Parkinson’s Disease Prognosis using Diffusion Tensor Imaging features Fusion

Prédiction de la Maladie de Parkinson basé sur la fusion des caractéristiques d’Images par Résonance Magnétique de Diffusion

Scientific Coordinators:
Université de Franche-Comté, Besançon, France
Prof.Dr.Eng. **Daniel RACOCEANU**
Prof.Dr.Eng. **Noureddine ZERHOUNI**
“Politehnica” University of Timisoara, Romania
Prof.Dr. Eng**. Vladimir Ioan CRETU**

Author:
Eng. **Roxana Oana TEODORESCU**

Summary

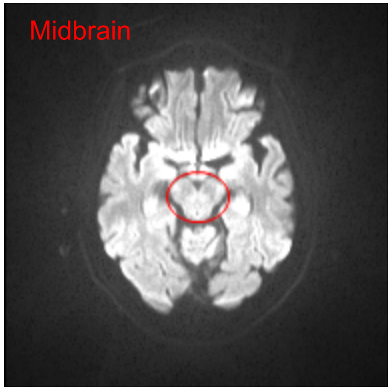
- Purpose
- Context
  - Medical premises for PD- hypothesis
  - Biomarkers for PD
  - Medical Image as biomarkers
- Research Objectives
- Feasibility study
- Approach on Medical Image handling
  - Technical challenges
  - Methods
  - Evaluation and results
- Conclusion
  - Scientific contribution
  - Future development and applications

Thesis presentation. Motivation. Purpose

- Proposing the usage of Medical Images as bio-marker for Parkinson's Disease (PD)
  - Characteristics
    - Introducing image-extracted data as measurable indicators
    - Providing values for estimation on the early PD cases
    - Complementary data to the congnitive testing

UFC UNIVERSITÉ DE FRANCHE-COMTÉ

Current Medical Diagnosis for Parkinson's Disease



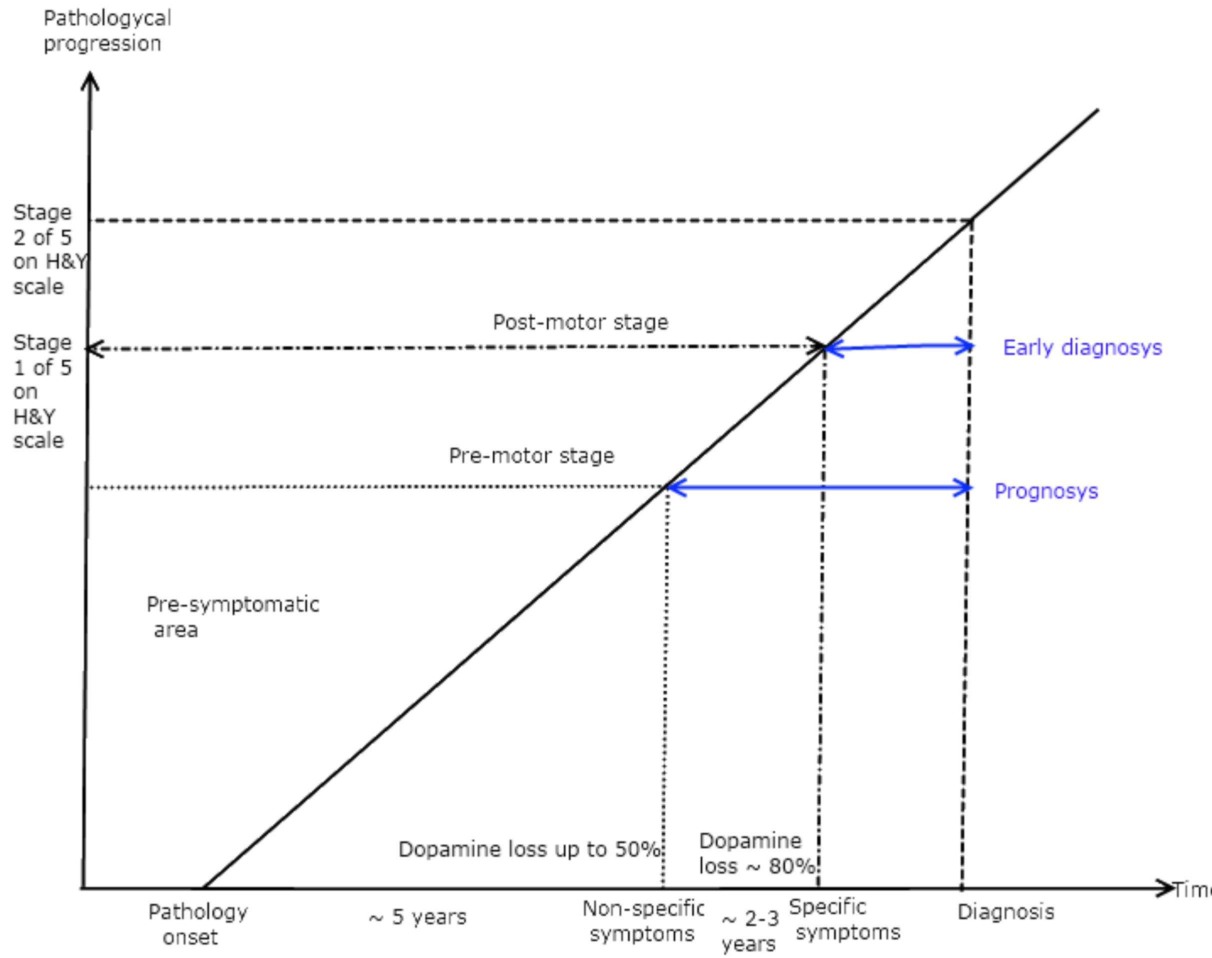
- Parkinson's Disease (PD)[1]
  - Dopamine
    - Neural impules on the motor tract
    - Substantia Nigra (SN)[1] anatomical area -the midbrain level
- Cognitive testing
  - After 80-90% of dopamine is lost[2]
  - At stage 2 at least on H&Y scale
- Unified Parkinson's Disease Rating Scale (UPDRS); Hoehn&Yahr (H&Y) scale

[1] Medical Dictionary. The Free Dictionary By Farlex. On-line, April 2010. http://encyclopedia.thefreedictionary.com/.

[2] Medical News Today. Brain bank Appeal aims to double number of brain donors.www.medicalnewstoday.com, March 2009. Parkinson's awareness week 2009, 20-26 April.

Current biomarkers for Parkinson's Disease

Biomarker	Imaging Technique
Cerebral blood flow (CBF)	MRI/ arterial spin labeling
Directed molecular probes	PET optical
Dopamine transporter (DAT) density	SPECT (using I-123 altropane)
Dopamine binding potential	SPECT (using I-123 altropane)
Dopaminergic neurotransmitter activity	fMRI PET
N-acetylaspartate (NAA) levels over time	MRS



[1]Mitchell RA, Lewis A.W et al. Biomarkers and Parkinson's Disease, Brain, vol.127, nr.8, pg. 1693-1705, 2004.
[2] Marck J., Jennings K., et al. Biomarker's for Parkinson's Disease: tools to asses Parkinson's Disease onset and progression, Ann Neurol, vol.65, nr.15,pg.232-21, 2009.

Reasoning in the PD context

PD Pathology onset
- Dopamine producing process starts to diminish
- Physiological changes in SN

Non-Specific Symptoms
- Up to 50% of dopamine is no longer produced
- Pre-motor stage

Specific Symptoms
- Motor stage
- Up to 80% of dopamine is no longer produced
- Motor fibers are affected – physiological changes

Clinical phenotype
- Diagnosis based on cognitive testing
- PD evaluation

Clinical
- Evaluation on PD rating scale
- Diagnosis

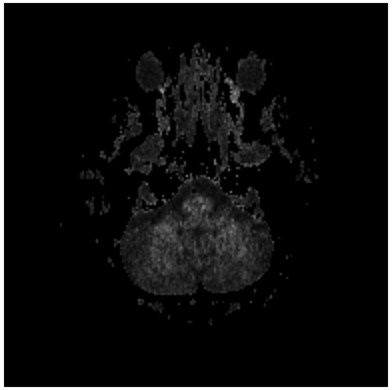
Specific symptom
- Tremor
- Dopamine loss (~80%)

Non-specific symptoms
- Pre-motor stage
- Dopamine loss (<50%)

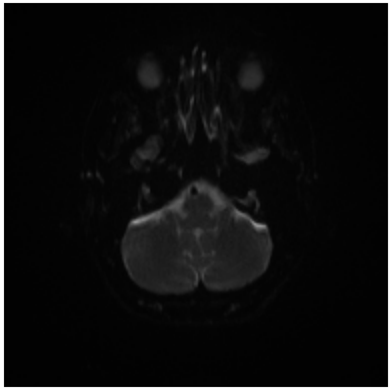
PD Pathology onset
- Deterioration on SN physiology
- Beginning of dopamine loss

Medical Imaging on PD

- Medical Imaging Standard
  - Digital Imaging Comunication in Medicine (DICOM)[5] :Header file + Image file
  - Analyze – separate files for header and image
- MRI – Medical Resonance Imaging
  - DTI – Diffusion Tensor Imaging
    - EPI – Echo-Planar Imaging
    - FA – Fractional Anisotropy



