Experimental Verification and Trials:
Brain & Liver MRI Images

Working Group 3

Issue Topics

- Glioblastomas
  - Tumor heterogeneity and margin
- Liver Fibrosis
  - Correlation with METAVIR grading
- Liver Volume
  - Segmentation

MRI Images

- Acquisition :
  - 3T MRI, Philips Achieva
  - Rennes University Hospital

LIVER

- 3D T1w THRIVE iso
  - Gradient Echo, Ultra-fast
  - TR/TE=2.76/1.36ms; α=10°
  - FOV=400x400mm, Mat=192x192
  - Isotropic voxel : 2x2x2mm
- 21 patients
  - With METAVIR grading
    - 7 F0
    - 3 F1
    - 1 F2
    - 2 F3
    - 8 F4
  - Confirmed by histological analysis

BRAIN

- 3D T1w
  - TR/TE=9.9/4.4ms ; α=8°
  - FOV= 256x256mm; Mat=256x256
  - Voxel: 1x1x1mm
  - Tacq=3’52
- 10 patients with Glioblastomas
  - 2 series of images for each patient
    - before and after Injection of a paramagnetic contrast agent
  - Confirmed by histological analysis

GLIOBLASTOMA

- **First step (data from Al Ain and Rennes): COM TA parameters, MI+PA+F - LDA, 3D>2D, better with normalization (128 grey level range = 7 bpp)**

- Second step (March-June 07)(Belgrade, Madrid, Szeged, Al Ain, Rennes, Martin, Dundee, London): two different works:
  - White matter heterogeneity in glioblastoma patients as evaluated by 2D and 3D MRI TA: COM TA parameters, MI+PA+F - LDA, normalization (7bpp):
    - 3D: 2 VOI x 3 (PH, HL, CL) x 10 patients (VOI= 7.7.7 voxels)
    - 2D: 2ROI x 3 (PH, HL, CL) x 10 patients (ROI = 15.15 pixels)
  - Glioblastomas heterogeneity as detected by 2D MRI TA:
    - 2 ROI x 4 (Oed., Tum., necr., peritum.)x 10 patients (ROI= 10.10 pixels)

