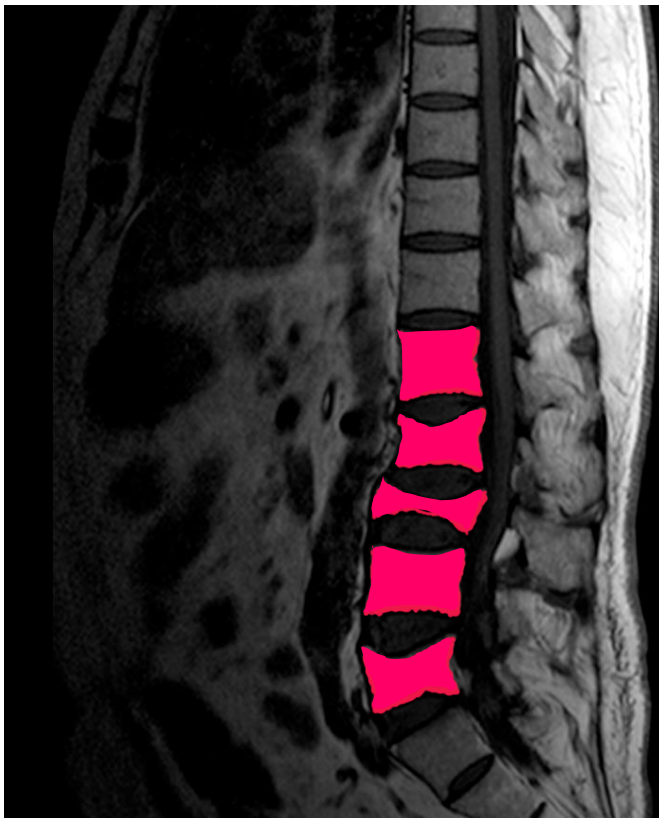
Normal

Benign VCFs

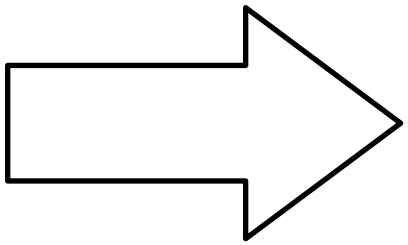
Malignant VCFs

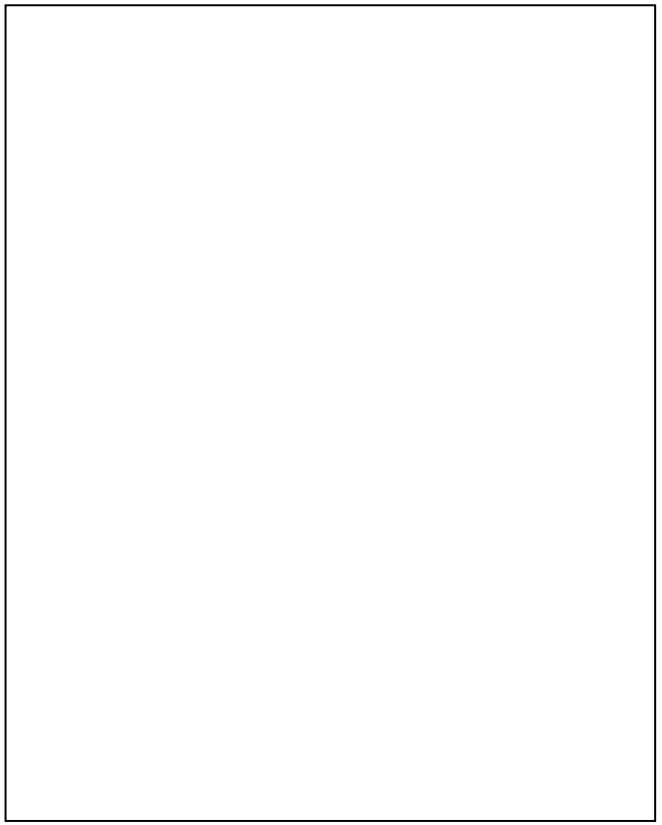


Manual segmentation



MRI exam





Vertebral body masks

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Software flow chart

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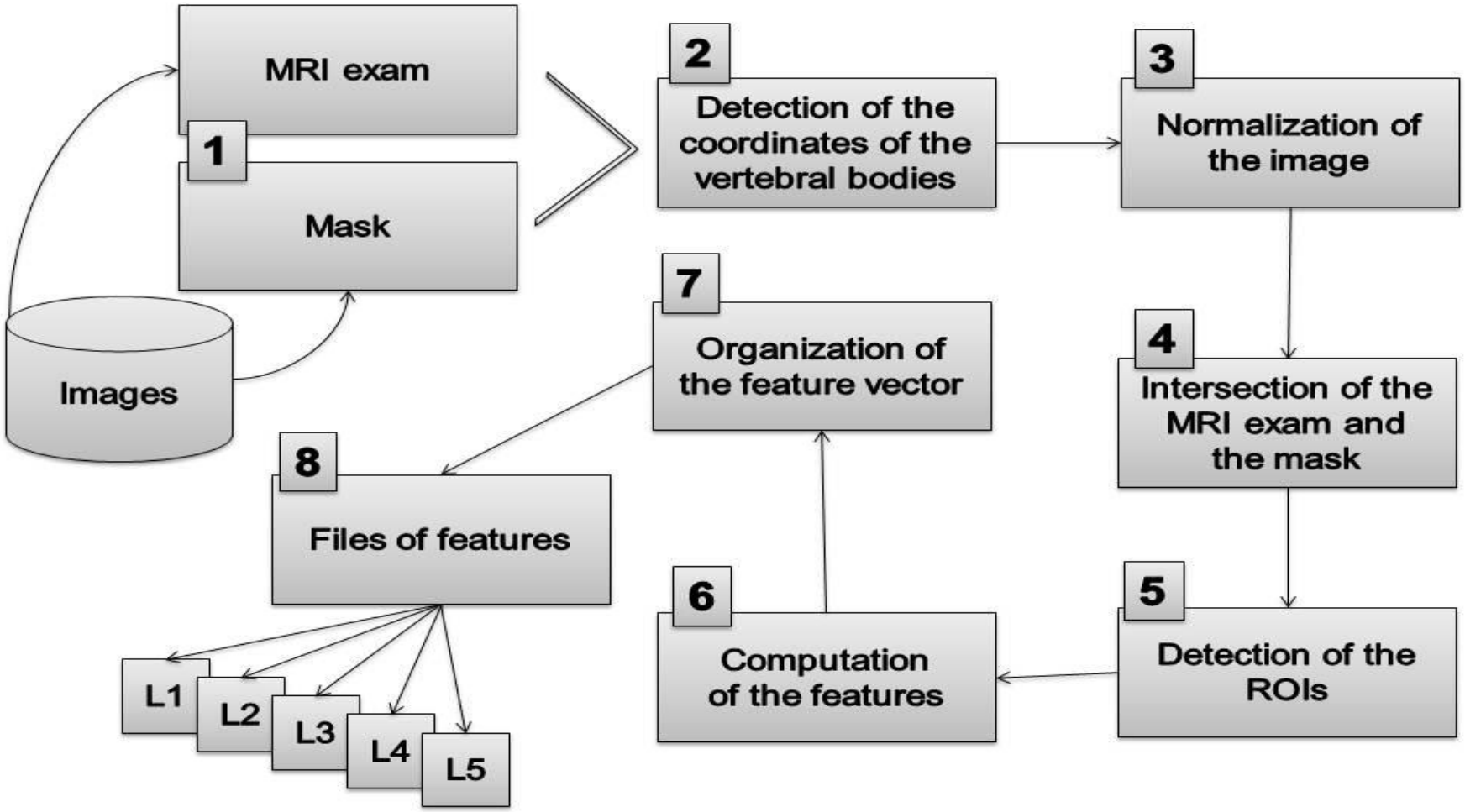