FA stack



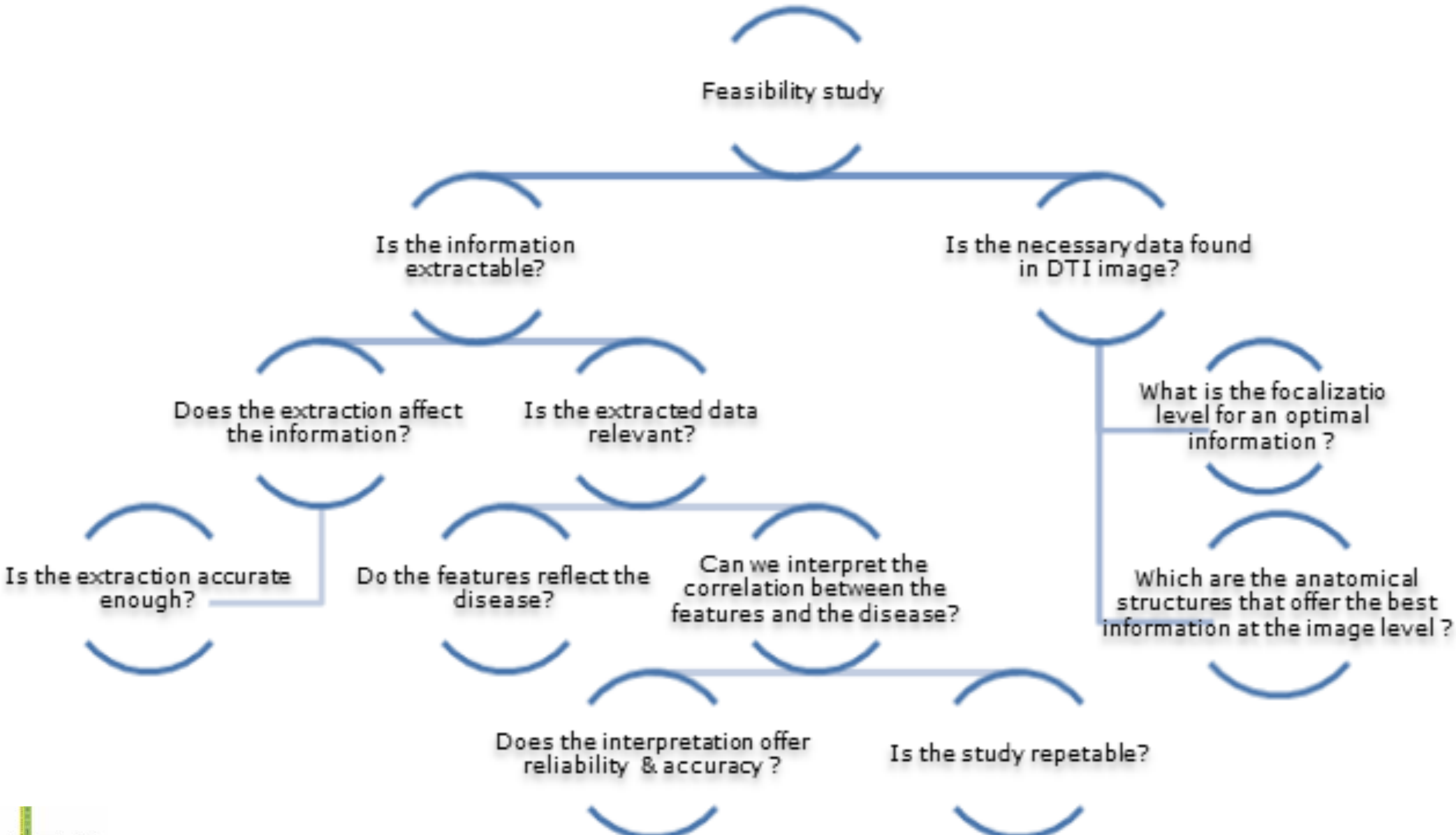
EPI B0 stack

[5] South Carolina University. The DICOM standard. Web presentation, December 2008. Technical Report. http://www.sph.sc.edu/comd/rorden/dicom.html - last accessed on May 2010.

Database and imaging protocol

- Singapore General Hospital (SGH)- database
  - 143 cases : 68 PD diagnosed subjects +75 control subjects
- DTI images
  - Siemens Avanto 1.5T; B0=800
  - Parameters: TR/TE 4300/90 ; 12 directions;4 averages; 4/0 mm/section; 1.2 x 1.2 mm in plane resolution
    - EPI : 351 images/patient : 27 axial slice/volume x 12 directions + B0
    - FA : 27 axial slices / patient
    - T1, T2, DWI etc.

Reasoning for including the DTI imaging as a new PD biomarker



Feasibility : Medical Premises that support our approach

I. Anisotropy on the Substantia Nigra highlights PD condition[3]
II. Motor fibers run from SN on Anterior-Posterior direction
III. Left hemisphere of the brain is more affected by PD [4]

- Metods:
  - Correlation :Substantia Nigra at the midbrain level and the PD
  - Determinig the correlation between neuromotor fibers and PD severity

[3] L-L Chan, H. Rumperl and K. Yap. Case Control study of Delusion tensor imaging in Parkinson's disease. J. Neurol. Neurosurg. Psychiatry, vol. 78, pages 1383–1386, 2007
[4] Parkinson's disease statistics. on-line, July 2009. http://parkinsons-disease.emedtv.com/parkinsonease-statistics.html.

Feasibility: Test batches

- Demographic elements
- Randomly take out 5 contol cases and 5 patients in each batch test
  - T1 – male/all difference
  - T2 – small H&Y
  - T3 –age difference
  - T4 – H&Y

Nr	H&Y value	Age		Male/ all	
		Patients	Control	Patients	Control
1	2.312	64.5	59.37	11/16	6/16
2	2.375	63.31	60.93	9/16	9/16
3	2.375	64.06	58.5	8/16	7/16
4	2.467	62.75	61.5	9/16	8/16

Feasibility: Midbrain analysis

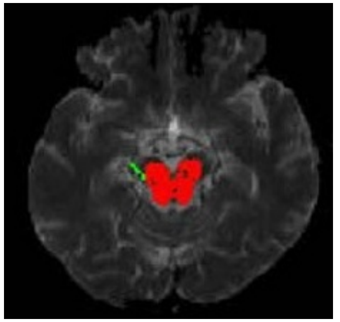
- Midbrain
  - FA image
    - Red Left-Right
    - Green Anterior- Posterior
    - Blue Down – Up
- Histogram of G channel elements
- Normalize & Eliminate the noise
- Correlation with H&Y scores

Nr.	Left Independent Sample T-Test [p %]	Right Independent Sample T-Test [p %]	Left Correlate Bivariate [%]	Right Correlate Bivariate [%]	Left ANOVA [Sig]	Right ANOVA [Sig]
1	24.4	74.0	13	8	0.872	0.937
2	12.2	69.3	7	8	0.906	1
3	75.5	65.3	3	6	0.937	1
4	83.6	71.4	7	7	0.937	0.906

UFC UNIVERSITÉ DE FRANCHE-COMTÉ

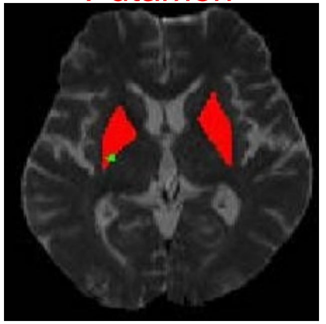
Thesis Objectives

Midbrain

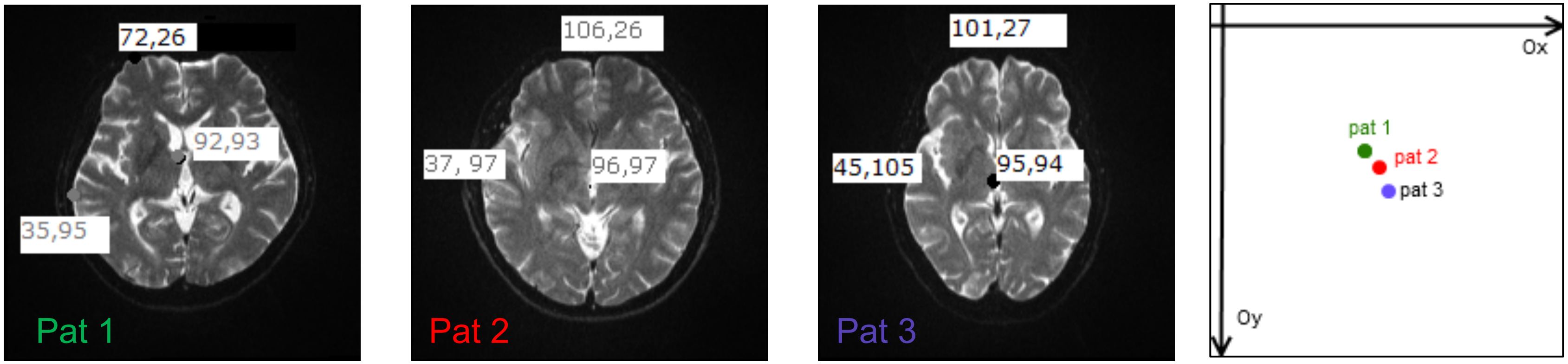


- Pre-Processing
- Processing : extracting the midbrain and the Putamen from images
- Analysis :
  - Detecting the motor fibers
  - Definig a measure for the fibers relevant for PD
- Diagnosis and Prognosis: definig a variation function of the fibers on the H&Y scale

Putamen

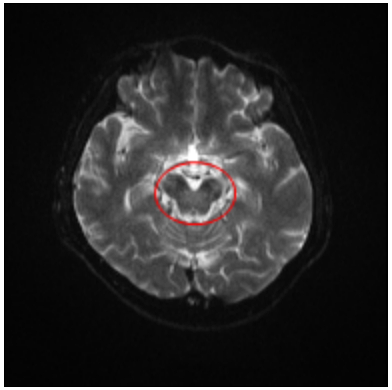


Definig challanges

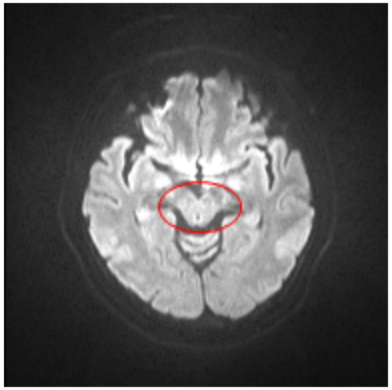


- Inter-patient variability
  - Positioning inside the image axes
    - Vertical
    - Horizontal

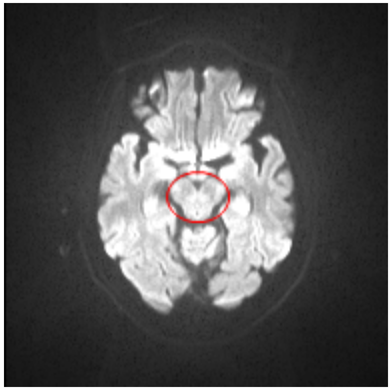
Inter-Patient variability



Slice 7/27 :midbrain



Slice 12/27 : midbrain

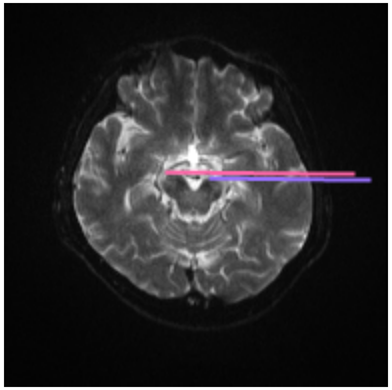


Slice 9/27 : midbrain

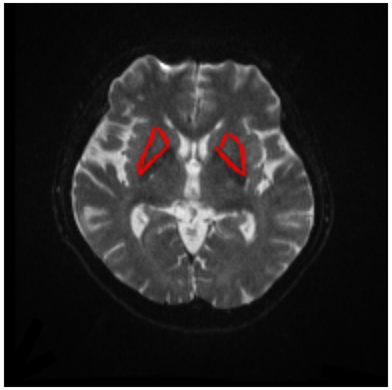
- Inter-patient variability
  - Shape /Volume / Surface
    - At the brain level
      - age difference (atrophy)
      - Sex difference
    - For the same anatomical structure

Intra-patient variability

- Intra-patient variability
  - Hemisphere difference
    - Orientation inside the image
    - Difference among the two lobes at the region of interest (ROI) level