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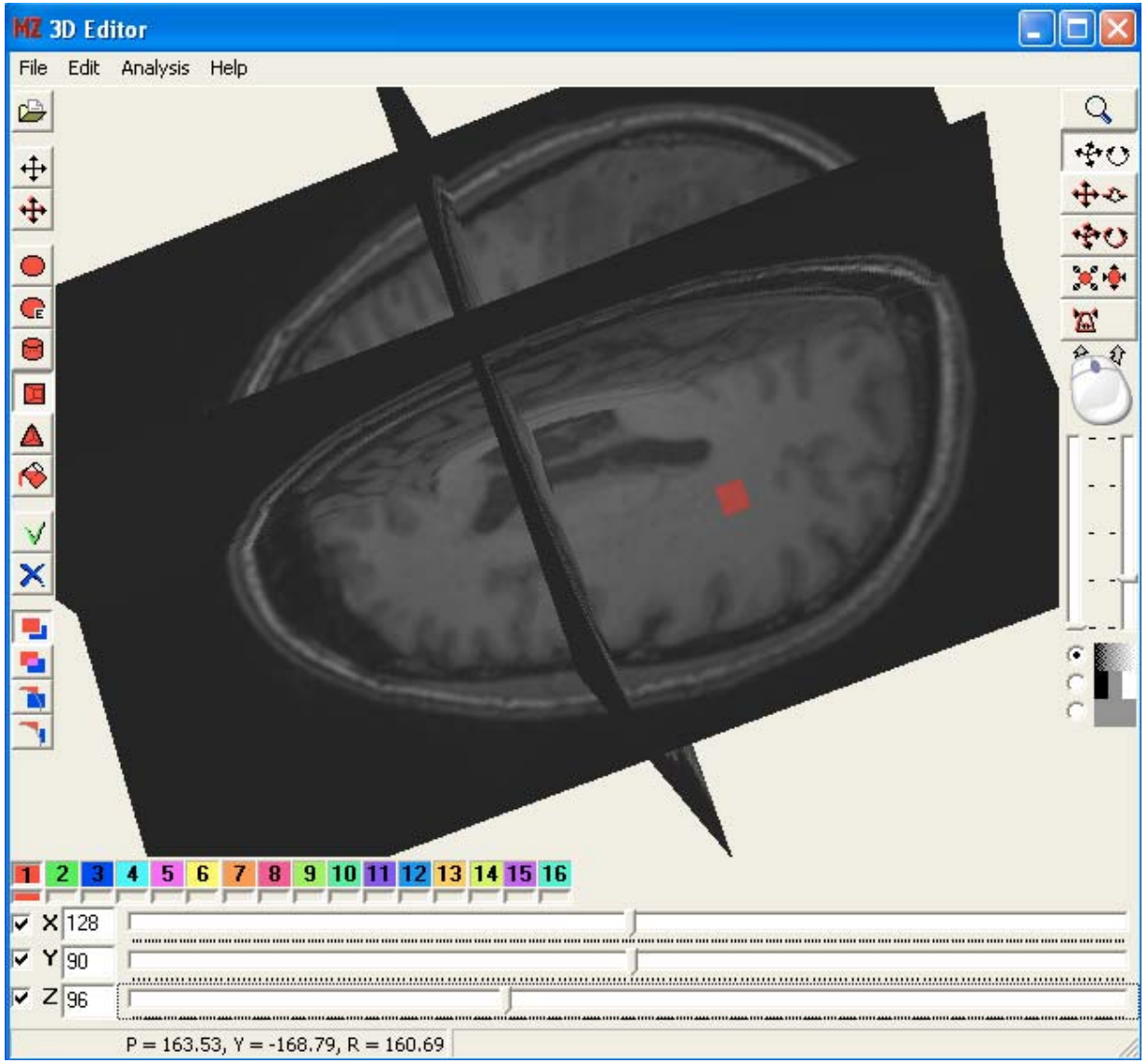
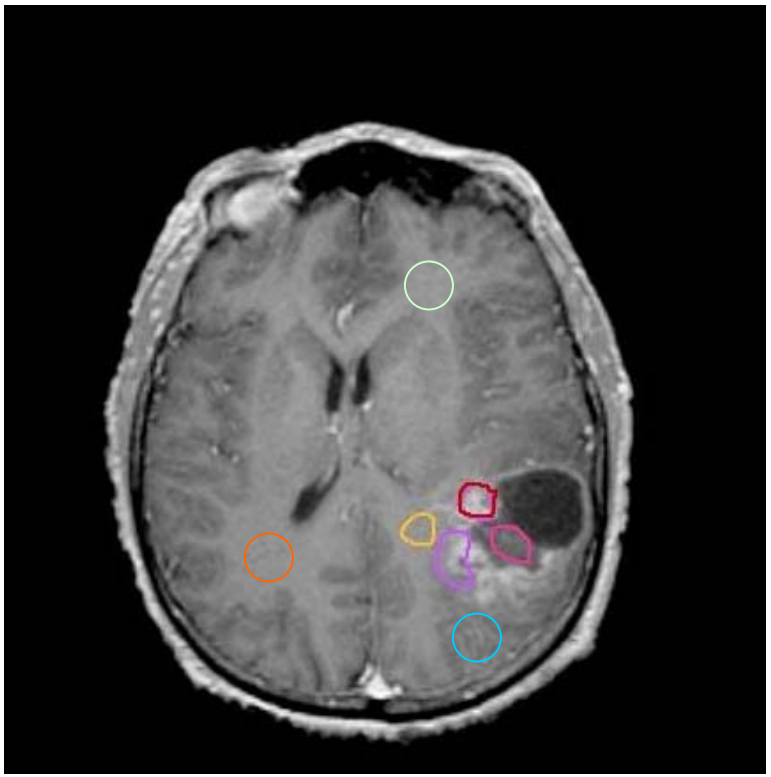

MZ 3D Editor
File
Edit
Analysis
Help
1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16
X 128
Y 90
Z 96
P = 163.53, Y = -168.79, R = 160.69

BRAIN: Glioblastomas

- Tumor Heterogeneity and Margin



Necrosis

Tumor

Margin (interface between the tumor and the parenchyma)

