Automatic Image Quantification Strategies in Nuclear Medicine and Neuroradiology

PhD Defense Presentation

F. Sampedro

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- Motivation, objectives and general framework

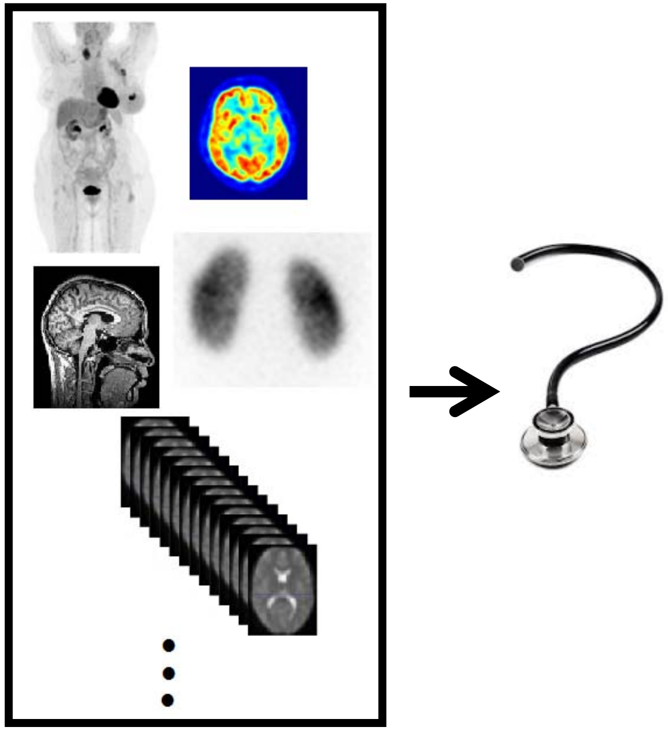
- Contributions to the design and application of automatic quantification strategies in nuclear medicine and neuroradiology

  - Quantification of cross-sectional breast cancer FDG-PET-CT scans
  - Quantification of longitudinal Non-Hodgkin lymphoma FDG-PET-CT scans
  - Quantification of DMSA scans with structural renal damage
  - Quantification of cerebral FDG-PET scans in Alzheimer's Disease
  - Quantification of cortical thickness from T1-MRI scans in Alzheimer's Disease
  - Quantification of gray matter volume from T1-MRI in Parkinson's disease
  - Quantification of task-related brain activation in fMRI in cannabis users