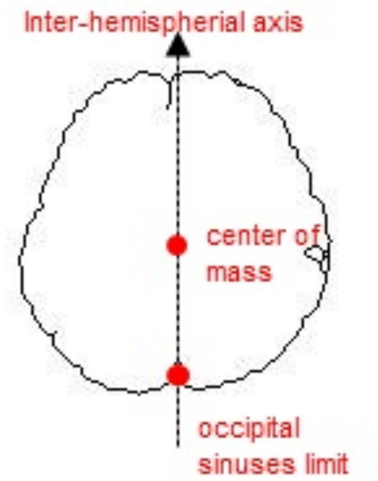


Slice with midbrain



Putamen on the two hemispheres

From feasibility to Features



- Eliminating the skull
  - Determining the brain contour: KMeans[6]
  - Determining the orientation
    - Occipital sinus – inflexion point <> Center of mass [7]
- Slice of interest
  - Relative to the center of mass :4 possibilities related to P_{slice}

$$P_{slice} = \frac{Vol_{Zslice}}{Vol_{Fslice}} * \frac{100}{ST}$$

    - P_{slice} - slice of interest position ; Vol_{Zslice}, Vol_{Fsice} – volumes of brain in the slice with the center of mass respectively the first slice; ST – slice thickness

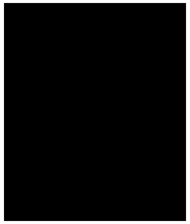
[6]KMeans in imageJ: http://ij-plugins.sourceforge.net/plugins/clustering/index.html - last accessed on June 2010
[7]ImageJ plug-in Object Counter : http://rsbweb.nih.gov/ij/plugins/track/objects.html - last accessed on June 2010

Image Segmentation- State of the art

- Segmentation
  - Intensity-based
    - Tissue segmentation
      - Grey Matter (GM) , White Matter (WM), Cerebral Blood Flow (CSF)
    - SPM (Statistical Parameter Mapping)[8]
    - VBM (Voxel Based Morphometry)[9]
  - Atlas-based

Intensity segmented stacks

SPM/VBM segmented stacks

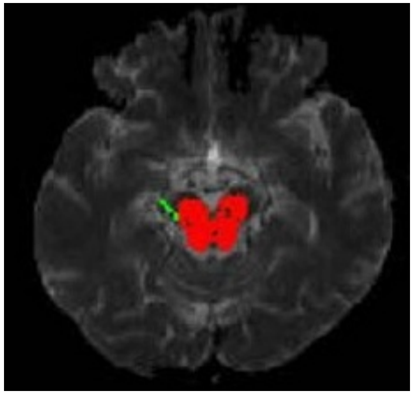


[8] SPM site -http://www.fil.ion.ucl.ac.uk/spm/ - last accessed on May 2010

[9] John Ashburner and Karl J. Friston. Voxel-Based Morphometry - The methods. Neuroimage, vol. 11, pages 805–821, 2000. The Welcome Department of Cognitive Neurology, Institute of Neurology.accessed on June 2010

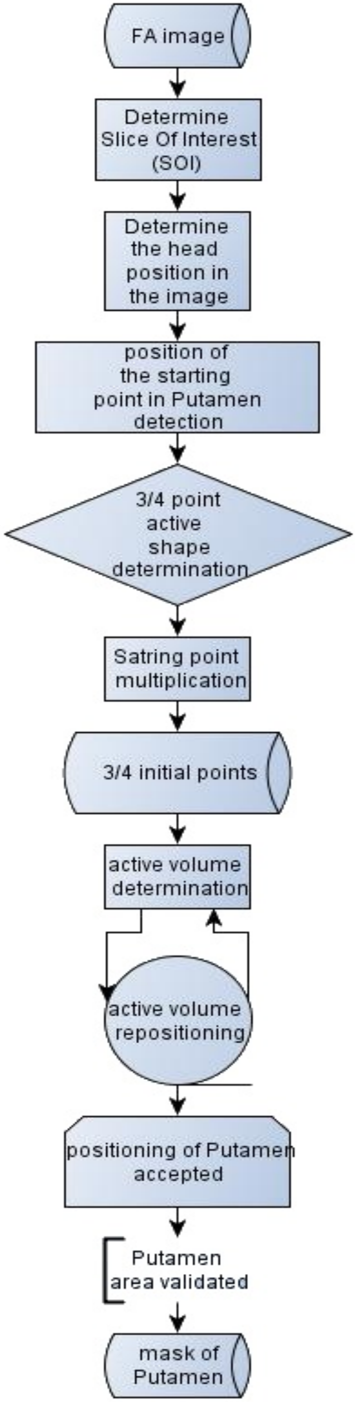
Image Segmentation Our Method

- Midbrain detection
  - ROI detection
  - Atlas approach
    - Not generating a mask
    - Adaptive for any patient
    - Limits set by intensity
    - Geometry-based limitations



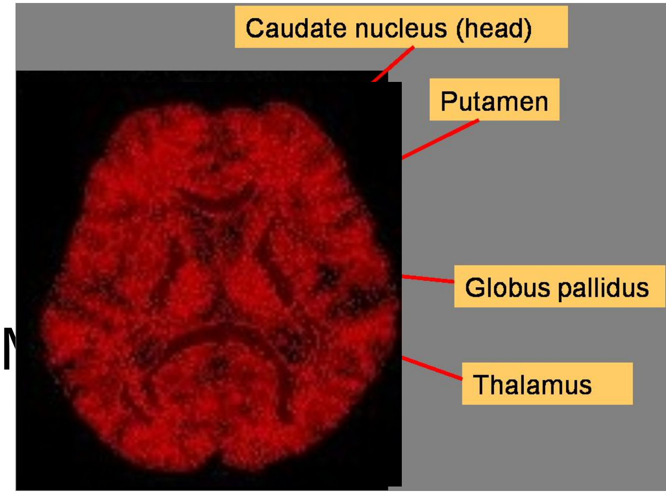
Processing

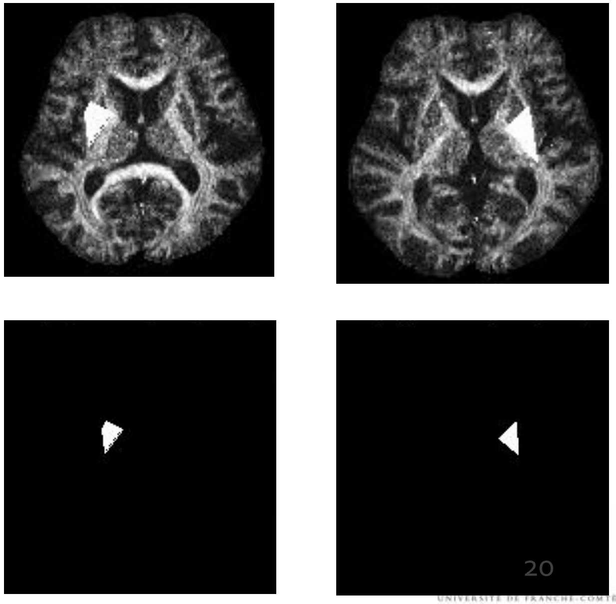
Image Segmentation : our approach



Putamen detection

- Detecting the ROI
  - KMeans (4 clusters): GM/WM CSF / noise
  - Center of mass - 2/3 Frontal Lobe
- Growing the seeds
  - Triangular approach
  - Quadrilateral approach





Registration – State of the Art

- Rigid registration[3,4,5]
- Geometry-based registration [3,4,5]
  - Determine automatically the checkpoints on the EPI Bo image and FA
    - Center of mass of the brain – for translation
    - Midline axis orientation – flip horizontal or vertical
    - Angle of the Midline axis and the image axis – for rotation
  - Rigid body transformation by matrix application on the 2D images of masked volume of the Putamen image

[3] Antoine J.B. Maintz and Max A. Viergever. A survey of medical image registration. Medical Image Analysis, vol. 1 and 2, pages 1–32, 2000..
[4] Barbara Zitova and Jan Flusser. Image Registration: A Survey. Image and Vision Computing, vol. 21, pages 977–1000, 2003. 63, 74
[5] Jan Modersitzki. Numerical methods for image registration, volume Oxford Science Publications of Numerical Mathematics and Scientific Computation. Oxford University Press, hardcover edition, 2004

Registration- our approach

- Parameters
  - Midline axis orientation – flip horizontal or vertical
    - Horizontal flip : $sign(x_{inflexion, FA} - x_{CM,FA}) != sign(x_{inflexion, EPI} - x_{CM, EPI})$
    - Vertical Flip: $sign(y_{inflexion, FA} - y_{CM,FA}) != sign(y_{inflexion, EPI} - y_{CM, EPI})$
  - Center of mass of the brain – for translation
    - $(d_x, d_y, d_z) = abs(CM_{FA}(x,y,z) - CM_{EPI}(x,y,z))$
  - Angle of the Midline axis and the image axis
    - for rotation(θ_x, θ_y)
- Rigid body transformation by matrix application on the 2D images of masked volume of the Putamen image

Registration -Determined parameters

- Transformation matrix

$$\begin{bmatrix} x` & y` & z` & 1 \end{bmatrix} = \begin{pmatrix} \cos\theta_x & \sin\theta_x & 0 & d_x \\ -\sin\theta_y & \cos\theta_y & 0 & d_y \\ 0 & 0 & 1 & d_z \\ 0 & 0 & 0 & 1 \end{pmatrix} * \begin{bmatrix} x \\ y \\ z \\ 1 \end{bmatrix}$$

  - θ :difference of the angle between the midline determined on the FA and EPI and the image coordinate axes

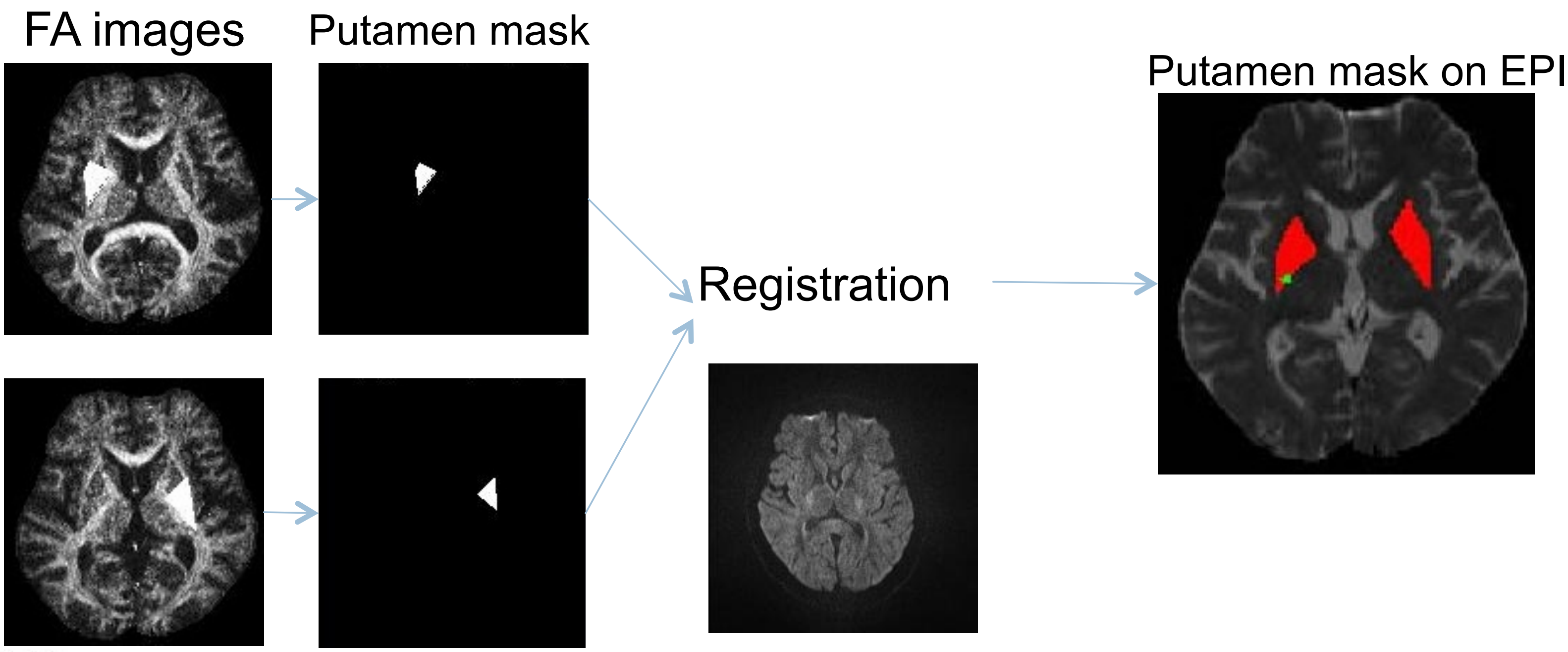
$$\theta_x = abs(\mathrm{S}\,(midline_{FA}, O_x) - \mathrm{S}\,(midline_{EPI,B0}, O_x))$$