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MRI exam and its mask

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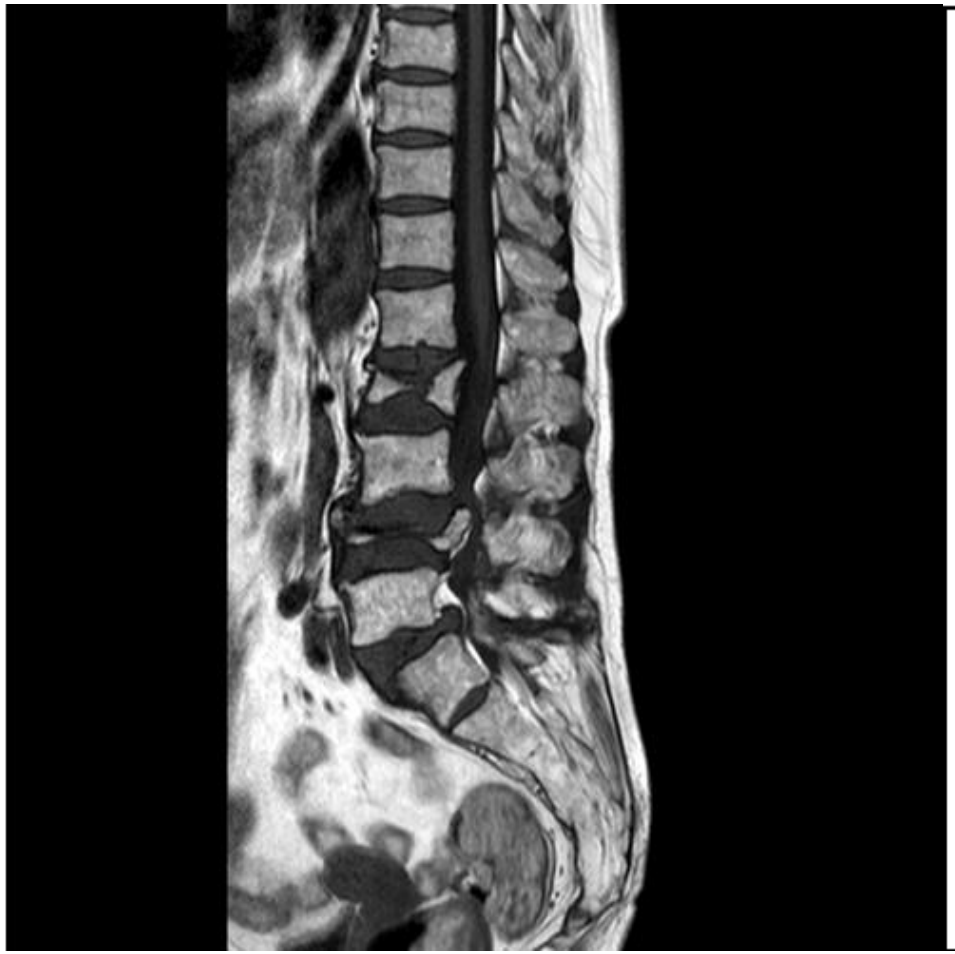

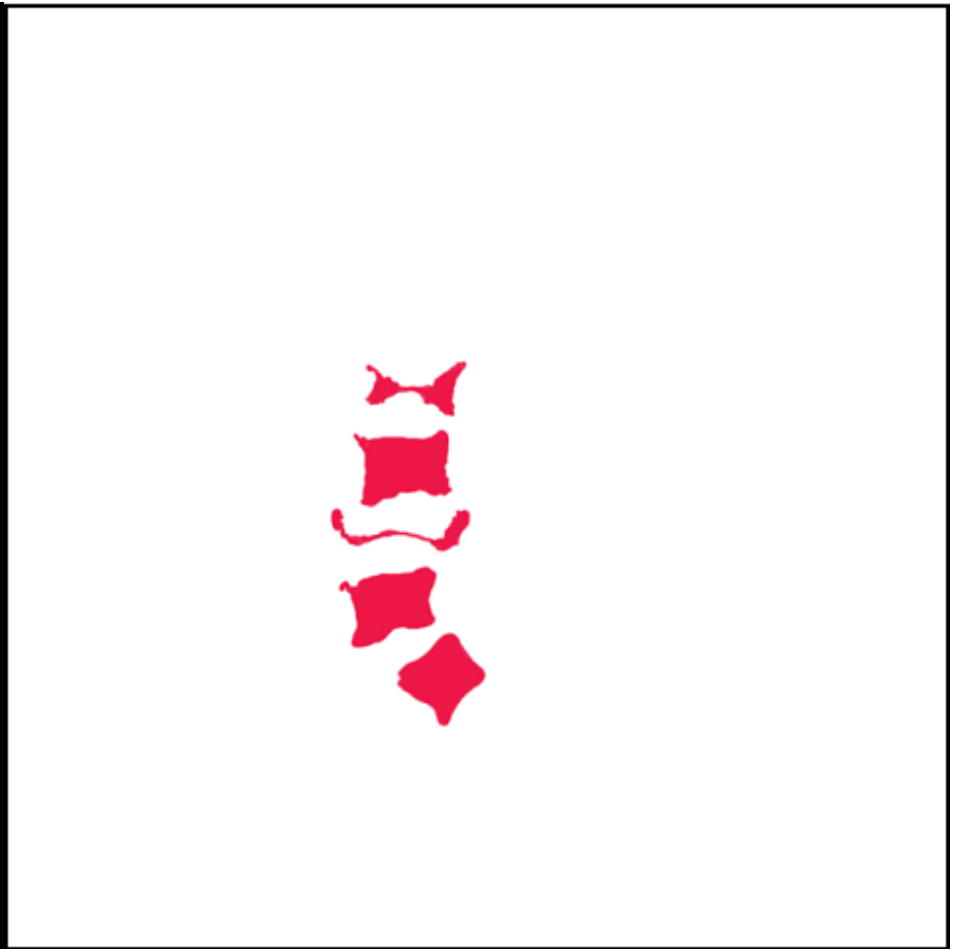

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Detection of the coordinates of the vertebral bodies

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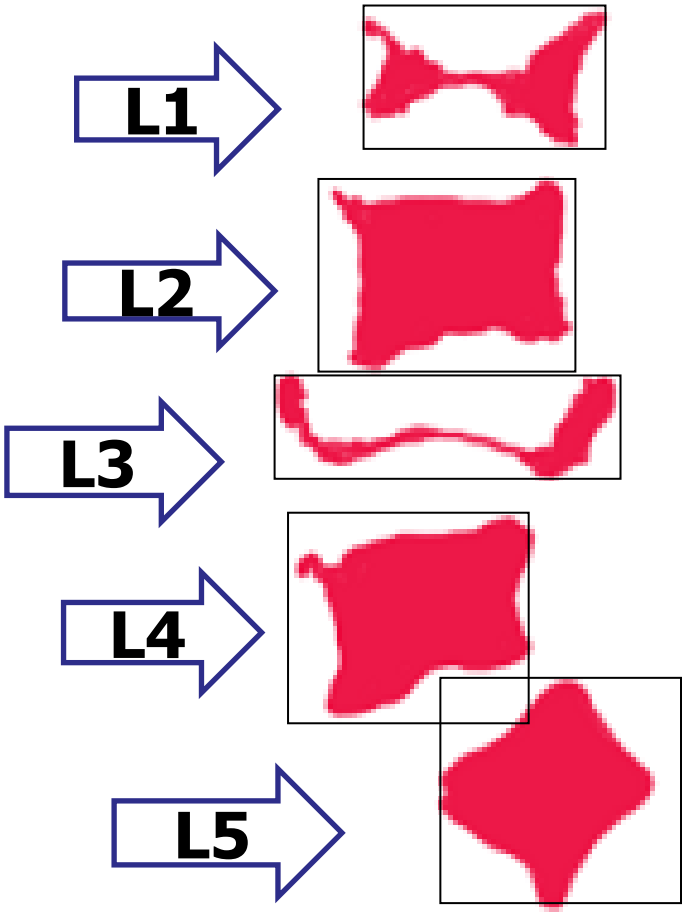

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Normalization of the MR images