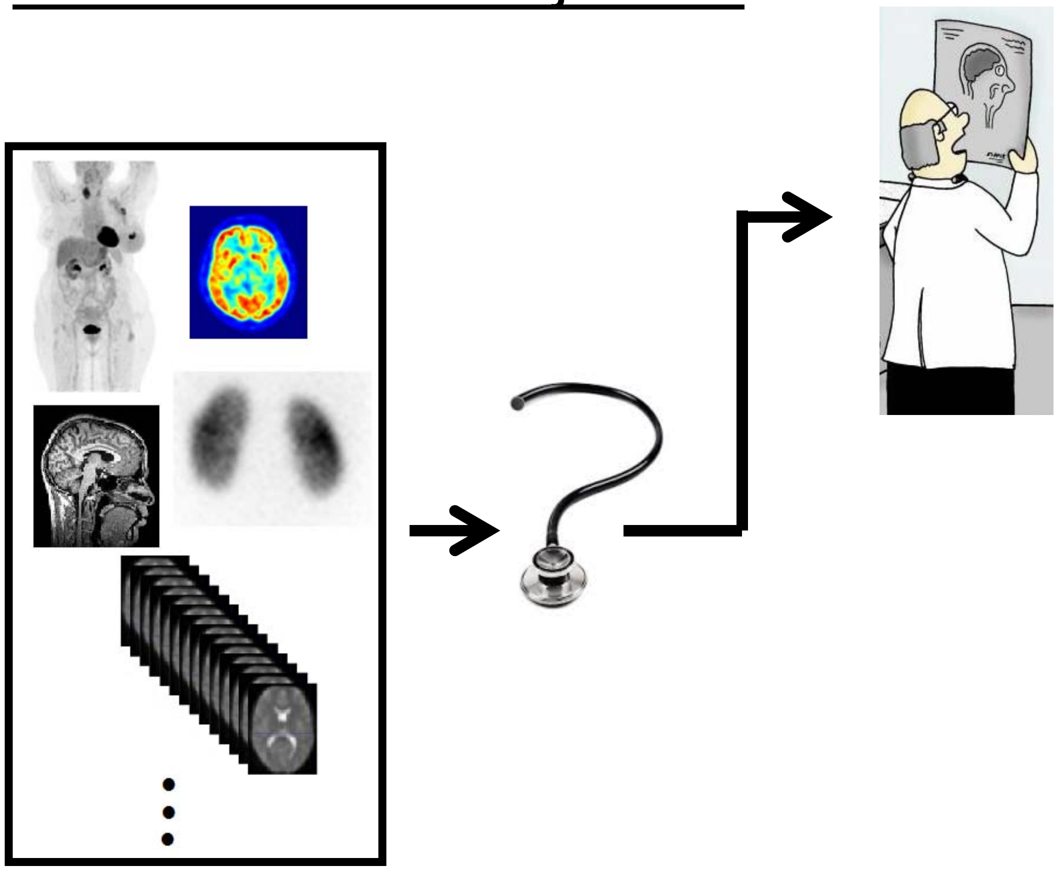
- Other contributions in the field

- General conclusions and future work

Motivation and objective



Motivation and objective



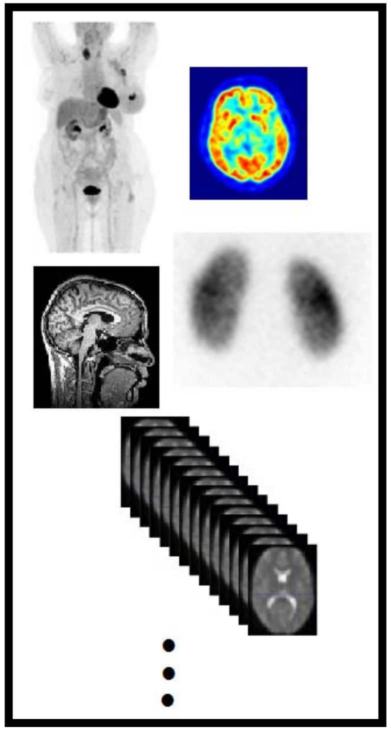
High accuracy at identifying complex image patterns relying on previous knowledge.

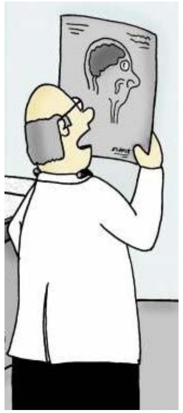
Observer-dependent

Categorical output

Limitation at handling large 4D datasets

Motivation and objective





High accuracy at identifying complex image patterns relying on previous knowledge.

Observer-dependent

Categorical output

Limitation at handling large 4D datasets

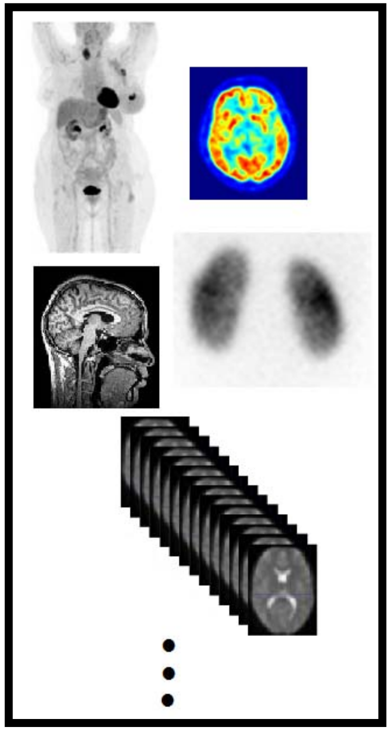
Observer-independent

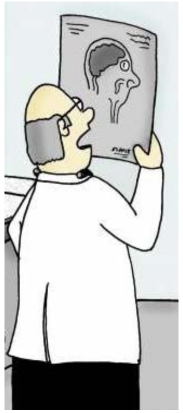
Continuous + categorical output.

Capable of handling large 4D datasets

Medium-low accuracy at identifying complex image patterns relying on previous knowledge.

Motivation and objective





High accuracy at identifying complex image patterns relying on previous knowledge.