$$\theta_y = abs(\mathrm{S}\,(midline_{FA}, O_y) - \mathrm{S}\,(midline_{EPI,B0}, O_y))$$

  - (d_x, d_y, d_z)= abs $(CM_{FA}(x,y,z) - CM_{EPI}(x,y,z))$

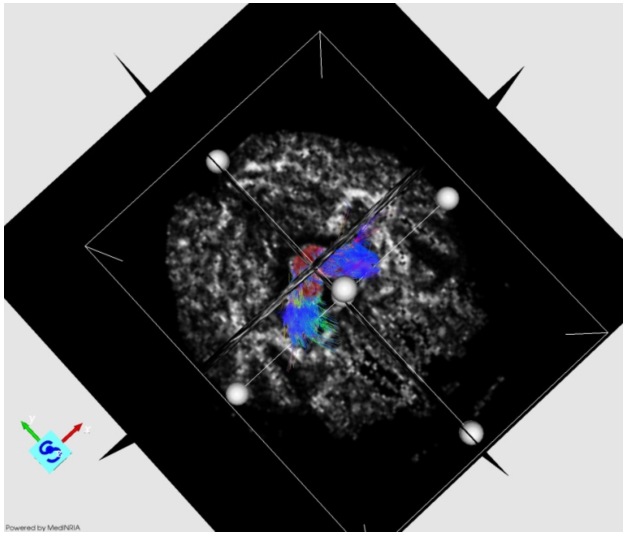
Fusion elements (Information Addition)

- Extraction of Putamen on FA
  - Registration on EPI
- Apply mask on the EPI

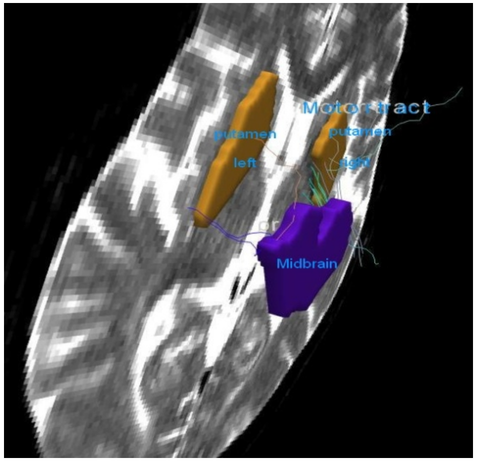


Fiber extraction and evaluation – state of the art

- Tractography process
  - Deterministic
  - Probabilistic
- Fiber validation
  - Local approach
  - Global approach



Obtained by local tractography: MedINRIA[10] – DTI Tracker Module

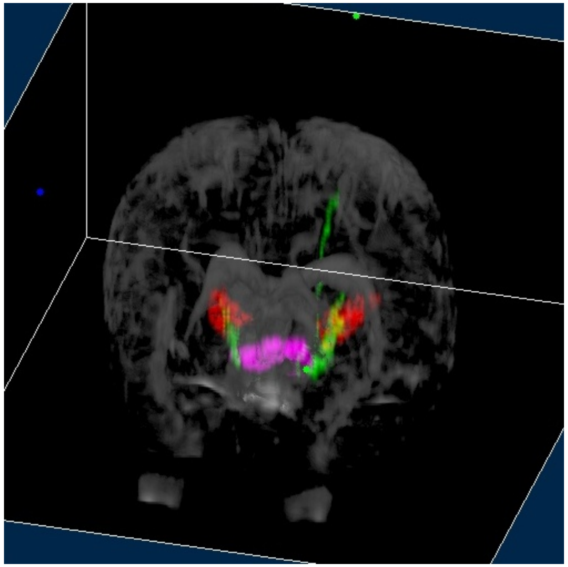


Obtained by global prbabilistic tractography: TrackVis[11] – Diffusion Toolkit Module

[10] MedINRIA - http://www-sop.inria.fr/asclepios/software/MedINRIA/ - last accessed on May 2010
[11] TrackVis - http://www.trackvis.org/-last accessed on July 2010

Tractography – our approach

- Global deterministic Algorithm[3,4]
- Our approach
  - Start from the determined volume of interest – midbrain
  - Grow the fibers only on anterior – posterior (AP) direction
  - Validate only the fibers that reach the Putamen volume
- Validation of fibers
  - Anisotropy values > 0.1
  - Angulations < 60 degree



[3] Peter J. Basser, Sinisa Pajevic, Carlo Pierpaoli, Jeffrey Duda and Akram Aldroubi. In vivo fiber Tractography using DT-MRI data. Magnetic Resonance in Medicine, vol. 44, pages 625–632, 2000.

[4] Denis Le Bihan, Jean-Francois Mangin, Cyril Pupon and Chris A. Clark. Diffusion Tensor Imaging : concepts and application. Journal of Magnetic Resonance Imaging, vol. 13, pages 534–546, 2001

Definig measures

- Evaluating the extracted data
  - Introducing the fiber evaluation values

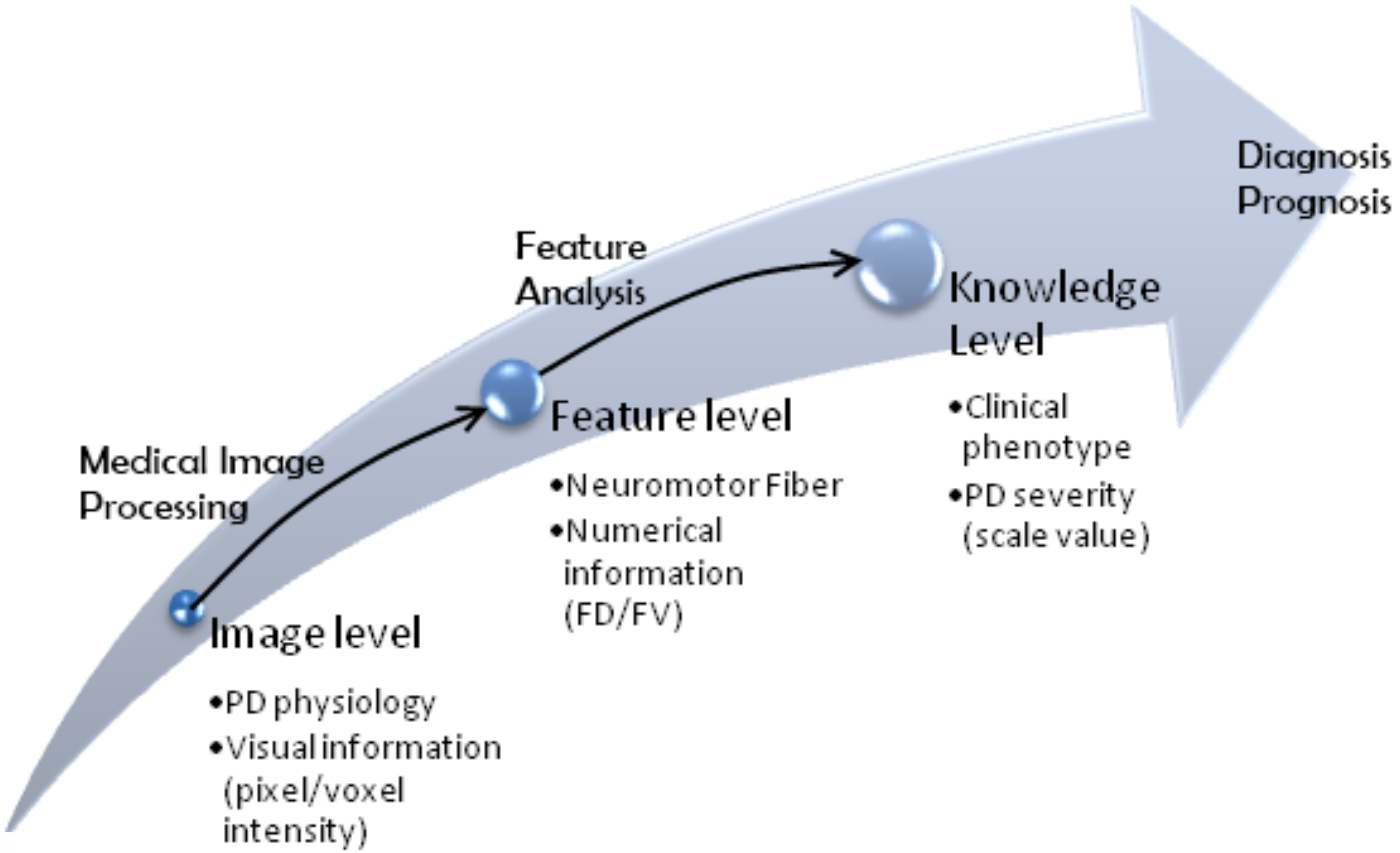
$$FD_{3D} = \frac{Nr_F * V}{Vol_{Brain}} \qquad FD_{rel} = \frac{F_{Nr}}{Vol_{VOI}} \qquad FD = \frac{F_{Nr}}{Vol_{Brain}}$$

$$FV = F_{Nr} * V_{height} * V_{width} * V_{depth} * F_{legth}$$

    - FD_{3D}-Fiber Density on the 3D perspective; Nr_F- Number of Fibers; Vol_{Brain} -brain volume; Fiber Volume (FV) ; Fiber density (FD) ; Number of fibers (F_{Nr}),Voxel measure (width/height/depth), Fiber Length (F_{length})

  - Correlation between the FD on the left side and the PD severity
    - ANOVA testing (0.8-1)
- Use FD for diagnosis and prognosis