Oedema

Peritumoral White Matter

Normal region in the cerebral hemisphere with tumor

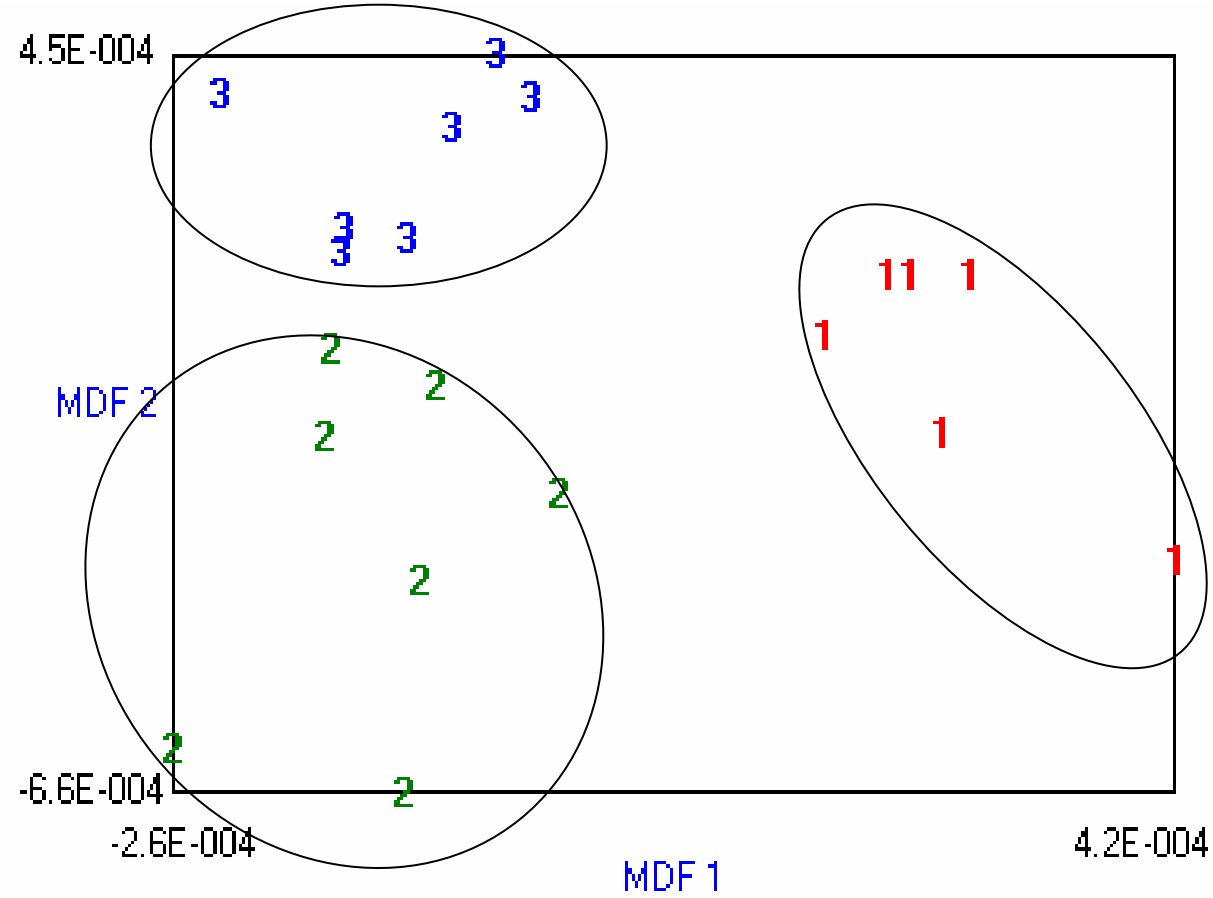
Normal region in the contralateral hemisphere