Observer-dependent

Categorical output

Limitation at handling large 4D datasets

+

Observer-independent

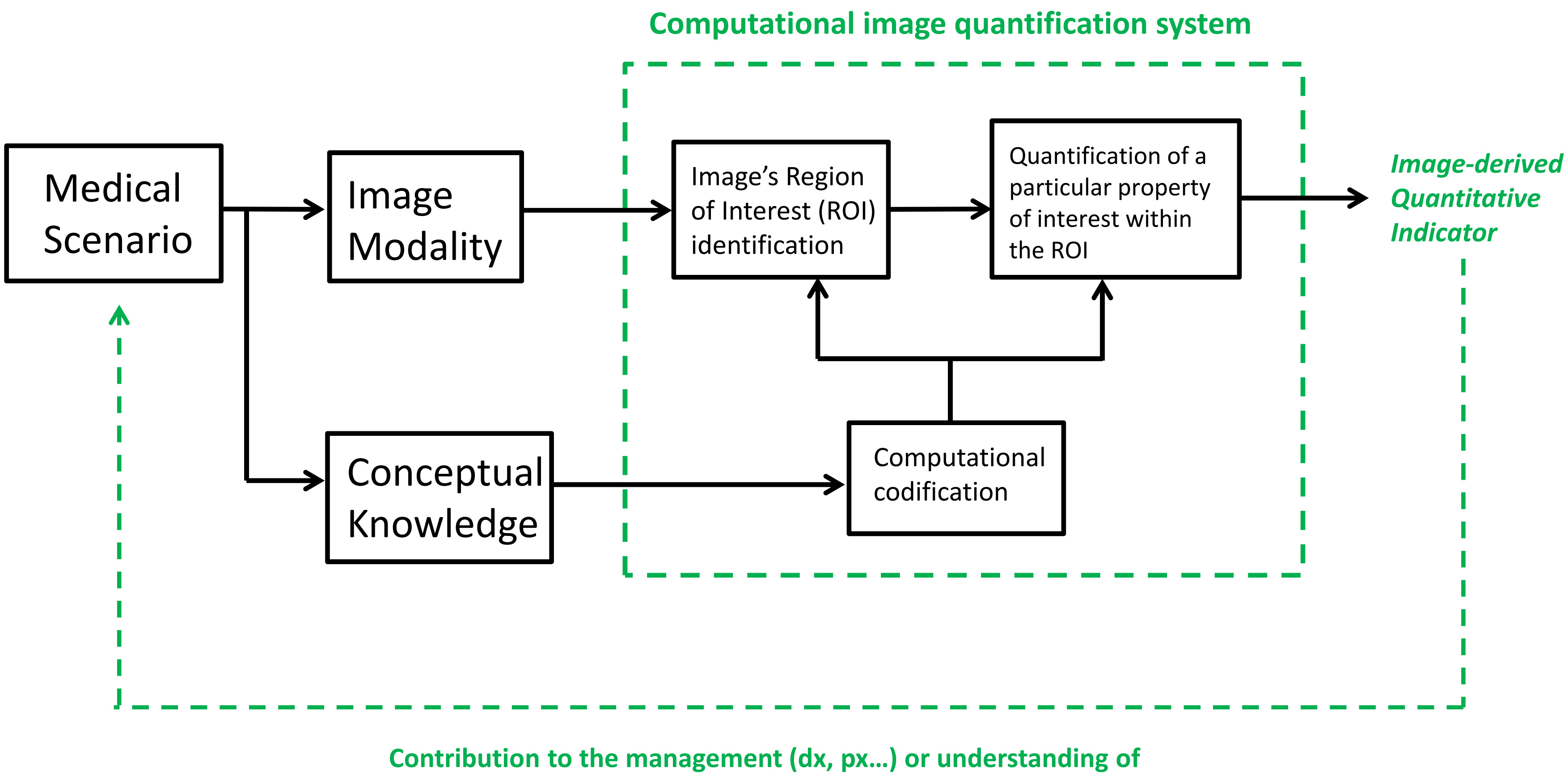
Continuous + categorical output.

Capable of handling large 4D datasets

Medium-low accuracy at identifying complex image patterns relying on previous knowledge.

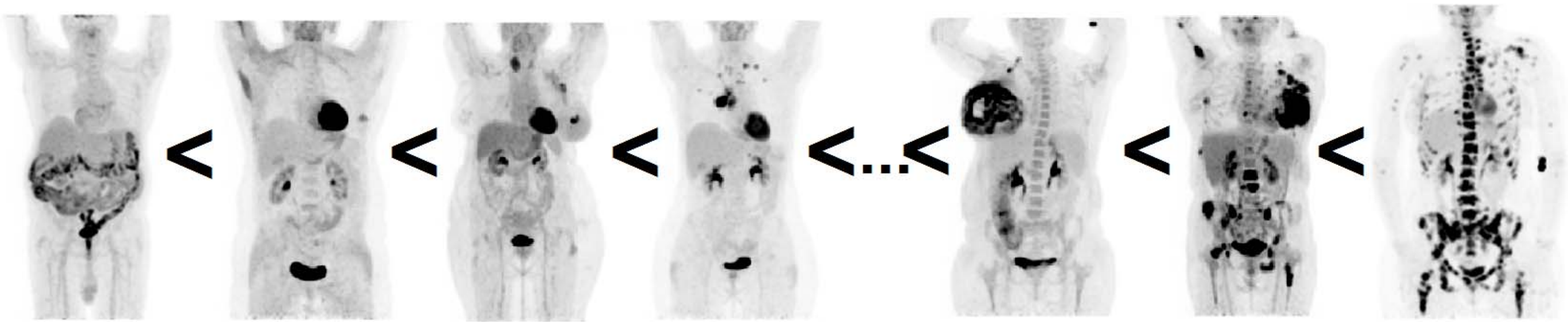
PhD Thesis Objective: To design, implement and validate computational image quantification strategies for a set of nuclear medicine and neuroradiological contexts.