Informational transfer



Diagnosis and Prognosis

- Diagnosis : which subjects are affected by PD and which are control cases
- Prognosis : determining the severity of PD on the patients
- Using the H&Y scale
- Ground truth : SGH provided values from cognitive testing on H&Y scale

Diagnosis

- Rules

  If $(HY_{FD}=HY_{VOIVol} \wedge HY_{FD}\neq -1$ then $HY= HY_{FD}$
  If$(HY_{FD}=-1 \wedge HY_{VOIVol}\neq -1$ then $HY=HY_{VOIVol}$
  If$(HY_{FD}\neq -1 \wedge HY_{VOIVol} =-1)$ then $HY= HY_{FD}$
  If $(HY_{FD}\neq -1 \wedge HY_{VOIVol}\neq -1)\wedge(HY_{FD}\neq -HY_{VOIVol})$ then
  If $(FD_{3D}\neq 0)$ then $HY=2$
  else $HY=0$;
  If$(HY_{FD}=-1 \wedge HY_{VOIVol}=-1)$ then Tractography invalid!♪

- Advantages
  - Includes the medical knowledge
  - Adaptive to any scale
- Disadvantages
  - Can rate only what it has learned – no perspective for prognosis from this point

Prognosis methodology

- Adaptive Neuro-Fuzzy Inference System (ANFIS)[12] architecture
  - Input layer- determines using a function the premise parameters
  - The rule strengths
  - Normalized firing strengths - weights definition
  - Consequent parameters - determined using the weights and the variation functions
  - Output - decisional output based on the computed consequence parameters

- Our approach:
  - Input layer : FD/FV
  - Rules strengths –H&Y scale
  - Weights – the polynomial degree
  - Consequence parameters : computed with Lagrange polynomials
  - Output : H&Y estimated value

[12] Piero P. Bonissone. Adaptive Neural Fuzzy Inference Systems (ANFIS): Analysis and Applications. GE CRD Schenectady, NY USA, 1 1997.

Prognosis methods

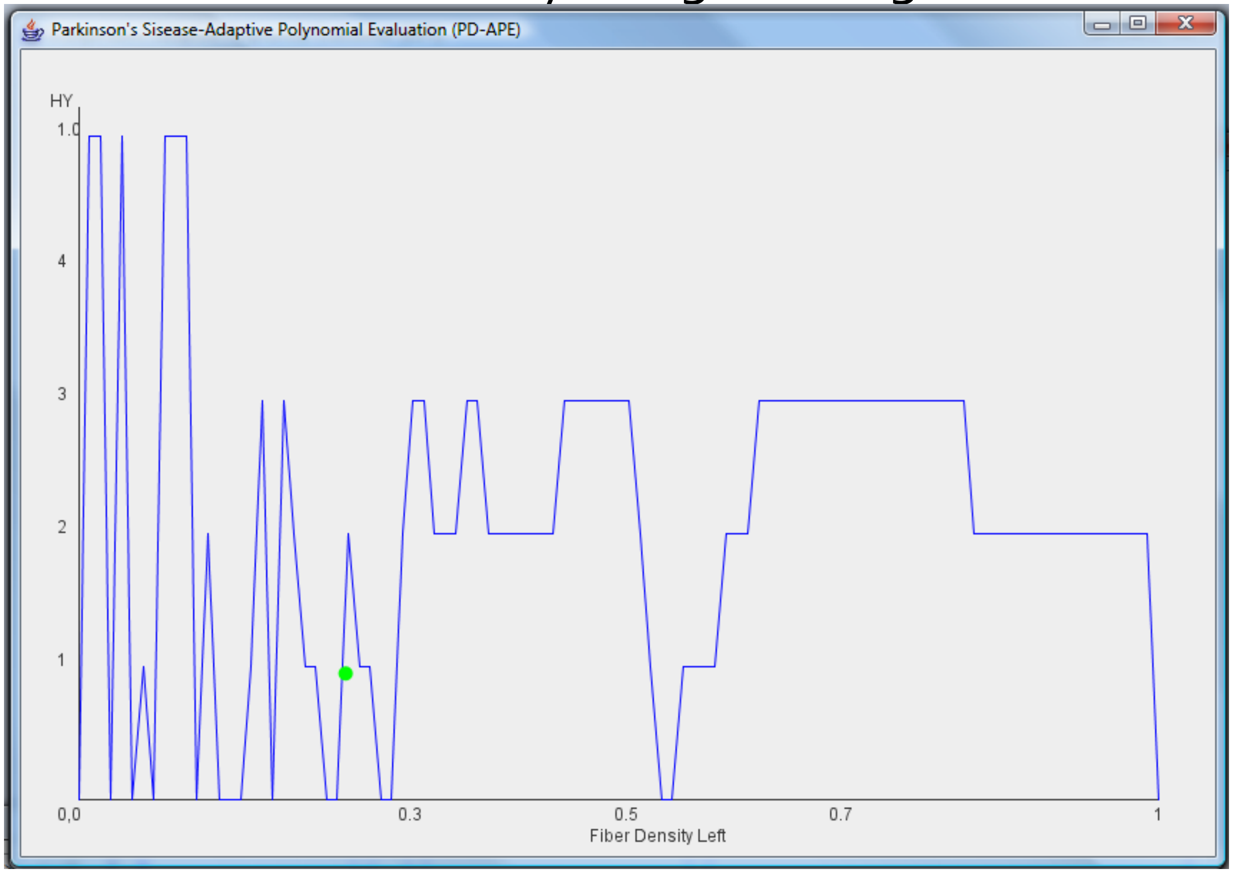
- Lagrange polynomials

$$L(x) = \sum_{i=0}^{N} y_i * \prod_{j=0, j \neq i}^{N} \frac{x - x_j}{x_i - x_j}$$

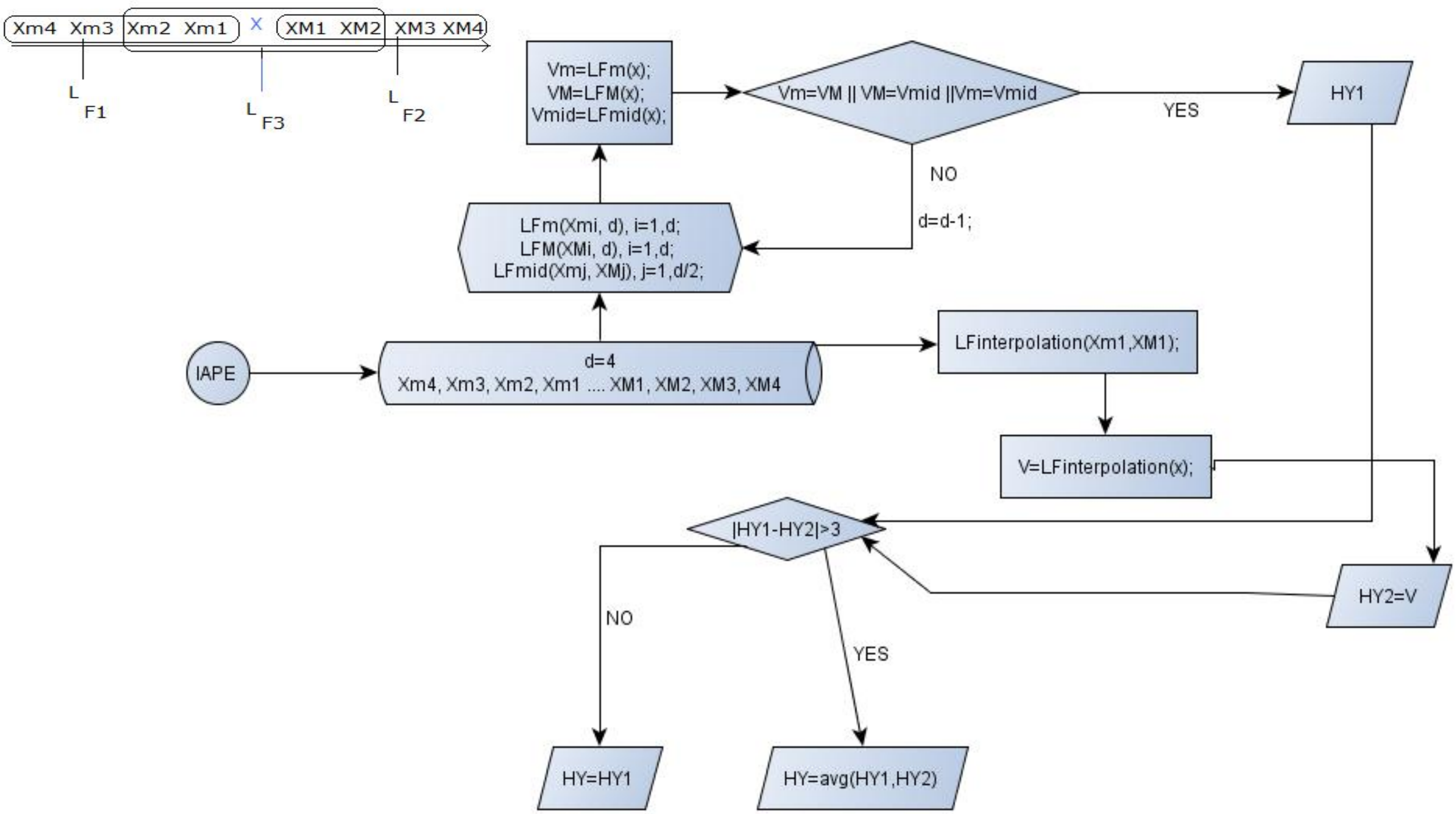
  - Determinig intervals – fuzzy sets
  - 2-nd and 4-th degree polynomials
- Independent Adaptive Polynomial Approach (IAPE)
- Parkinson's Disease- Adaptive Polynomial Evaluation (PD-APE)