Characterizing Peritumoral WM from other WM

Calculation approach	32 bpp		64 bpp		128 bpp	
	PT vs. (HL and CL) Misclassification	HL vs. CL overlapping	PT vs. (HL and CL) Misclassification	HL vs. CL overlapping	PT vs. (HL and CL) Misclassification	HL vs. CL overlapping
3D	1	4	1	0	0	0
2DM (average of all ROIs)	1	6	3	3	1	1
ROI3	0	2	0	3	0	2
ROI2	5	2	2	0	0	1
ROI1	0	2	0	1	0	3

- For most classification results for all methods, PT was separated from other two overlapping WMs.
- HL and CL were totally separated using 64 and 128 bpp in 3D method (feature overestimation? or true histological evidence?).
- The number of errors decreased for increasing the number of bits-per-pixel (bpp).
- The averaging method 2DM didn't improve results compared to single slice 2D method.
- Higher dynamic range might be better for simple 2D calculation but could be misleading for more complex calculations.

Three classes were separated using 3D COM with 128 bpp



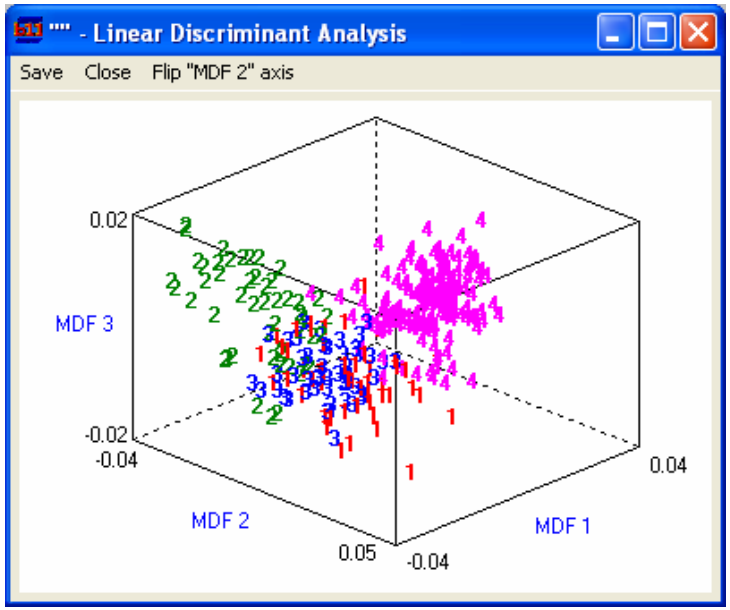
1 Peritumoral WM

2 Homolateral WM

3 Contralateral WM

Necrosis(1) / Tumor(2) / Oedema(3) / WM(4)

MI+PA+F/LDA

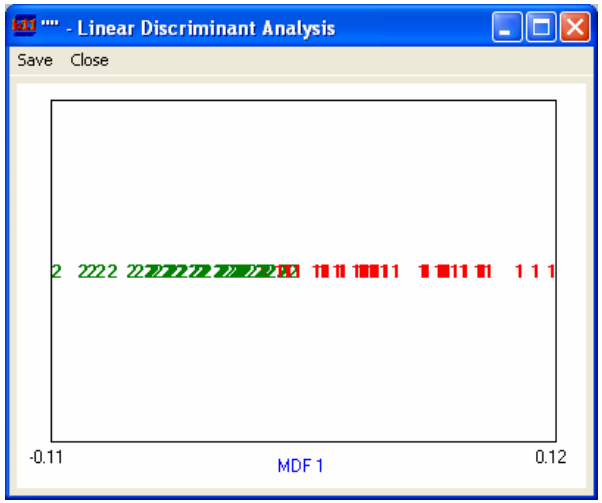


Misclassified data : 10%

- Ability of TA with proper method to highlight tumor heterogeneities

Necrosis (1) / Tumor (2)