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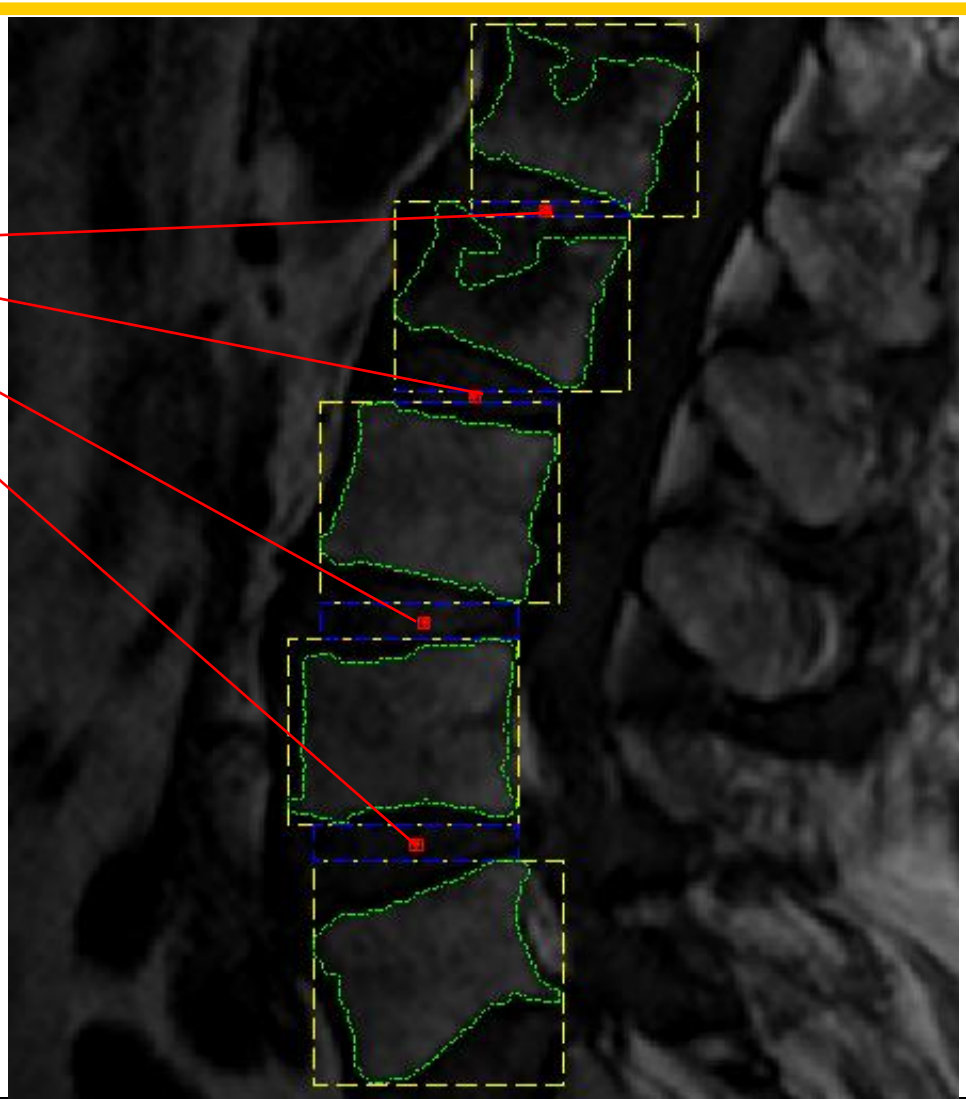
DiscsMean

Extraction of blocks of intervertebral discs using the mask ROIs as reference

5x5 disc block



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Normalization of the MR images

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$$newImg(i,j) = \frac{imgOriginal(i,j)}{discsMean}$$

$$\boldsymbol{imgNorm(i,j)} = 255 \times \frac{newImg(i,j) - \min(newImg)}{\max(newImg) - \min(newImg)}$$

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MRI exam ∩ Mask

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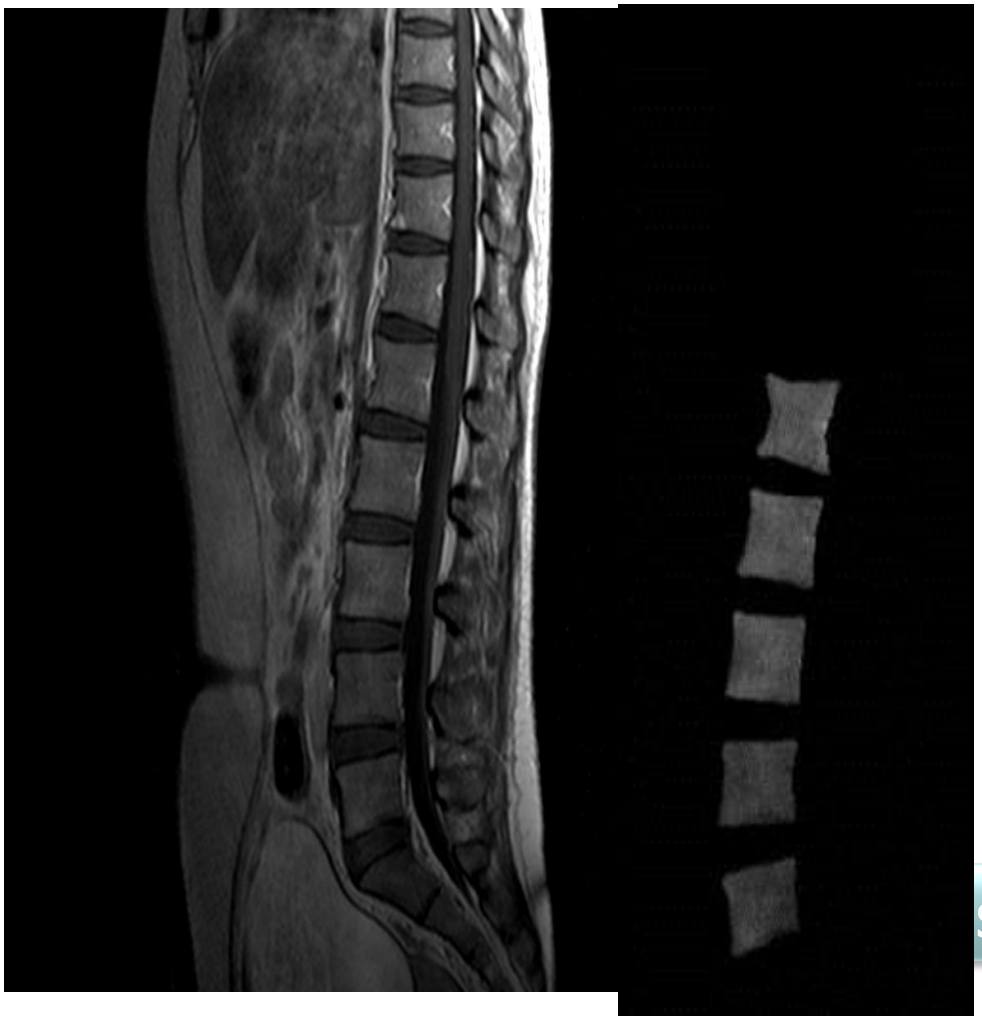

ssing new image...

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Detection of the ROIs

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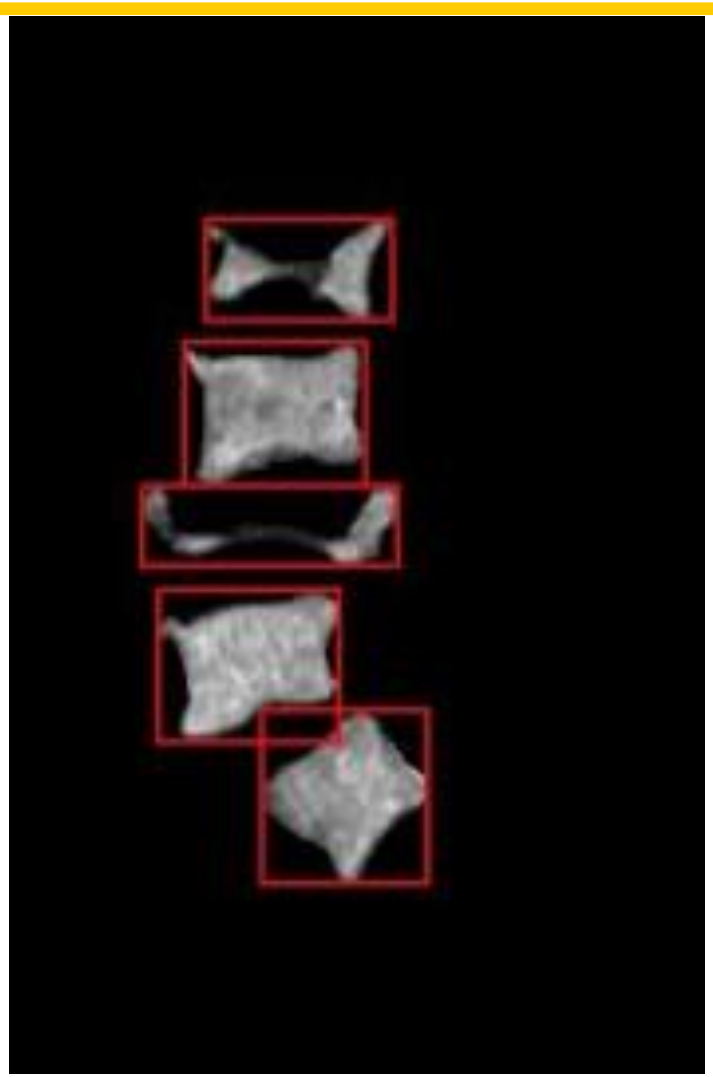

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ROIs of the vertebral bodies