Prognosis methods – PD-APE

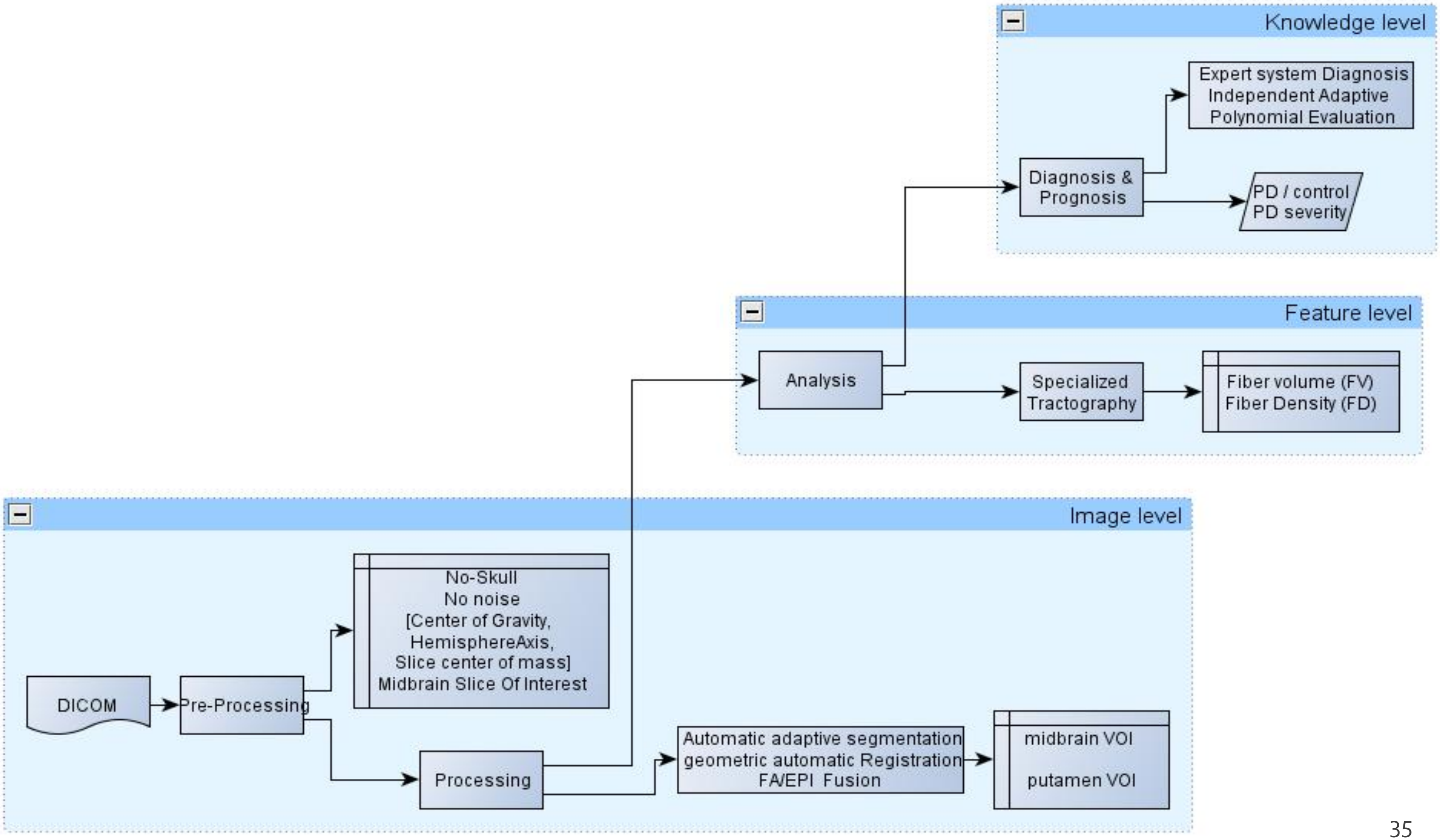
- Diagnosis based on rules : does the patient have PD?
  - NO – duble check aplying the 2-nd degree polynomial
  - YES – evaluate the severity using the neighbour values



Independent Adaptive Polynomial Evaluation (IAPE)



From image level to knowledge level



Evaluation metrics

- Learning set: Ideal cases with the manual extracted Putamen: 41 cases – 20 PD and 21 control
  - Used for correlation testing
  - On validation and relative error computation for segmentation

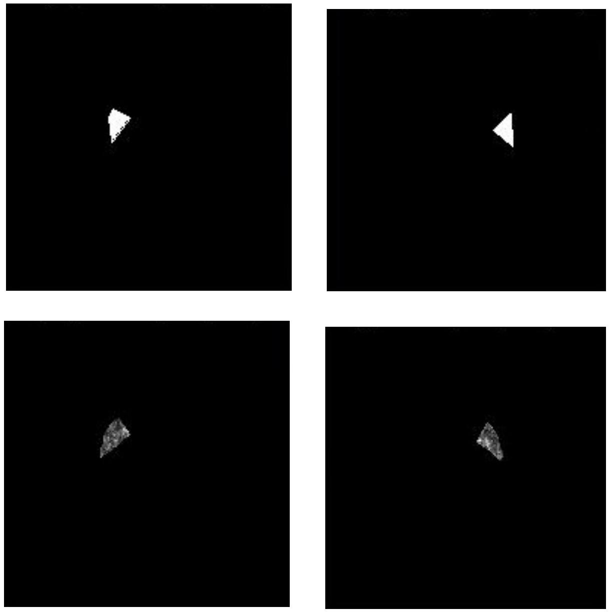
$$Err_{rel} = \frac{x - X}{X} * 100[\%]$$

    - Where x is the measured value and X is the average value of all measurements
    - For setting up the diagnosis expert system
    - For defining the prognosis functions

- Database : 68 PD cases and 68 controls totally automatic processing and analysis trough PDFibAtl@s

Segmentation results

- Midbrain area
  - validates by the neurologist
- Putamen segmentation
  - AND between the manual segmentation and the automatic detection
  - Relative error on the Putamen detection
    - Triangular+ quadrilateral approach : 34.66% left side detection, 35.75% for right side volume
    - Aligned Volume approach: 37.16% on the left side, 39.16% for the right side



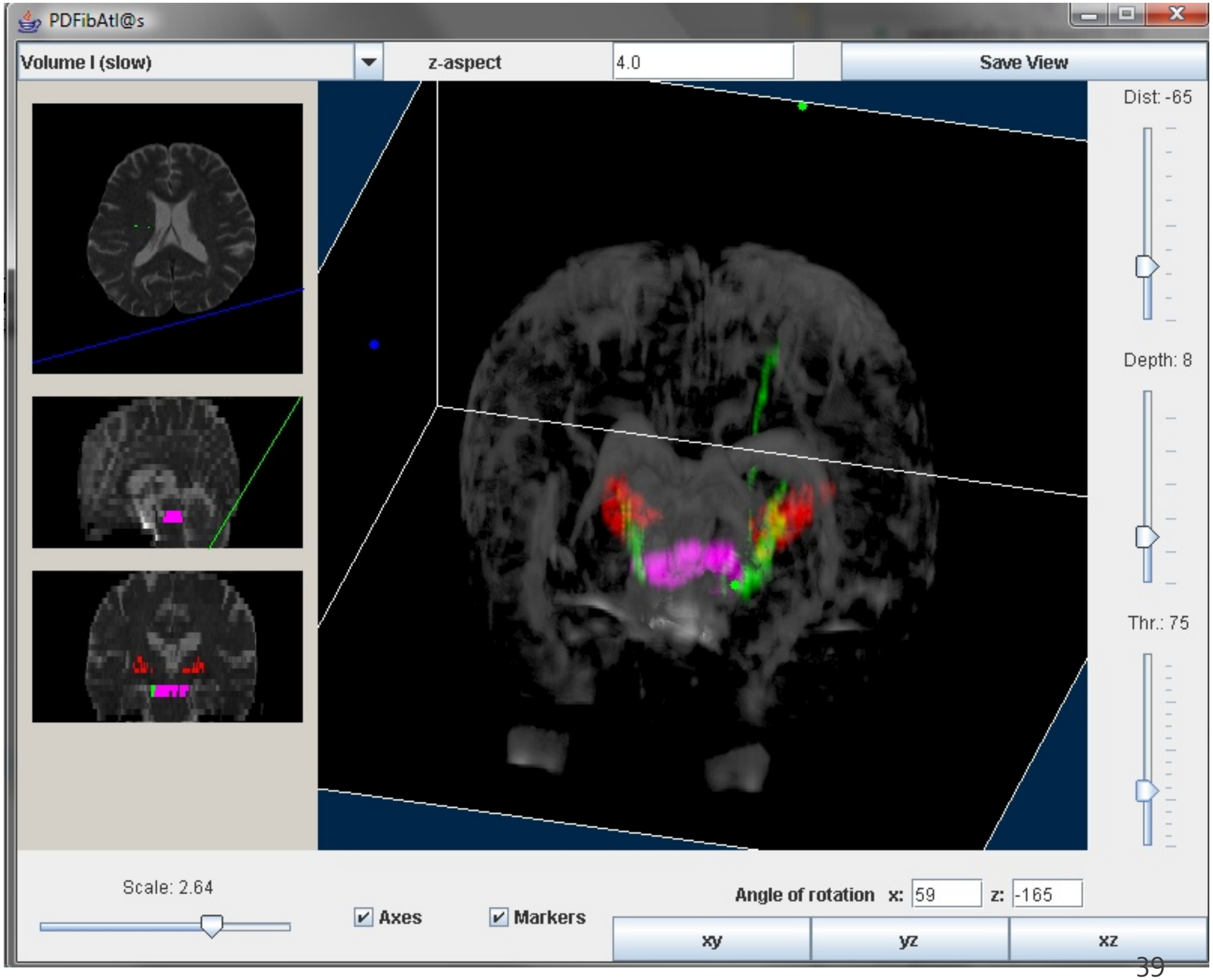
Tractography relevance at the image level

- Determining if the fibers from the Midbrain and Putamen can be used as a PD indicator
  - Homogeneity using 80% of the ideal test-set p=0.05
  - ANOVA test (N=35 subjects) - the correlation with H&Y scale : significance is 83%

Test Nr.	One Way ANOVA				MANOVA	
	FV		FD		FD	
	Left	Right	Left	Right	Left	Right
1	0.00	0.00	0.00	0.00	0.105	0.515
2	0.00	0.00	0.00	0.00	0.638	0.067
3	0.00	0.00	0.00	0.00	0.138	0.404
4	0.00	0.00	0.00	0.00	0.329	0.404
Total	0.00	0.00	0.00	0.00	0.149	0.629

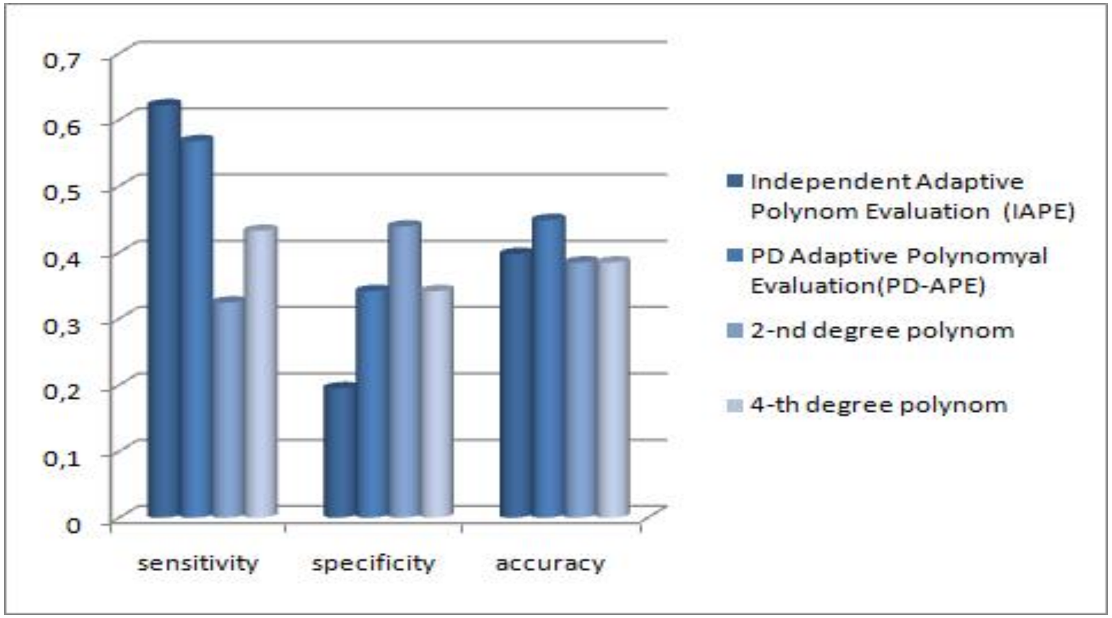
Tractography evaluation

- Relevance as method
  - Determining correctly the fibers
- Overall performances
  - Specificity : 63%
  - Sensitivity : 81%
  - Accuracy: 78.5 %