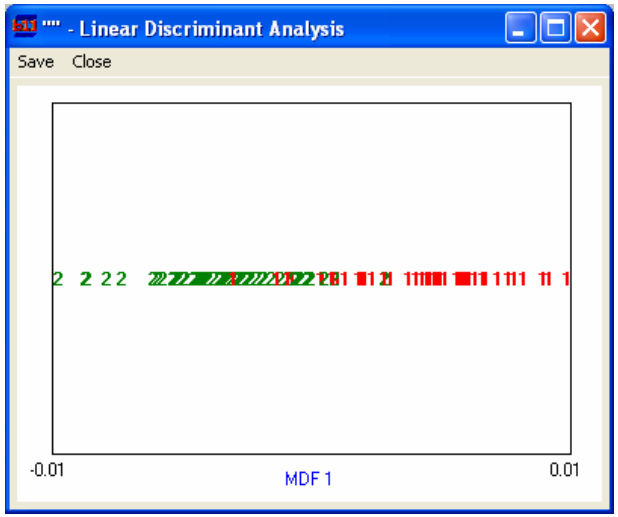
MI+PA+F/LDA



- With MI+PA+F/LDA : 10% misclassified (F score=8)
- Overlapping between regions
  - Due to irregularities of necrosis
  - Tumoral cells in necrosis regions?

Tumor(1) / Oedema(2)

MI+PA+F/LDA



Misclassified : 12%

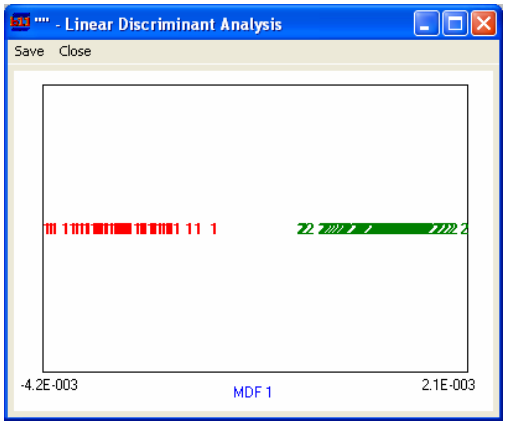
Fisher coefficient = 8

Tumor(1) / WM(2)

MI+PA+F/LDA

(1) Tumor

(2) White Matter WM (PT+HL+CL)

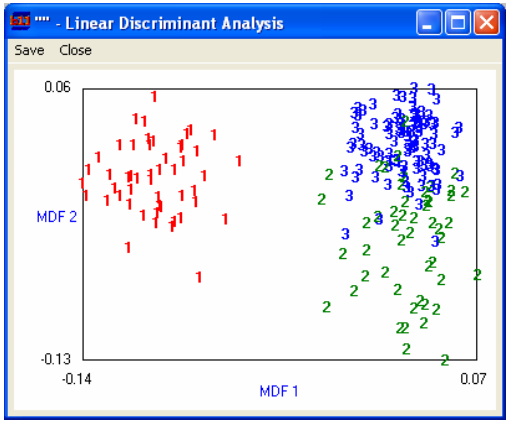


MI+PA+F/LDA

(1) Tumor

(2) Peritumoral White Matter

(3) White Matter WM (HL+CL)



MI+PA+F

*features
1 Perc.01%
2 Perc.10%
3 Perc.50%
4 Mean
5 Horzl_RLNonUni
6 S(1,0)Entropy
7 135dr_RLNonUni
8 Vertl_RLNonUni
9 45dgr_RLNonUni
10 Perc.90%
11 135dr_GLevNonU
12 Sigma
13 S(0,1)AngScMom
14 S(5,5)AngScMom
15 S(4,4)AngScMom
16 Perc.99%
17 45dgr_GLevNonU
18 Teta1
19 S(5,5)SumOfSqs
20 S(1,0)AngScMom
21 S(0,1)Entropy
22 S(1,-1)Entropy
23 S(2,0)Entropy
24 S(1,1)Entropy
25 S(0,2)Entropy
26 Variance
27 S(3,0)Entropy
28 S(2,-2)Entropy
29 S(4,0)Entropy
30 S(2,2)Entropy

Synthesis of results

	MI+PA+F/ LDA method	
Classes	% of misclassified data	Comments / Hypothesis
Necrosis / Tumor / Oedema / WM	10%	Highlight heterogeneities of brain glioblastoma
Tumor vs Necrosis	10%	Potential tumoral cells in necrosis?
Tumor vs Oedema	12%	Potential tumoral cells in oedema?
Tumor vs WM	0%	Strong discrimination
Peritumoral WM / Far extratumoral WM	5%	Moderate differentiation
Peritumoral WM / HL-WM / CL-WM	26%	Overclass : HL-WM and CL-WM data are similar