General framework



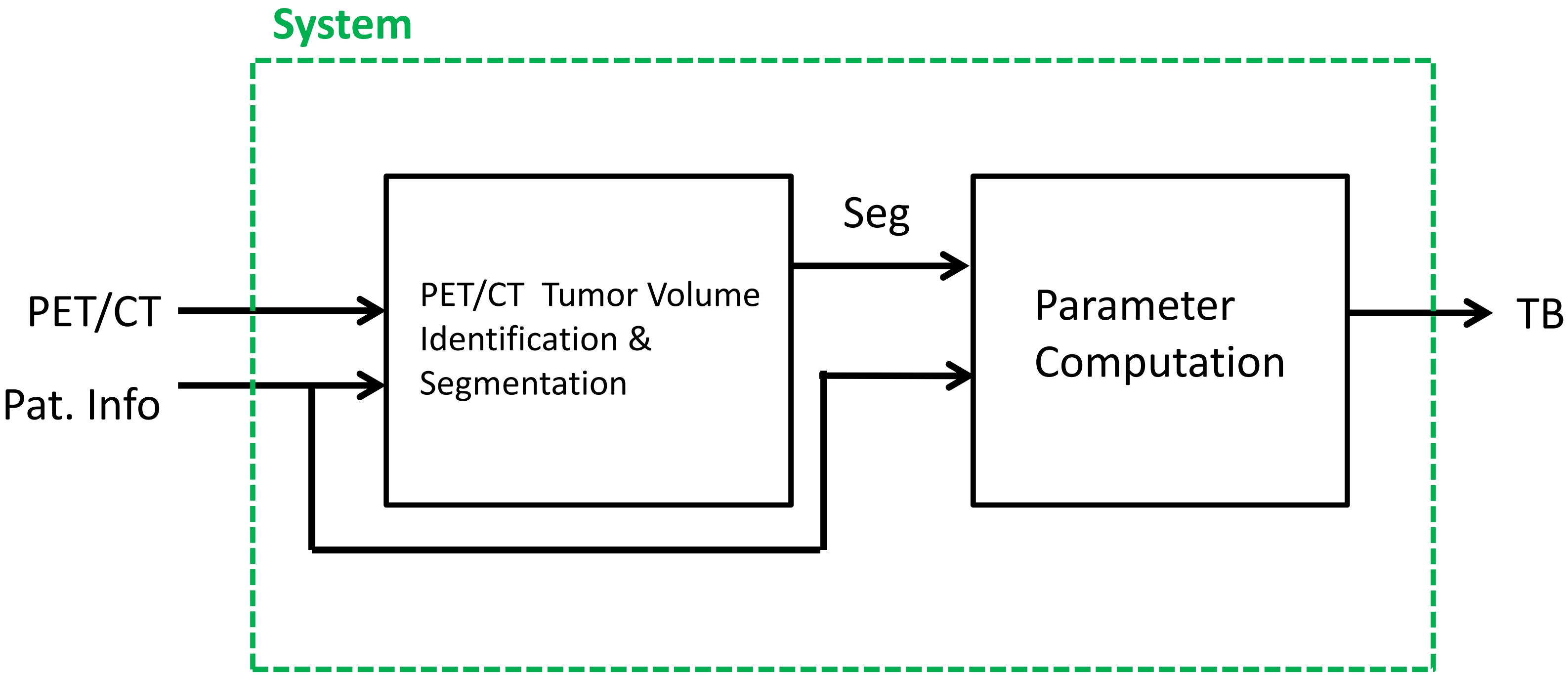
Scenario 1

Oncological PET/CT: Tumor burden (TB) quantification