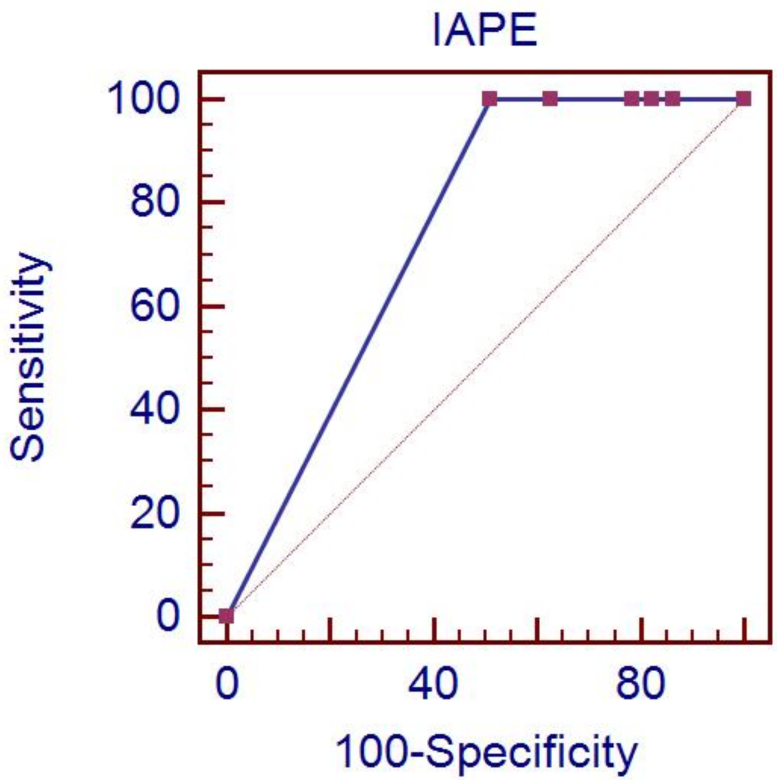
Prognosis evaluation

- Maximum sensitivity: 62.16% for IAPE on the PD cases and 43.9% for second degree polynomial on the controls
- Accuracy is the best on the PD-APE : 44.87%