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LIVER FIBROSIS GRADING

- **First step (data from Madrid, Prague, Martin, Dundee, Lodz and Rennes(2)): 4 + results against 2 - for fibrosis grading and questions about liver segmentation.**

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  Liver fibrosis grading by 3D vs 2D MRI TA: 21 patients (8 F0 vs 6 F1+F2+F3 vs 8 F4)

  – 2D: 5 ROI (out of main vasculature or artefacts, and from at least 3 pixels from the limits of the liver) x 18.18 pixels, standardization: Yes, normalization: +/-3σ, selection of 10-15 parameters by MI+PA+F, LDA analysis

  – 3D: 3 spherical VOI (20 pixels= 4cm in diameter)

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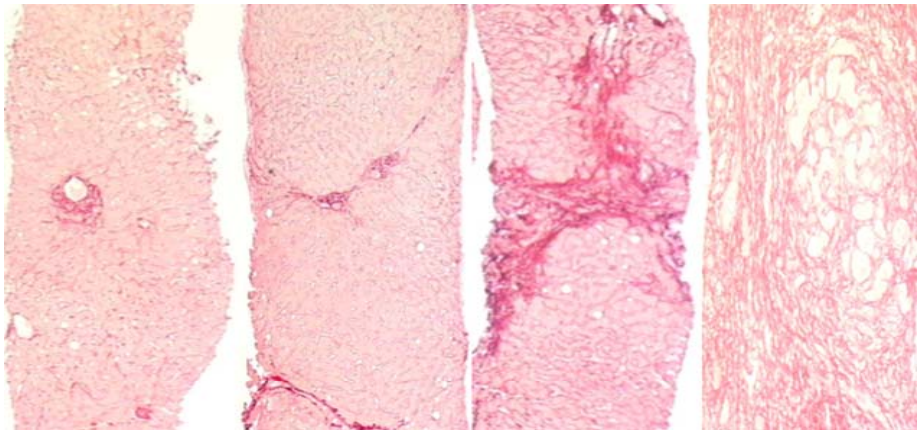
Liver Fibrosis

- METAVIR Fibrosis Grading Scale

Finding	Score F
No Fibrosis	0
Portal Fibrosis	1
Bridging fibrosis, slight	2
Bridging fibrosis, marked	3
Cirrhosis	4



F1 F2 F3 F4

F0 vs (F1+F2) vs (F3+F4)

MaZda v4.5

2D-TA

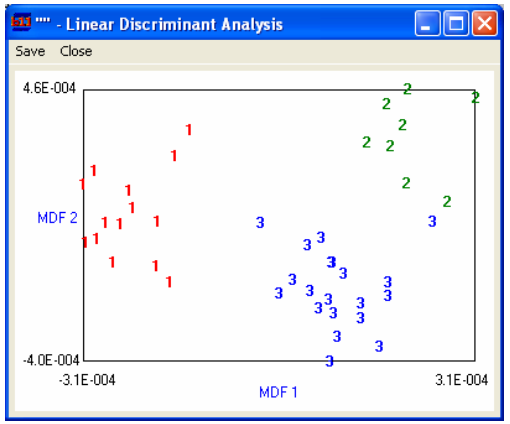
Misclassified (%)								
	Fisher		PA		MI		MI+PA+F	
Standardization	No	Yes	No	Yes	No	Yes	No	Yes
Raw+kNN	58	45	64	53	51	36	51	42
LDA+kNN	43	43	53	53	42	41	33	32
PCA+kNN	58	46	63	53	59	34	59	41

3D-TA

Misclassified (%)								
	Fisher		PA		MI		MI+PA+F	
Standardization	No	Yes	No	Yes	No	Yes	No	Yes
Raw+kNN	62	60	69	62	60	50	60	50
LDA+kNN	36	36	36	38	55	50	5	5
PCA+kNN	62	62	69	64	60	50	60	50