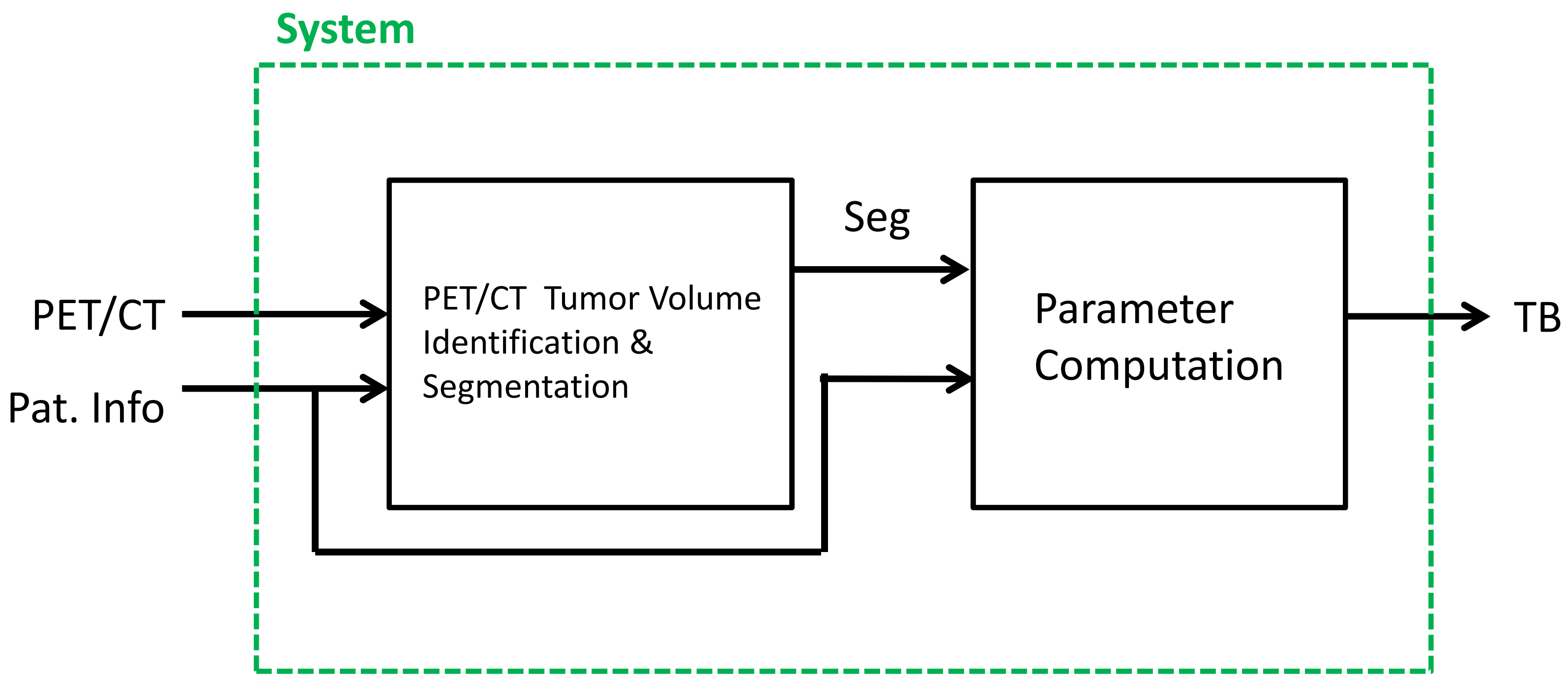


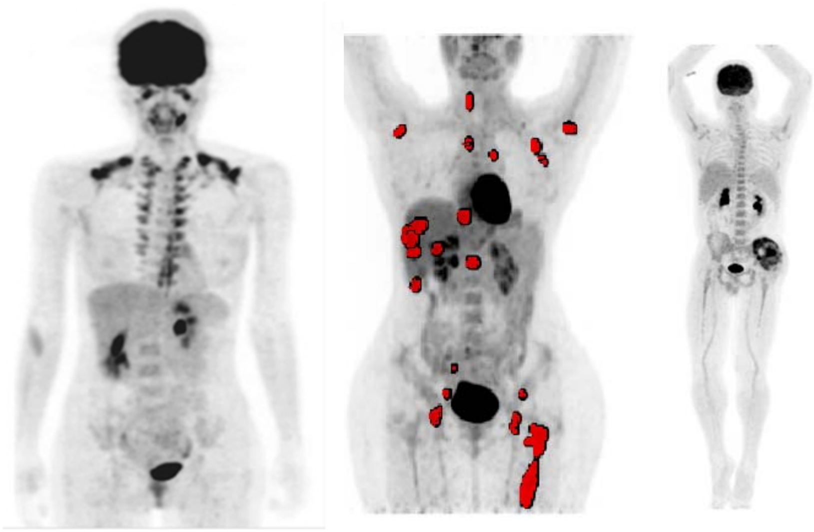
$0 < TB_1 < TB_2 < TB_3 < \ldots < TB_{N-2} < TB_{N-1} < TB_N$