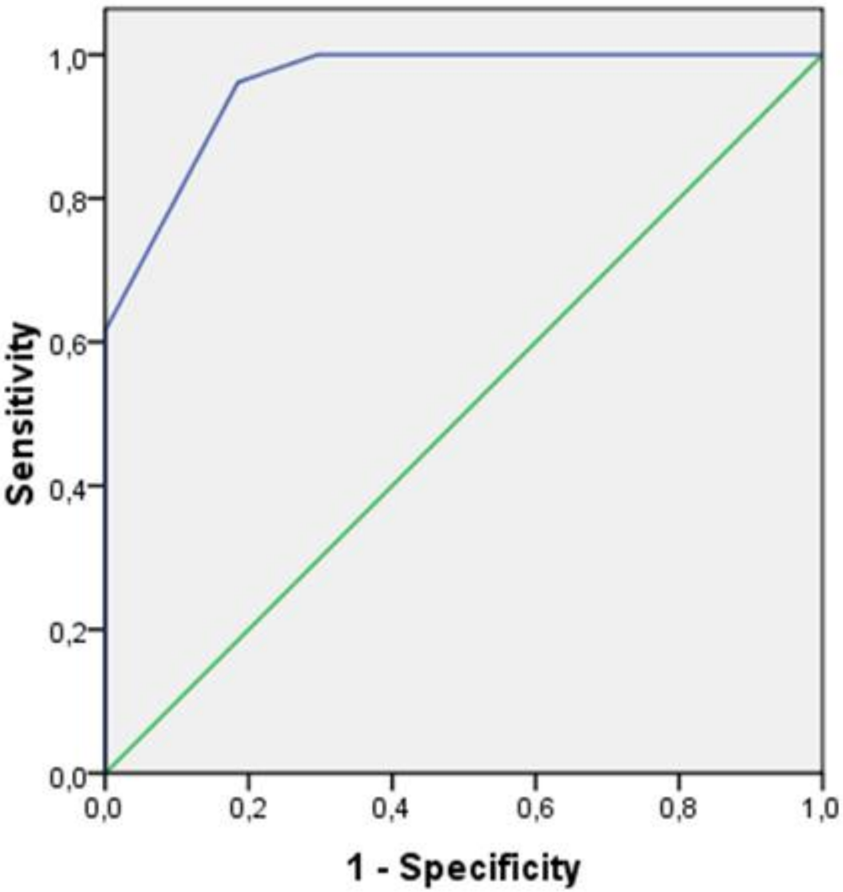
UFC
UNIVERSITÉ DE FRANCHE-COMTÉ

Prognosis evaluation – IAPE vs. PD-APE

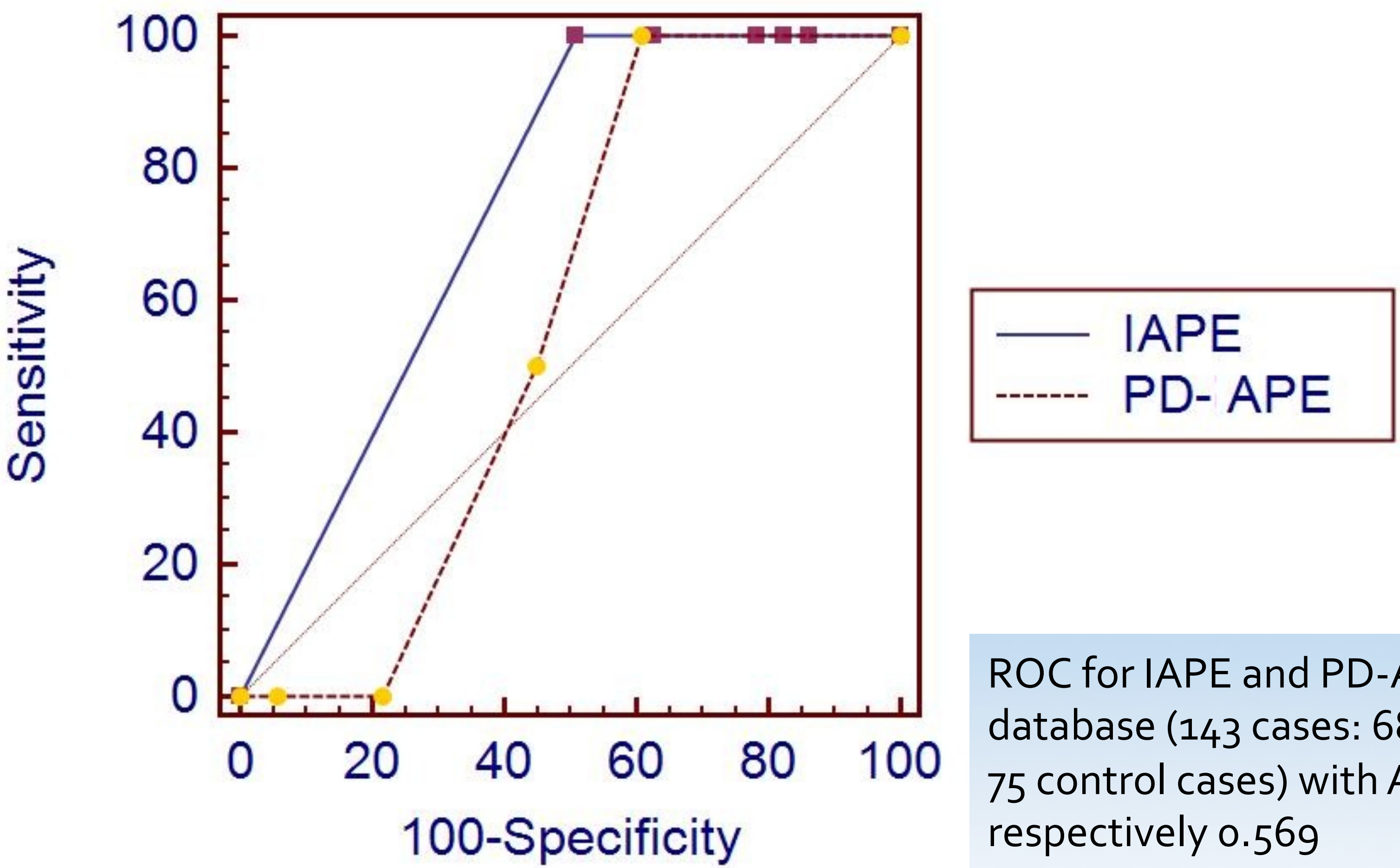


ROC for IAPE on the whole database (68 PD cases+ 75 controls) AUC value 0.745

ROC for PD-APE on the patient data (68 cases) AUC value 0.959

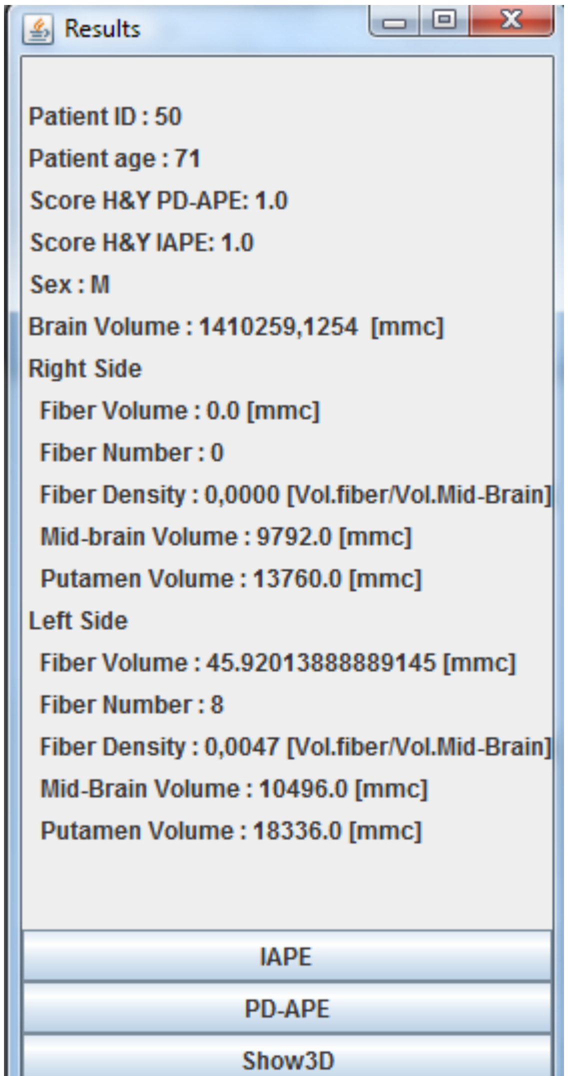


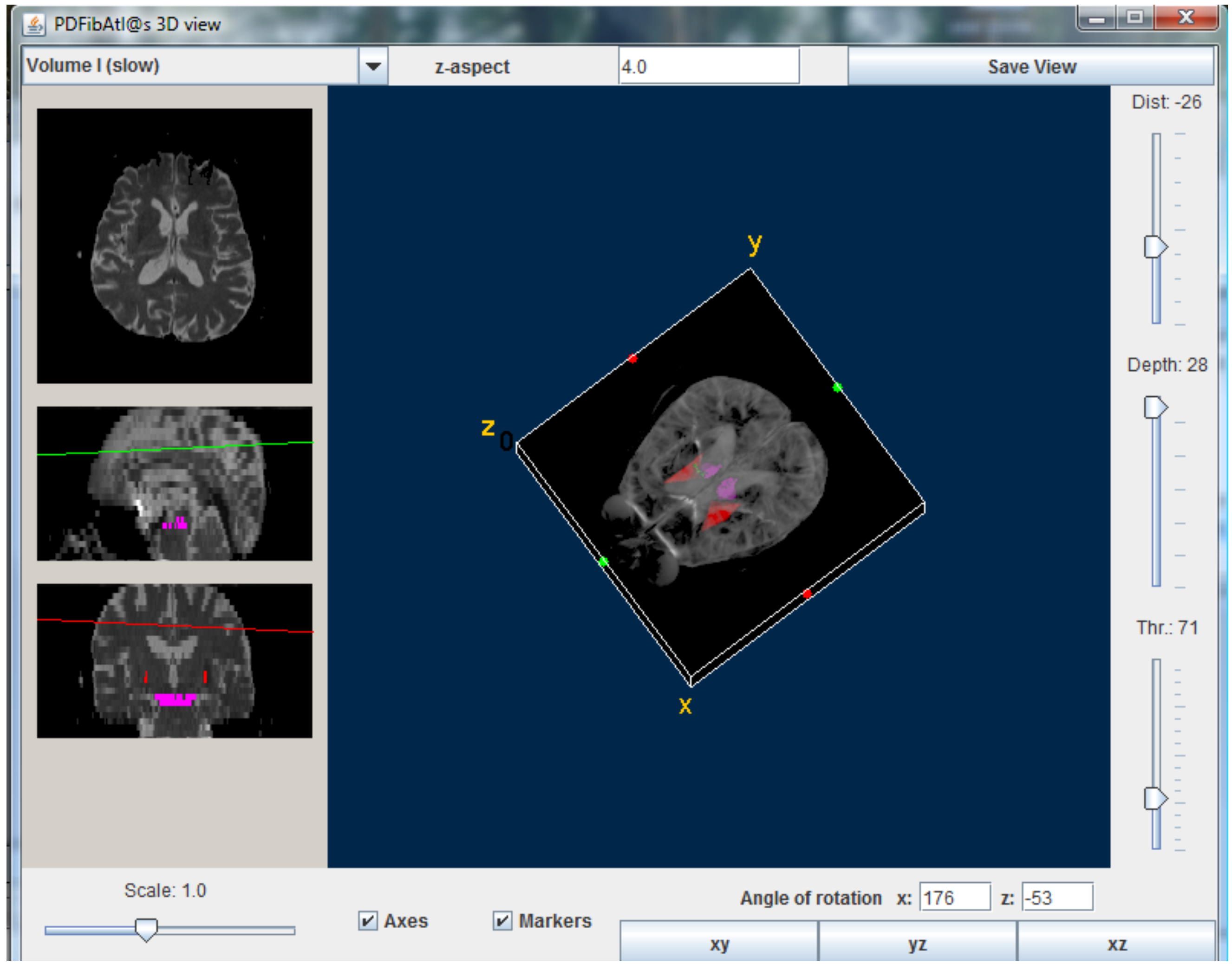
Overall prognosis performance



ROC for IAPE and PD-APE on the database (143 cases: 68 PD patients + 75 control cases) with AUC values 0.745 respectively 0.569

Results with the PDFibAtl@s prototype





Conclusion - Global Contributions

- Pioneering contribution to the use of medical image as a bio-marker for PD
  - Consistent and heterogeneous database
  - Integrated system
- Alternative automatic approach to the cognitive testing
  - Measurable values for the disease
  - Correlated with the H&Y scale
  - Complementary to the classical approach
- Automated system for PD prognosis
- Specialized PD atlas

Conclusion – Scientific contribution Pre-processing level

- Eliminating
  - Inter-patient variability
    - Method determining geometrical landmarks for each patient
    - Inter-hemispherial axis automated algorithm
    - Relative positioning method at the volume level
  - Intra-patient variability
    - Specific algorithms for each hemisphere
    - Intuitive methods for segmentation

Conclusion – Scientific contributions Processing level

- Segmentation approach
  - Midbrain
    - Automatic and hemispherical independent
    - Adapted for each shape
  - Putamen
    - Automatic detection of ROI for each hemisphere
    - Independent and intuitive treatment for each side
    - Adapter for each slice (triangular vs. quadrilateral approach)
    - Controlled alignment for the extracted volume
- Registration
  - Fully automatic
  - Using detected variables
  - Providing information fusion (FA and EPI)

Conclusion – Scientific contributions Knowledge level

- Diagnosis and Prognosis
  - Possibility to evaluate the mild cases
  - Value of PD at the image level
  - Adaptive and intuitive new methods (IAPE / PD-APE)

Conclusion – Perspectives and applications

- Medical Image used as a marker for **other neurodegenerative diseases**
  - Automatic Segmentation extended to **other anatomical regions**
  - **Fusing** several medical images

Conclusion – Perspectives and applications

- Tractography level
  - Determining **another volume of interest (**Globus Pallidus)
- Diagnosis and Prognosis
  - **Dedicated function** for evaluation
  - Using the prognosis function in **an Radial Basis Function Network**

Conclusion – New Perspectives

- Study in time on the patients at the image level can provide
  - **A function of PD evolution** at the fiber level and/or the volumes of interest
  - Determine the **rate of deterioration** of the fibers
  - A **function of atrophy**
  - A map for a **healthy patient** and one for a **PD affected** patient extracting
    - aging parameters (the way the volume and the regions are affected)
    - the disease specific parameters and their evolution
    - Providing another prognosis using these additional data

Publications (1/2)

1. Roxana Oana Teodorescu, Vladimir Ioan Cretu & Daniel Racoceanu. *Diagnosis and Prognosis on Parkinson's desease using an automatic image-based approach*. Book chapter., title "Biomedical Engineering, Trends in Electronics, Communications and Software", Ed. Anthony N. Laskovski, ISBN 978-953-307-475-7, published by INTECH, 2011.

2. Anda Sabau, Roxana Oana Teodorescu and Vadimir Ioan Cretu. *A New Cerebral Anatomical-Based Automated Active Segmentation Method* - to appear, Scientific Bulletin of the Politehnica University of Timisoara, Transactions on Automatic Control and Computer Science, ISSN 1224-600X, 2010.

3. Roxana Teodorescu. *H&Y Compilant for PD Diagnosis and Prognosis using EPI and FA images.* Phd report no. 2, Politehnica University of Timisoara, February 2010.

4. Anda Sabau, Roxana Oana Teodorescu and Vadimir Ioan Cretu. *Automatic Putamen Detection on DTI Images*. Application to Parkinson's Disease. ICCC-CONTI, vol. 1, pages 1-6, may 2010.

5. Teodorescu, R.; Racoceanu, D.; Smit, N.; Cretu, V. I.; Tan, E. K. & Chan, L.-L. *Parkinson's disease prediction using diusion based atlas* - poster session SPIE - Computer Aided Diagnosis [7624-78] PS2, 13-18 Febr., San Diego CA, USA 2010.

6. Roxana Oana Teodorescu. *Feature extraction and Ontology use for Brain medical images* - PhD Report No 1. Rapport technique 1, UPT and UFC, January 2009.

7. Teodorescu, R.; Racoceanu, D.; Chan, L.; Lovblad, K. & Muller, H. Parkinson's disease detection using 3D Brain MRI FA map histograms correlated with tract directions - oral presentation Neuroradiology (Brain: Movement and Degenerative Disorders SSC13 - 09) RSNA,95th Radiological Society of North America Scientific Conference and Annual Meeting, November 29 to 4 December, McCormick Place, Chicago IL, USA, 2009.

8. Teodorescu, R. O. & Racoceanu, D. Prognosis of Parkinson's Disease – poster session, A*STAR Scientic Conference, 28-29 Oct., Biopolis, Singapore 2009.

Publications (2/2)

9. Teodorescu, R. O.; Racoceanu, D. & Chan, L.-L. H&Y compliant for PD detection using EPI and FA analysis - poster session, NIH Workshop Inter-Institute Workshop on Optical Diagnostic and Biophotonic Methods from Bench to Bedside, 1-2 Oct, Washington DC, USA 2009.

10. Teodorescu, R.; Cernazanu-Glavan, C.; Cretu, V. & Racoceanu, D. The use of the medical ontology for a semnatic-based fusion system in Biomedical Informatics - Application to Alzheimer disease ICCP Proceedings, 2008, 1, 265-268.

11. Teodorescu, R.; Cretu, V. & Racoceanu, D. The use of medical ontology in a semantic-based fusion system CONTI, 2008, 1, 48-52.

12. Teodorescu, R.; Racoceanu, D.; Leow, W.-K. & Cretu, V. Prospective study for semantic Inter-Media Fusion in Content-Based Medical Image Retrieval Medical Imaging Technology, 2008, 26, 48-58

13. R. Teodorescu and D. Racoceanu. *Semantic Inter-Media Fusion Design for a Content-Based Medical Image Retrieval System*. Japanese Society of Medical Imaging Technology - JAMIT-ONCO-MEDIA workshop, vol. Tsukuba, Japan, pages 43-47, 21 - 22 july 2007.

14. Lacoste, C.; Chevallet, J.-P.; Lim, J.-H.; Hoang, D. L. T.; Wei, X.; Racoceanu, D.; Teodorescu, R. & Vuillenemot, N. *Inter-media concept-based medical image indexing and retrieval with umls at IPAL* Lecture Notes in Computer Science, Evaluation of Multilingual and Multi-modal Information Retrieval, 2007, 4730, 694-701.

15. Racoceanu, D.; Lacoste, C.; Teodorescu, R. & Vuillemenot, N. A *semantic fusion approach between medical images and reports* using umls Lecture Notes in Computer Science, (Eds.): Asian Information Retrieval Symposium, 2006, 4182, 460-475.