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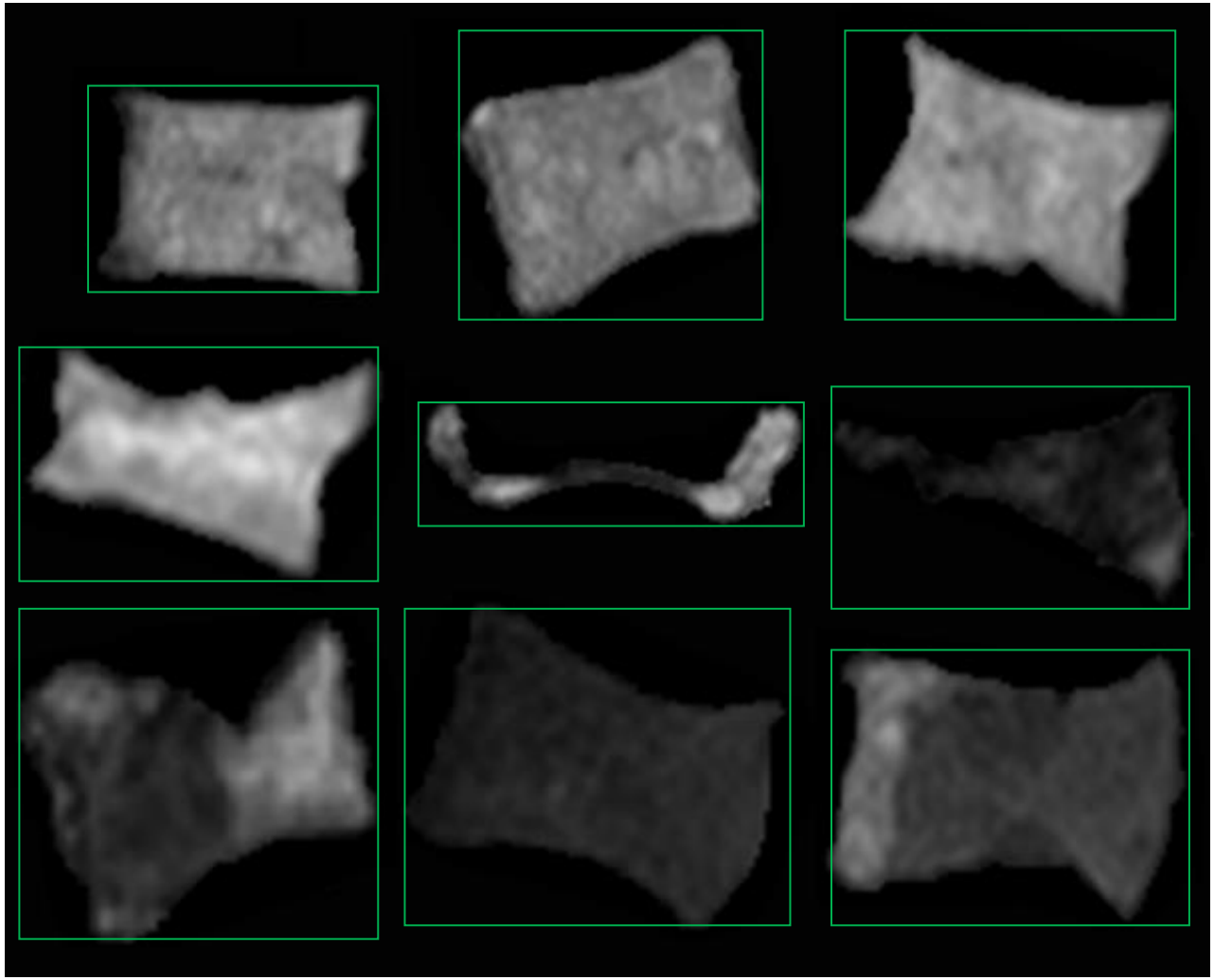
Normal

Benign VCFs

Malignant VCFs



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Computation of the features

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- 3 Statistical gray-level features
- 14 Texture features
- 10 Shape features

27 Features

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Statistical gray-level features

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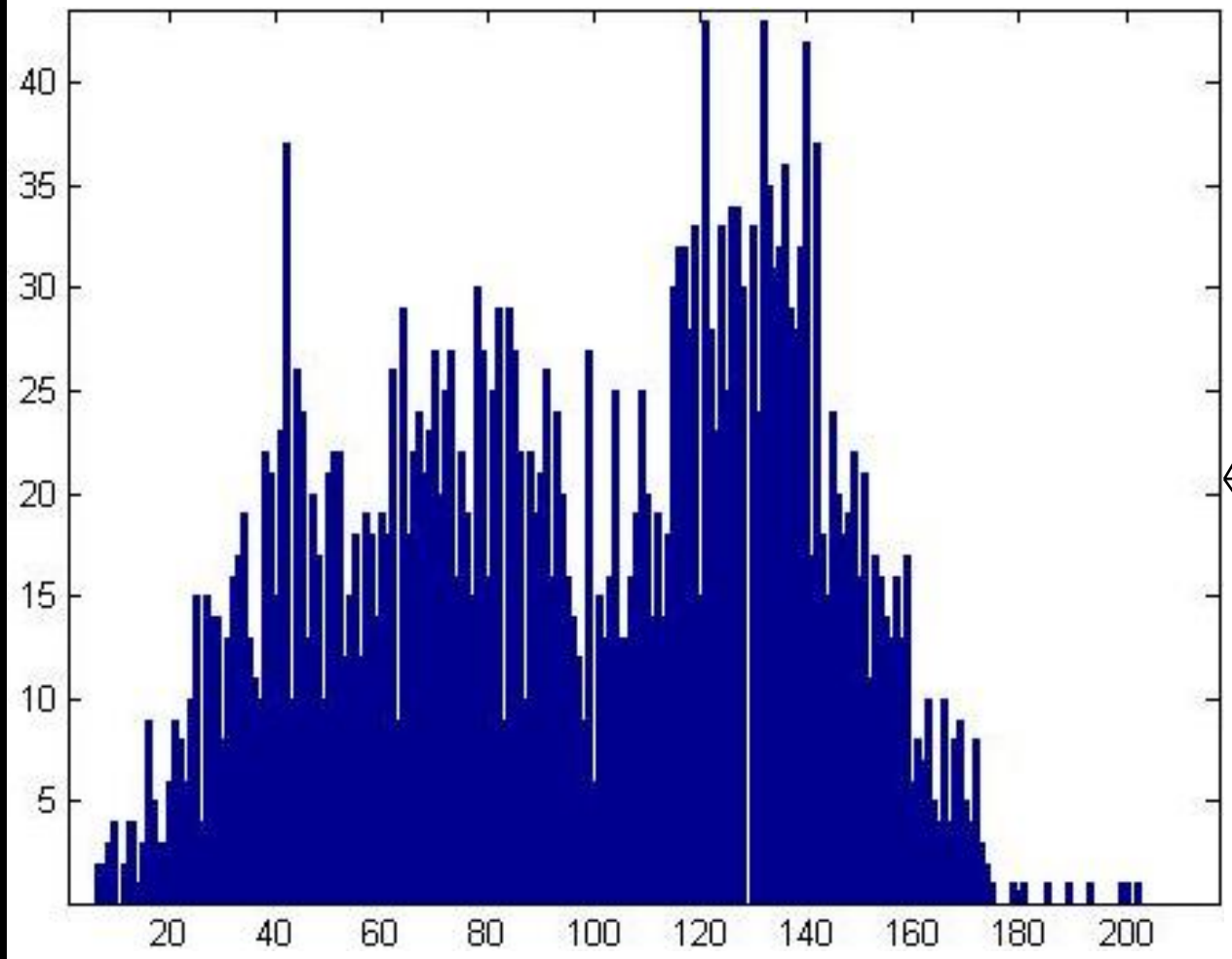

- Coefficient of variation
- Skewness
- Kurtosis

Statistical gray-level features

- Coefficient of variation (CV)

$$\mu = \sum_{l=0}^{L-1} l\, p(l)$$

$$\sigma = \sqrt{\sum_{l=0}^{L-1} (l-\mu)^2\ p(l)}$$

$$CV = \frac{\sigma}{\mu}$$

l = gray level, $[0, L-1]$

$p(l)$ = probability of occurrence of gray level l

Statistical gray-level features

- Skewness

$$skewness = \frac{1}{\sigma^3} \sum_{l=0}^{L-1} (l - \mu)^3 \, p(l)$$

Statistical gray-level features

- Kurtosis

$$kurtosis = \frac{1}{\sigma^4} \sum_{l=0}^{L-1} (l - \mu)^4 \, p(l)$$

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Differences in texture between normal and VCFs