TB computation system

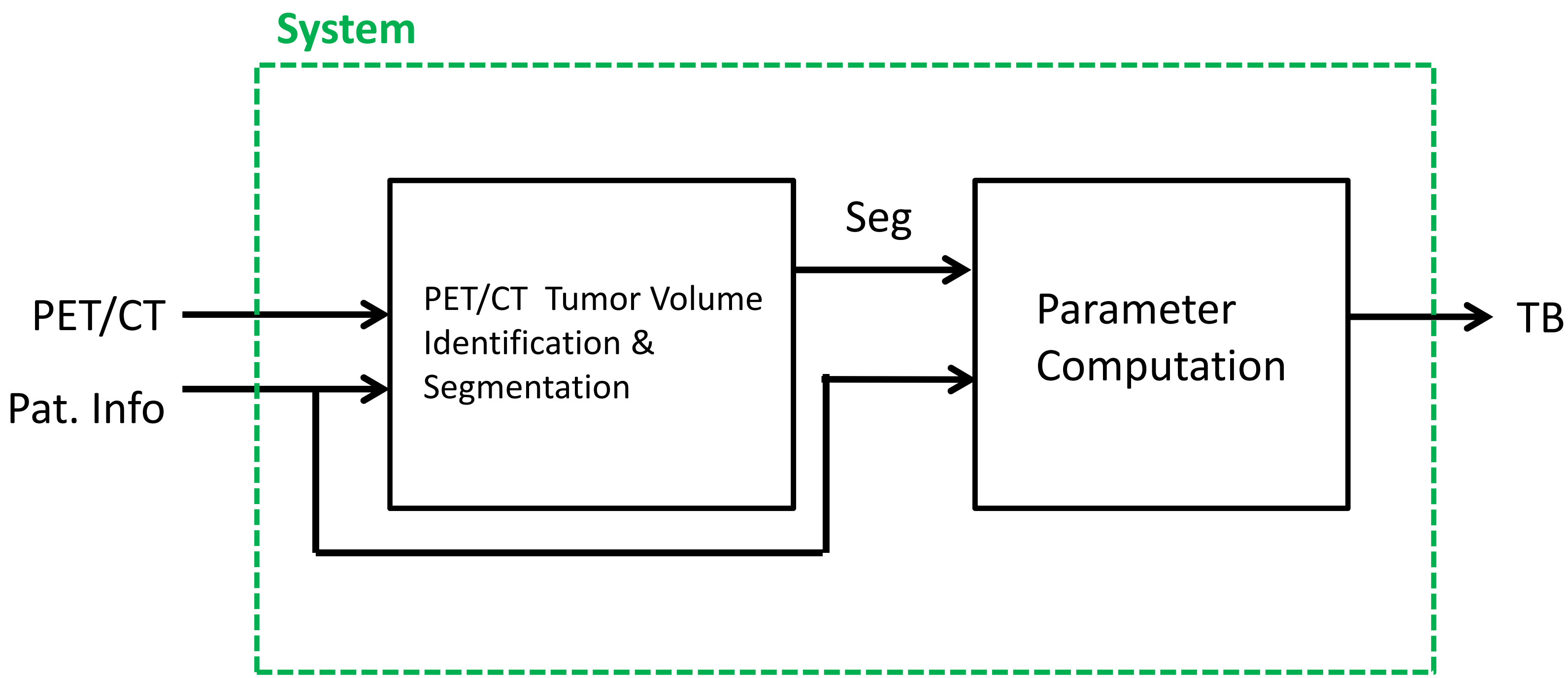


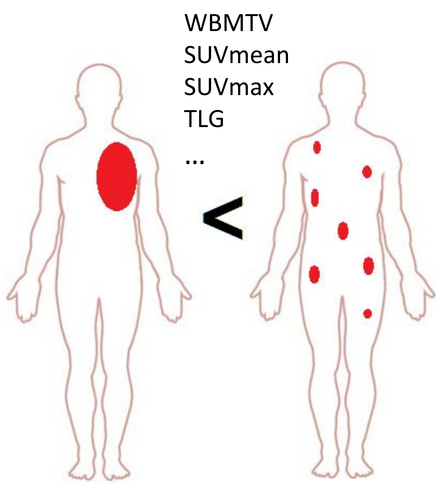
TB computation system



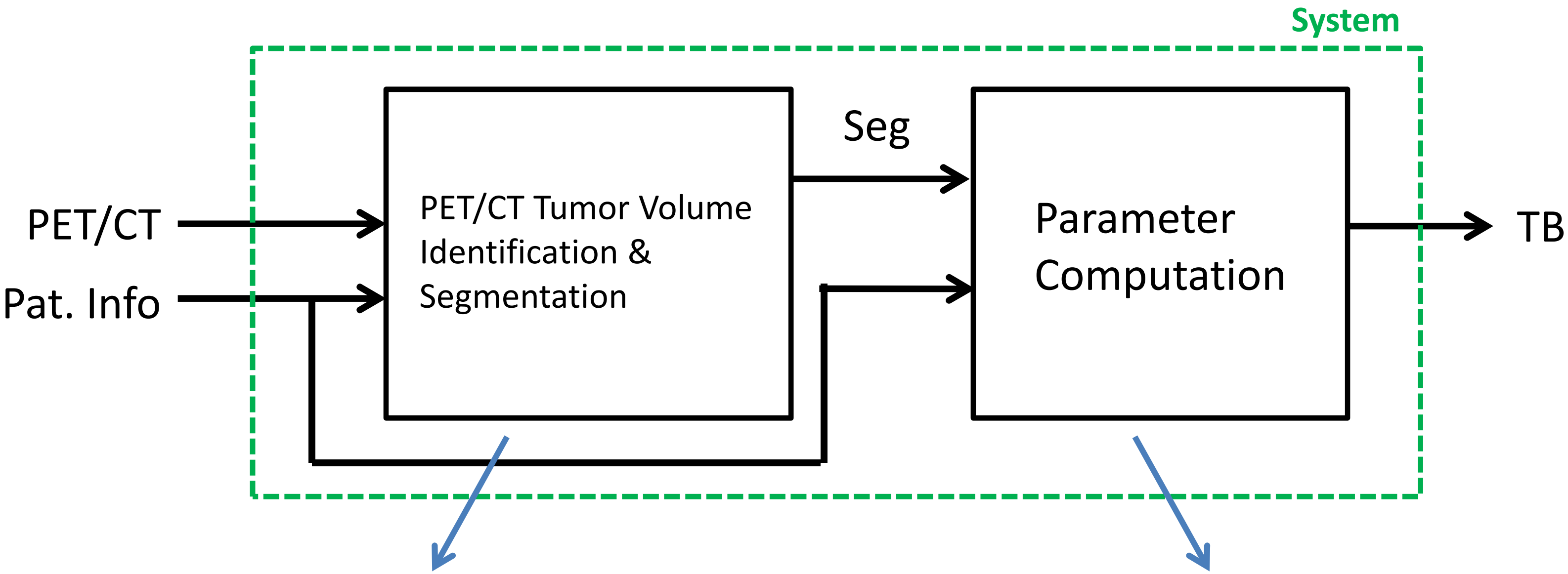


TB computation system





Scientific output



- Artificial intelligence: Machine Learning
- Knowledge codification (feature design)
- Contextual Learning (MSSL)