3D-TA

MI+PA+F/LDA



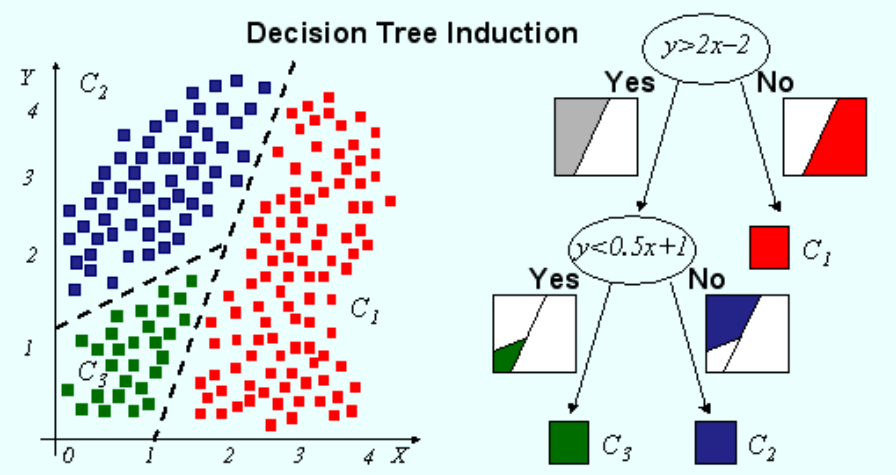
Misclassified : 5%

*features
1 S(0,0,2)SumOfSqs
2 S(4,4,0)DifEntrp
3 S(3,3,0)DifVarnc
4 S(5,-5,0)Correlat
5 S(0,0,2)SumVarnc
6 S(4,-4,0)DifEntrp
7 S(3,3,0)Contrast
8 S(4,4,0)AngScMom
9 S(0,3,0)SumEntrp
10 S(4,-4,0)Correlat
11 S(1,-1,0)Entropy
12 S(0,0,1)SumOfSqs
13 S(0,5,0)InvDfMom
14 Kurtosis3D
15 S(5,5,0)Correlat
16 S(5,0,0)SumAverg
17 Skewness3D
18 S(4,-4,0)SumEntrp
19 S(0,0,4)Entropy
20 S(3,3,0)SumAverg
21 S(5,-5,0)AngScMom
22 S(5,-5,0)Entropy
23 S(0,1,0)AngScMom
24 S(0,1,0)Entropy
25 Perc.10%3D
26 S(1,0,0)SumOfSqs
27 S(2,-2,0)Entropy
28 Perc.90%3D
29 S(2,-2,0)AngScMom
30 S(0,0,5)InvDfMom

Other TA Method

- **Texture Analyser** (software developped by M Kretowski and D Duda)

- **Classifier :** Decision induction trees by using dipolar criteria



- **Feature selection :**

  Sequential Forward Selection method applied separately for each non-terminal tree node

Results

- Experiments
  - Each experiment was repeated 20 times
  - 10-fold cross-validation was used to estimate the classification accuracy
- Results
  - Classification of 5 classes of liver tissue: F0, F1, F2, F3, F4

    Classification accuracy (with standard deviation) was 95.89 ± 0.59 %
  - Classification of 3 classes of liver tissue: F0 vs (F1 and F2) vs (F3 and F4)
    - F1 and F2 was put in the same class
    - F3 and F4 was put in the same class

    Classification accuracy (with standard deviation) was 97.32 ± 0.61 %

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Three steps to evaluate a new clinical method:

- I - Validation of the concept: for instance, TA could contribute to in-vivo liver fibrosis grading (Basic concepts, models, test-objects…)
- II - Methods standardization and validation: for instance, best TA method is… and potential artefacts are… (multicenter evaluation on a limited data set, open strategies…)
- III - Clinical evaluation: large multicenter evaluation in real clinical situation with fixed protocol.

TA : when, why and how?

- When classical methods are either traumatic (for instance, liver biopsy) or not enough efficient or too expensive (MRI????)
- Because MRI-TA corresponds to a not already explored space scale (500 microns - 2 mm) between histology (10-100 microns) and organ morphology (cm) but we have to explore the meaning of MRI-TA for clinicians (close collaboration with pathologists, biologists and clinicians)
- With well standardized methods, validated on large clinical trials and comprehensive for clinicians.