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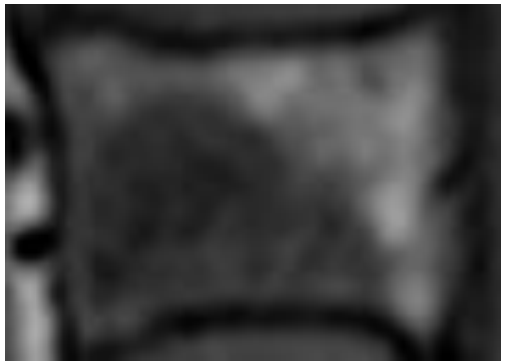
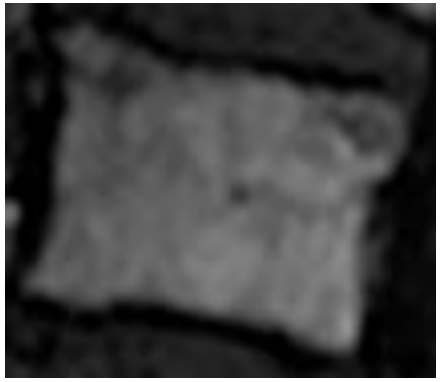
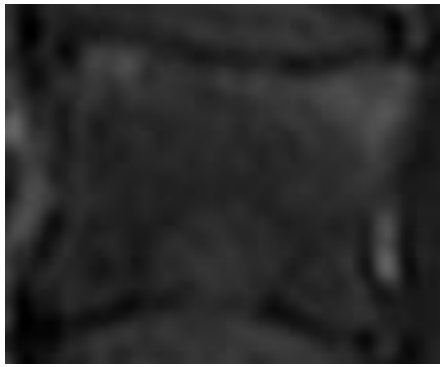


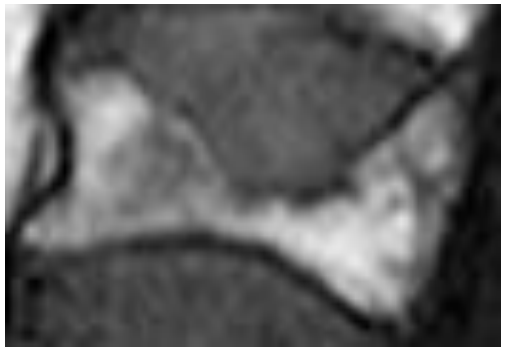
Malignant VCF



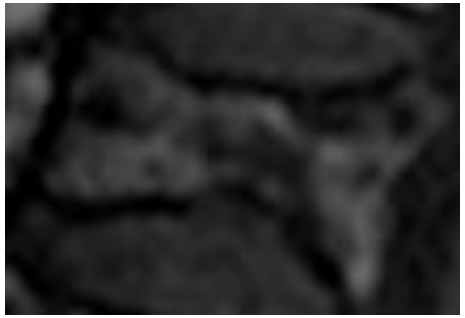
Normal



Malignant VCF



Benign VCF



Malignant VCF

Malignant VCF

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Texture features

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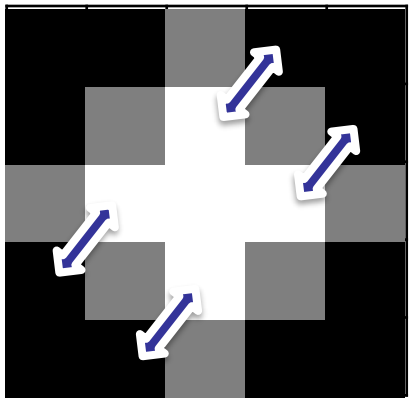
Gray-level cooccurrence matrix

14 texture features of Haralick et al.

Cooccurrence matrix

Ex: Image 5x5 pixels, 3 gray levels

Cooccurrence matrix $p(i,j)$ for $i = 0,\ \ j = 2$



0	1	2

Distance = 1 pixel

Angle = ±45°

	0	1	2
0	2	2	4
1	2	4	2
2	4	2	2

Number of pixels of intensity 0 that are at ±45 degrees and distance 1 of pixels of intensity 2

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- Angular second moment (Energy)

$$f_1 = \sum_i \sum_j \{p(i,j)\}^2$$

- Contrast

$$f_2 = \sum_{n=0}^{Ng-1} n^2 \left\{ \sum_{i=1}^{Ng} \sum_{j=1}^{Ng} p(i,j) \right\}; n = |i-j|$$

Ng: number of gray levels in the quantized image
p(i,j): normalized to probability density function

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- Correlation

$$f_3 = \frac{\sum_i \sum_j (ij)\, p(i,j) - \mu_x\, \mu_y}{\sigma_x\, \sigma_y}$$

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- μ_x , μ_y means
- σ_x , σ_y standard deviations

$$p_x(i) = \sum_{j=1}^{Ng} p(i,j) \qquad p_y(j) = \sum_{i=1}^{Ng} p(i,j)$$

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- Sum of squares: Variance

$$f_4 = \sum_i \sum_j (i - \mu)^2 \, p(i,j)$$

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- Inverse difference moment

$$f_5 = \sum_i \sum_j \frac{1}{1 + (i - j)^2} p(i, j)$$

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- Sum average

$$f_6 = \sum_{i=2}^{2Ng} i\, p_{x+y}(i)$$

- Sum variance

$$f_7 = \sum_{i=2}^{2Ng} (i - f_6)^2\, p_{x+y}(i)$$

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$$p_{x+y}(k) = \sum_{\substack{i=1 \\ k=i+j}}^{Ng} \sum_{j=1}^{Ng} p(i,j) \qquad k = 2,3,\ldots,2Ng$$

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- Sum entropy

$$f_8 = -\sum_{i=2}^{2Ng} p_{x+y}(i)\ \log\{\, p_{x+y}(i)\}$$

- Entropy

$$f_9 = -\sum_{i}\sum_{j} p(i,j)\ \log\{\, p(i,j)\}$$

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- Difference variance

$$f_{10} = \text{variance of } p_{x-y}$$

- Difference entropy

$$f_{11} = -\sum_{i=0}^{Ng-1} p_{x-y}(i) \log\{p_{x-y}(i)\}$$

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$$p_{x-y}(k) = \sum_{\substack{i=1 \\ k=|i-j|}}^{Ng} \sum_{j=1}^{Ng} p(i,j) \qquad k = 0,1,\ldots,Ng-1$$

14 texture features of Haralick et al.

- Information measures of correlation 1

$$f_{12} = \frac{HXY - HXY1}{\max\{HX, HY\}}$$

- Information measures of correlation 2

$$f_{13} = \{\, 1 - \exp[\, -2(HXY2 - HXY)\,]\, \}^{1/2}$$

14 texture features of Haralick et al.

$$HXY = -\sum_i \sum_j p(i,j) \log\{ p(i,j) \}$$

HX and HY are entropy of p_x and p_y

$$HXY1 = -\sum_i \sum_j p(i,j) \log\{ p_x(i)\, p_y(j) \}$$

$$HXY2 = -\sum_i \sum_j p_x(i)\, p_y(j) \log\{ p_x(i)\, p_y(j) \}$$

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- Maximal correlation coefficient

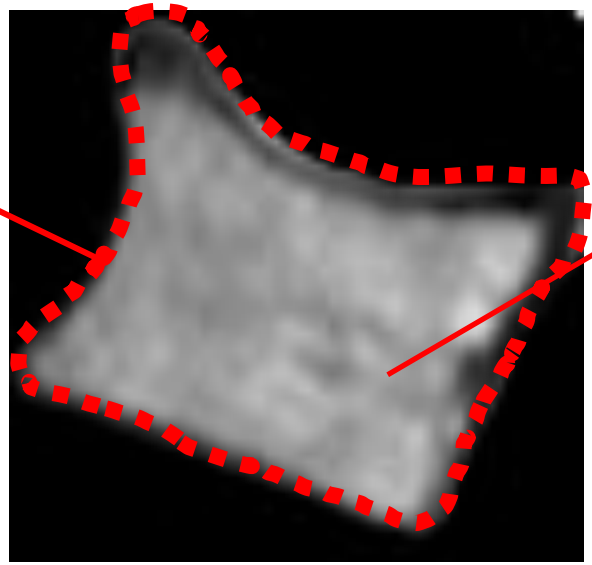
$$f_{14} = (\text{second largest eigenvalue of } Q)^{1/2}$$

where $$Q(i,j) = \sum_k \frac{p(i,k)\, p(j,k)}{p_x(i)\, p_y(k)}$$

Shape features

- Compactness C_o

$$C_o = 1 - \frac{4\pi A}{P^2}$$



Perimeter P

Vertebral area A

Shape features

- Fourier-descriptor-based feature *FDF*

$$Z(k) = \frac{1}{N} \sum_{n=0}^{N-1} z(n) \exp\left[- j \frac{2\pi}{N} nk \right]$$

$k = -N/2+1, \ldots, -1, 0, 1, 2, \ldots, N/2$

$z(n) = x(n) + j\, y(n)$

$n = 0, 1, \ldots, N-1$

Shape features

- Fourier-descriptor-based feature *FDF*

$$FDF = \frac{\sum_{k=k1}^{N/2} |Z(k)|^2 + \sum_{-N/2+1}^{k=-k1} |Z(k)|^2}{\sum_{k=-N/2+1}^{N/2} |Z(k)|^2}$$