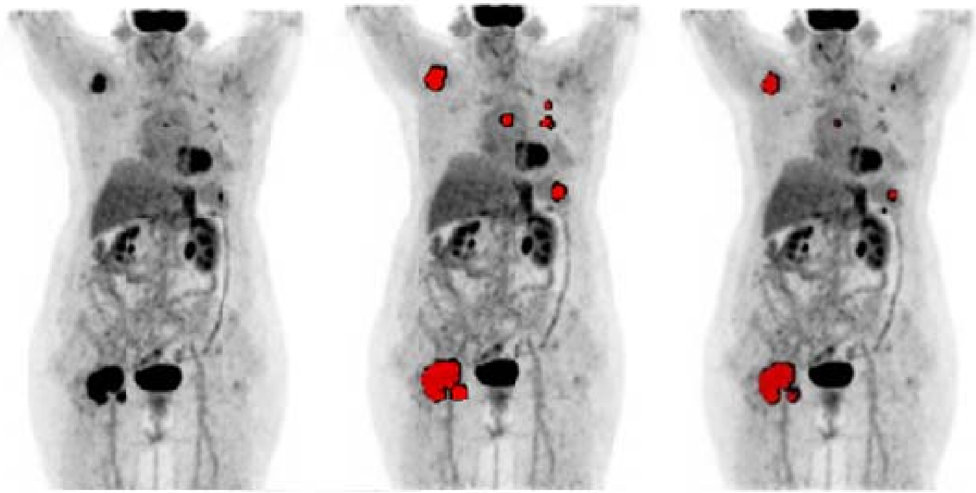
- Computational modeling of Tumor Spread
- Image Processing
- Combination of TB indicators

- **Sampedro et al. Automatic metabolic tumor volume segmentation in whole body PET/CT scans: a supervised learning approach. Journal of Medical Imaging and Health Informatics. 2015.**

- **Sampedro et al. Obtaining quantitative global tumoral state indicators based on whole-body PET/CT scans: a breast cancer case study. Nuclear Medicine Communcations. 2013.**