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Shape features

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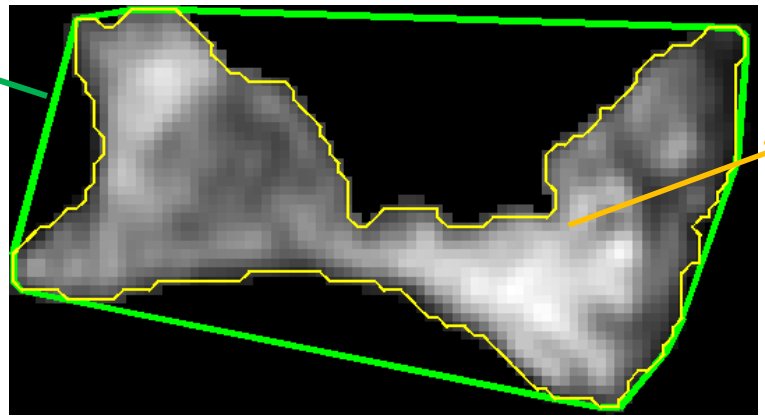
- Convex deficiency *CD*

$$CD = \frac{CH - VA}{VA}$$

Convex hull *CH*



Vertebral area *VA*

Shape features

Moments:

$$m_{pq} = \sum_i \sum_j i^p j^q img(i,j) \quad , \qquad p,q = 0,1,2,\ldots$$

$$\bar{x} = \frac{m_{10}}{m_{00}} \qquad \bar{y} = \frac{m_{01}}{m_{00}}$$

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Shape features

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Central Moments:

$$\mu_{00} = m_{00} = \mu$$

$$\mu_{10} = \mu_{01} = 0$$

$$\mu_{20} = m_{20} - \mu\bar{x}^2$$

$$\mu_{11} = m_{11} - \mu\overline{xy}$$

$$\mu_{02} = m_{02} - \mu\bar{y}^2$$

$$\mu_{30} = m_{30} - 3m_{20}\bar{x} + 2\mu\bar{x}^3$$

$$\mu_{21} = m_{21} - m_{20}\bar{y} - 2m_{11}\bar{x} + 2\mu\bar{x}^2\bar{y}$$

$$\mu_{12} = m_{12} - m_{02}\bar{x} - 2m_{11}\bar{y} + 2\mu\bar{x}\,\bar{y}^2$$

$$\mu_{03} = m_{03} - 3m_{02}\bar{y} + 2\mu\bar{y}^3$$

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Shape features

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Seven invariant moments (Hu):

$$M_1 = \mu_{20} + \mu_{02}$$

$$M_2 = (\mu_{20} - \mu_{02})^2 + 4\mu_{11}^2$$

$$M_3 = (\mu_{30} - 3\mu_{12})^2 + (3\mu_{21} - \mu_{03})^2$$

$$M_4 = (\mu_{30} + \mu_{12})^2 + (\mu_{21} + \mu_{03})^2$$

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Shape features

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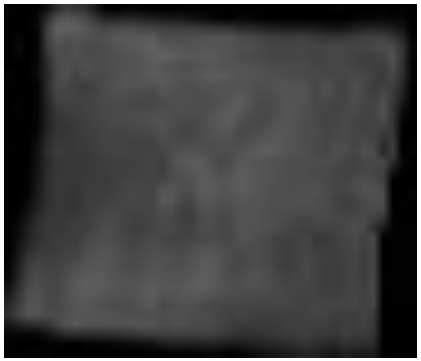
$$M_5 = (\mu_{30} - 3\mu_{12})(\mu_{30} + \mu_{12})[(\mu_{30} + \mu_{12})^2 - 3(\mu_{21} + \mu_{03})^2] + (3\mu_{21} - \mu_{03})(\mu_{21} + \mu_{03})[3(\mu_{30} + \mu_{12})^2 - (\mu_{21} + \mu_{03})^2]$$

$$M_6 = (\mu_{20} - \mu_{02})[(\mu_{30} + \mu_{12})^2 - (\mu_{21} + \mu_{03})^2] + 4\mu_{11}(\mu_{30} + \mu_{12})(\mu_{21} + \mu_{03})$$

$$M_7 = (3\mu_{21} - \mu_{03})(\mu_{30} + \mu_{12})[(\mu_{30} + \mu_{12})^2 - 3(\mu_{21} + \mu_{03})^2] - (\mu_{30} - 3\mu_{12})(\mu_{21} + \mu_{03})[3(\mu_{30} + \mu_{12})^2 - (\mu_{21} + \mu_{03})^2]$$

Organization of the feature vector

1	2	3	...	27
Coefficient of variation	Skewness	Kurtosis	...	M_7



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Files of features

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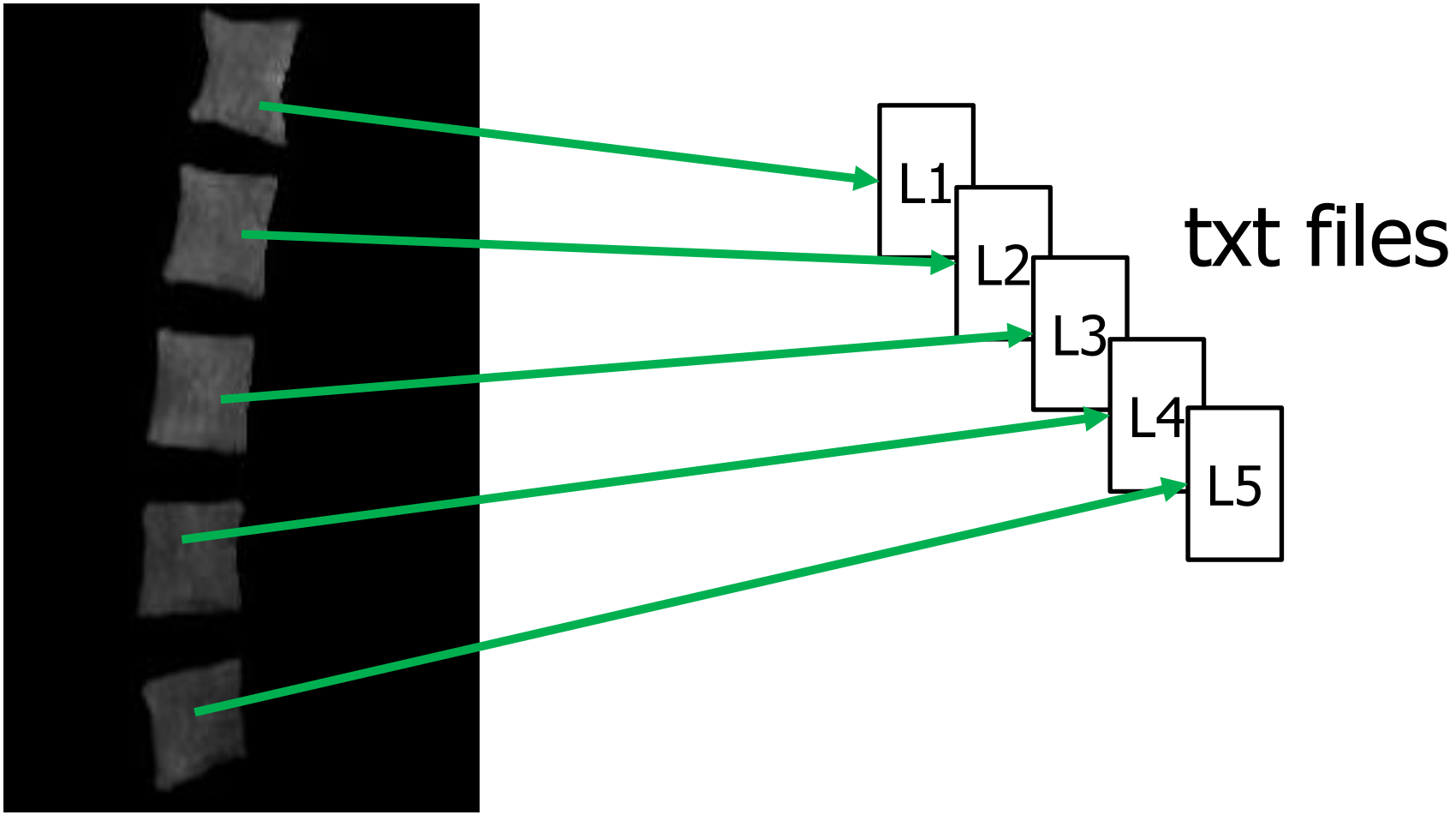
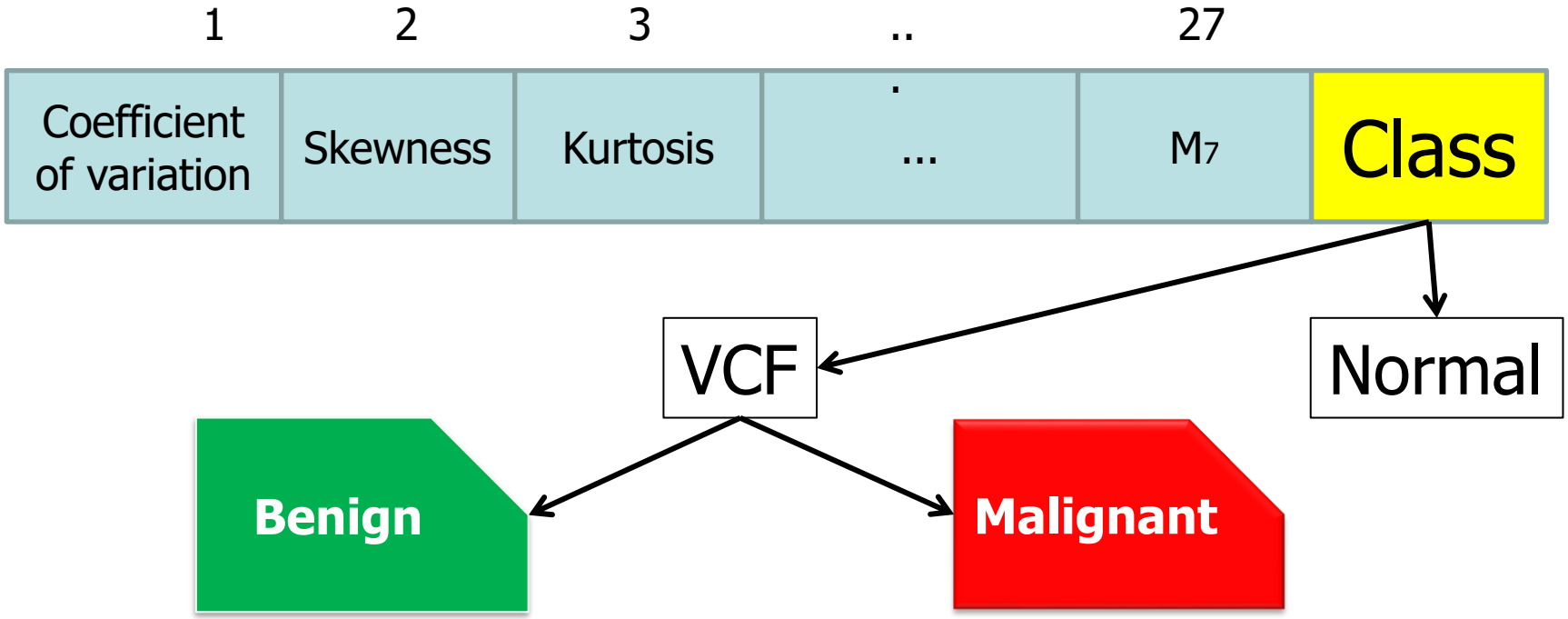


Inserting the reference classification

- Manual addition of the class
- Classification according to radiologist and biopsy



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Feature selection

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- Software WEKA
- Wrapper method for feature selection
  - kNN with k = 1, 3, ..., 13
  - Naïve Bayes
  - RBF network
- Best first as search method
  - Greedy search for the best subset of features

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Classification

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- Software WEKA
- Classifiers:
  - k-nearest neighbor: k = 1, 3, 5, 7, 9, 11, 13
  - Naïve Bayes
  - RBF network
- Stratified 10-fold cross-validation
  - 9 folds for training, 1 fold for test

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Clinical Classes

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- VCF vs Normal
- Benign VCF vs Malignant VCF
- Malignant VCF, Benign VCF, and Normal

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Validation

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- Confusion Matrix
  - Sensitivity
  - Specificity
  - AUROC
  - % of correct classification

A_z and p-values

- p-values obtained using Wilcoxon rank-sum test
- NS indicates no significant difference
- NA indicates that A_z could not be obtained

- * for $0.01 \leq p < 0.05$
- ** for $0.001 \leq p < 0.01$
- *** for $p < 0.001$

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A_z and p-values

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	Benign VCF versus Malignant VCF		All VCFs together versus Normal	
Feature	Significance	A_z	Significance	A_z
CV	NS	0.580	***	0.751
$Skew$	***	0.861	*	0.549
$Kurt$	***	0.824	NS	0.532
H_1	***	0.849	NS	0.625
H_2	***	0.866	*	0.661
H_3	NS	0.480	NS	0.629
H_4	***	0.874	NS	0.642
H_5	***	0.844	*	0.577
H_6	***	0.829	***	0.731
H_7	***	0.871	NS	0.640
H_8	***	0.854	**	0.620
H_9	***	0.858	***	0.647
H_{10}	***	0.871	**	0.674

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A_z and p-values

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	Benign VCF versus Malignant VCF		All VCFs together versus Normal	
Feature	Significance	A_z	Significance	A_z
H_{11}	***	0.868	**	0.632
H_{12}	***	0.731	NS	0.524
H_{13}	***	0.854	***	0.614
H_{14}	NS	0.566	NS	0.462
C_o	***	0.722	***	0.864
FDF	***	0.837	NS	0.449
CD	***	0.700	***	0.881
M_1	NS	0.567	***	0.964
M_2	NS	0.518	***	0.932
M_3	**	0.655	*	0.887
M_4	*	0.617	NS	0.936
M_5	NS	0.389	NS	NA
M_6	NS	0.480	NS	0.498
M_7	NS	0.538	NS	NA

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A_z and p-values

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- Benign VCFs versus Malignant VCFs
  - High statistical significance and A_z for texture and gray-level features
  - *FDF* is also highly significant
- All VCFs versus Normal vertebral bodies
  - Poor performance of texture and gray-level features
  - More of the shape features showed high significance and A_z

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Mean and standard deviation of features

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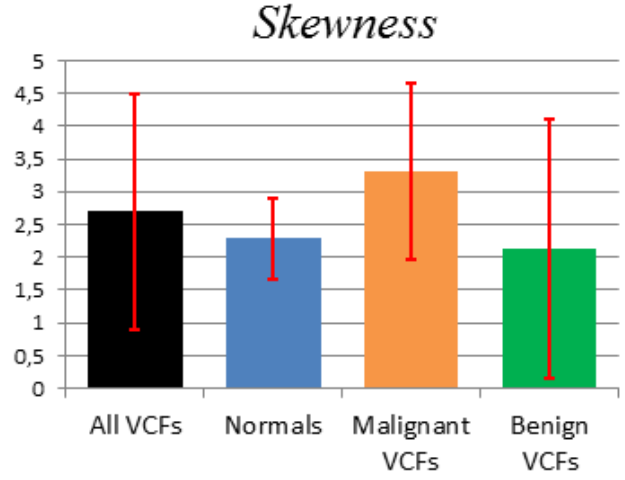

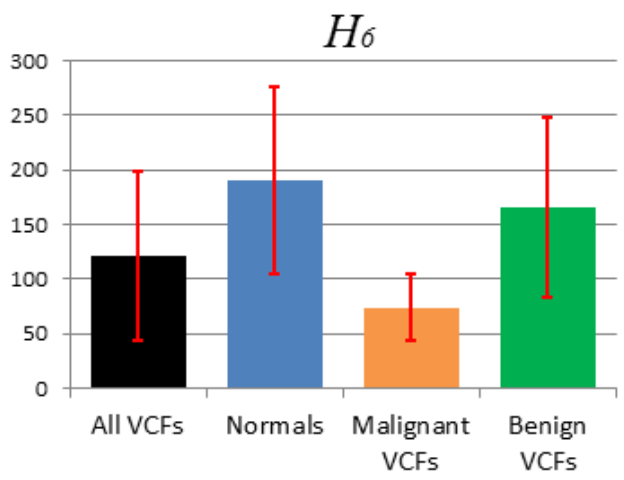

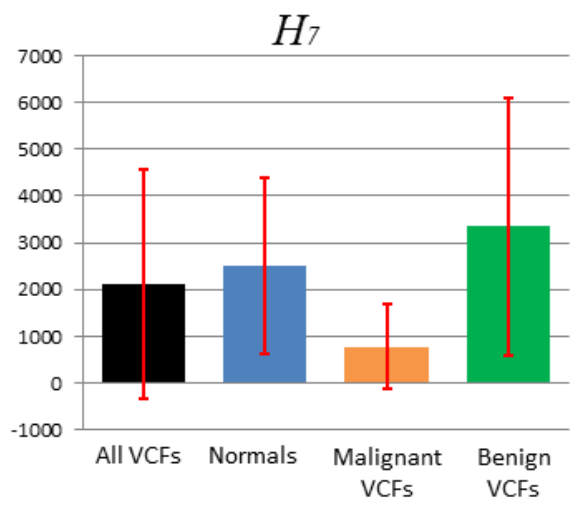

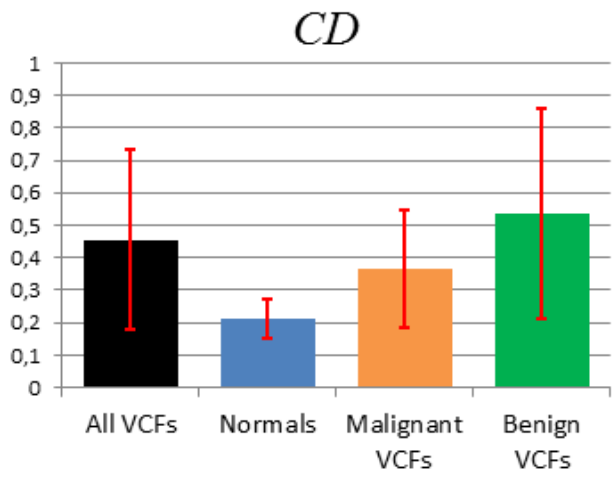

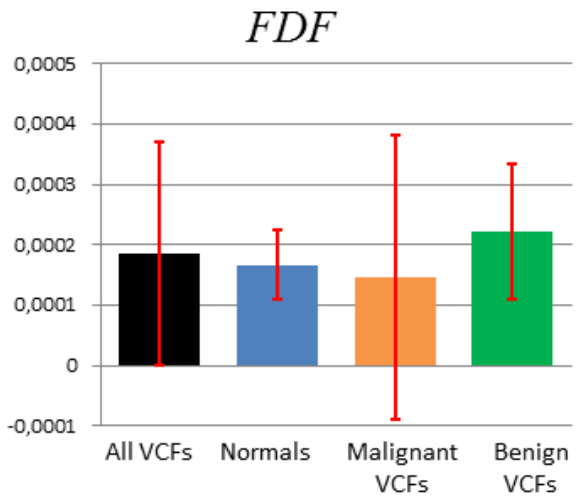

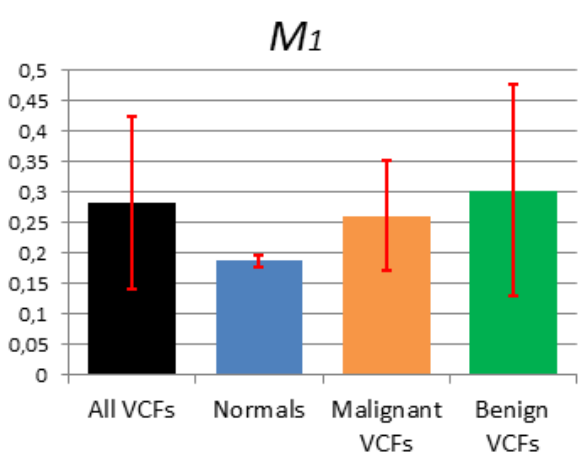

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Mean and standard deviation of features

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- Mean skewness of malignant VCFs is higher than that for benign VCFs
  - T1 signals are distributed more on the lower side of the histogram for malignant VCFs
- H_6 and H_7 show large differences in their mean values for malignant VCFs versus benign VCFs

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Mean and standard deviation of features

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- CD and M_1 show large differences in their mean values for classification of all VCFs together against normal vertebral bodies
- FDF values are, on the average, higher for benign VCFs than for normal vertebrae
- FDF values are lower for malignant VCFs than for normal vertebral bodies

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Feature selection

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- *FDF* is significant for benign vs malignant VCFs
  - *FDF* was selected for all cassifiers of this purpose
- *FDF* is not significant for all VCFs vs normal vertebral bodies
- M_1 is significant for all VCFs vs normal vertebral bodies
  - M_1 was selected for all classifiers of this purpose

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Feature selection

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- *k*-NN did not select the gray-level features for benign vs malignant VCFs
  - FDF, M_5, H_{10}, and H_{13}were selected at least three times
- *CV* is statistically significant for all VCFs vs normal vertebral bodies and was selected for all classifiers

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Feature selection

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- Various texture features were selected for both types of classification

- Naïve Bayes selected the highest number of features for both types of classification

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Classification

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- Benign *vs* malignant VCFs

Classifier		ACC rate %	AUROC
k-NN	k = 7	82.4	0.84
	k = 9	81.4	0.90
	k = 11	84.3	0.90
	k = 13	84.3	0.90
Naïve Bayes		85.3	0.92
RBF network		78.4	0.86

- All VCFs *vs* normal vertebral bodies

Classifier		ACC rate %	AUROC
k-NN	k = 7	90.1	0.95
	k = 9	89.0	0.92
	k = 11	89.0	0.92
	k = 13	89.5	0.94
Naïve Bayes		90.6	0.97
RBF network		91.1	0.94

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Classification

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- RBF network classifier for benign vs malignant VCFs
  - ACC rate was the lowest obtained
  - AUROC is only better than that of 7-NN
- RBF network classifier for all VCFs vs normal vertebral bodies
  - ACC rate is the highest obtained

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Classification

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- AUROC for classification of all VCFs together vs normal vertebral bodies is at least 0.92
- AUROC of the naïve Bayes classifier is 0.97 for this purpose
  - Better than the previous study using only shape features in which AUROC was 0.945
- This shows the importance of texture and gray-level features for this purpose

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Classification

UNIVERSIDADE DE SÃO PAULO

- AUROC for classification of benign vs malignant VCFs is 0.92 for naïve Bayes
  - Better than the previous study in which the highest AUROC was 0.91 for 3-NN
- In a previous study using only shape features the highest AUROC was 0.78
  - This shows the importance of texture and gray-level features for this purpose

Benign VCFs, malignant VCFs, and normal vertebral bodies

Predicted classification			True classification
Malignant VCFs	Benign VCFs	Normal vertebral bodies	
39	5	5	Malignant VCFs
13	35	5	Benign VCFs
4	1	84	Normal vertebral bodies

- Features selected:
  - *CV, Skew, H_2, H_3, H_5, H_6, H_8, H_9, H_{11}, H_{12}, H_{13},H_{14},C_o, FDF, CD, M_1, M_3, and M_7*
- Weighted average AUROC of 0.94
- ACC rate of 82.7%

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Limitations of the study

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- Manual segmentation of the vertebral bodies
  - Automatic segmentation methods could lead to the realization of a clinically useful CAD system
- Individual and separate analysis of the vertebral bodies ignores important information outside their regions

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Limitations of the study

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- The use of only the median sagittal slice
- Some lateral VCFs may be misclassified
- Extension of segmentation and feature extraction methods to 3D is desirable

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Limitations of the study

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- Analysis of only T1-weighted MRI
  - Benign VCFs
    - isointense vertebra in T2-weighted and T1-weighted MRI after gadolinium contrast
  - Malignant VCFs
    - heterogeneous or high signal in T2-weighted and in T1-weighted MRI after gadolinium contrast

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Conclusion

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- Most of the features presented are important for both types of VCF classification
- For benign vs malignant VCFs
  - A_z values of texture and gray-level features are higher than those shape features
- For all VCFs vs normal vertebral bodies
  - A_z values of shape features are higher than those of texture and gray-level features

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Conclusion

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- The features *FDF* and *CV* follow the opposite trend
- The naïve Bayes method was the best classifier in both types of classification
- The proposed methods are promising for CAD of VCFs

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Conclusion

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- Future works:
  - Evaluate our methods with the inclusion of an automatic segmentation method
  - Extend the methods to 3D analysis of vertebral bodies

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Acknowledgment

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- São Paulo Research Foundation (FAPESP)
  - 2014/12135-0 and 2015/08778-6
- National Council of Technological and Scientific Development (CNPq)
- Natural Sciences and Engineering Research Council of Canada
- Ph.D students
  - Rafael de Menezes-Reis
  - Faraz Oloumi

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Feature selection: benign vs malignant VCFs

Feature	k-NN				Naïve Bayes	RBF Network
	k = 7	k = 9	k = 11	k = 13		
CV						
$Skew$					X	X
$Kurt$						
H_1						
H_2	X	X				X
H_3	X	X			X	X
H_4						
H_5						
H_6	X				X	X
H_7						
H_8						
H_9						
H_{10}		X	X	X		
H_{11}					X	
H_{12}					X	
H_{13}	X	X	X	X	X	
H_{14}					X	X
C_o					X	X
FDF	X	X	X	X	X	X
CD					X	
M_1					X	
M_2						
M_3						

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Feature selection: all VCFs vs normal vertebral bodies

Feature	k-NN				Naïve Bayes	RBF Network
	k = 7	k = 9	k = 11	k = 13		
CV	X	X	X	X	X	X
$Skew$					X	
$Kurt$						
H_1						
H_2					X	
H_3					X	
H_4					X	X
H_5					X	
H_6					X	
H_7						
H_8					X	
H_9					X	
H_{10}					X	
H_{11}		X	X		X	X
H_{12}						
H_{13}						
H_{14}						
C_o						
FDF						
CD						X
M_1	X	X	X	X	X	X
M_2		X	X	X		
M_3		X	X		X	X