Illustrative results

PET Manual Seg Automatic Seg



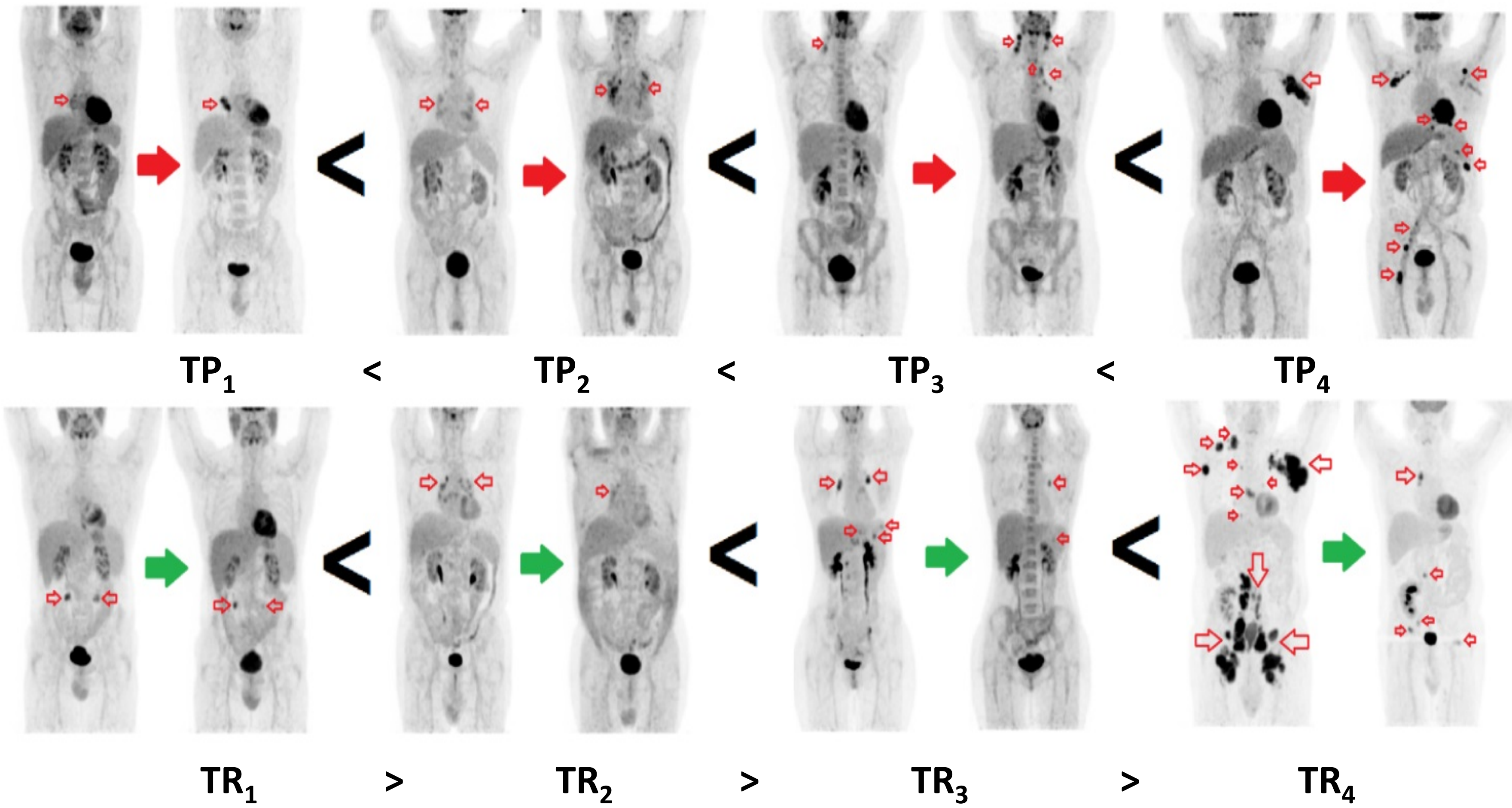
False positive

TB indicator	*Man Seg*	*TB indicator*	*Man Seg*	*Auto Seg*
SUVmean	48%	nTSUV	80%	58%
SUVmax	60%	nTSUV*NCC	85%	62
WBMTV	80%	nTSUV*aNCC	84%	61
TLG	79%	**nTSUV*NORG**	**87%**	**64%**

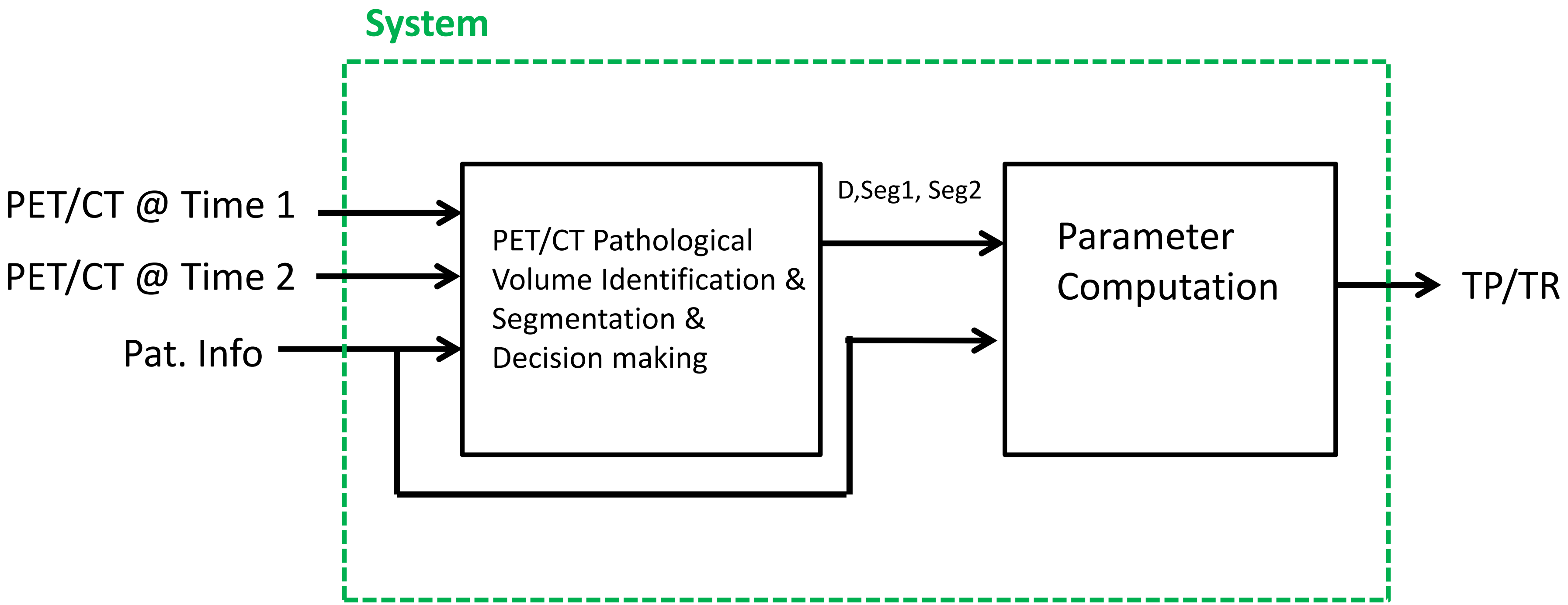
Main conclusion: Automatic tumor segmentation of whole-body PET-CT scans is a computational challenge, showing excessive performance variance to be used in the clinical routine. TB indicators that take into consideration the tumor spread properties offer higher performance at modeling the underlying pathology.

Scenario 2

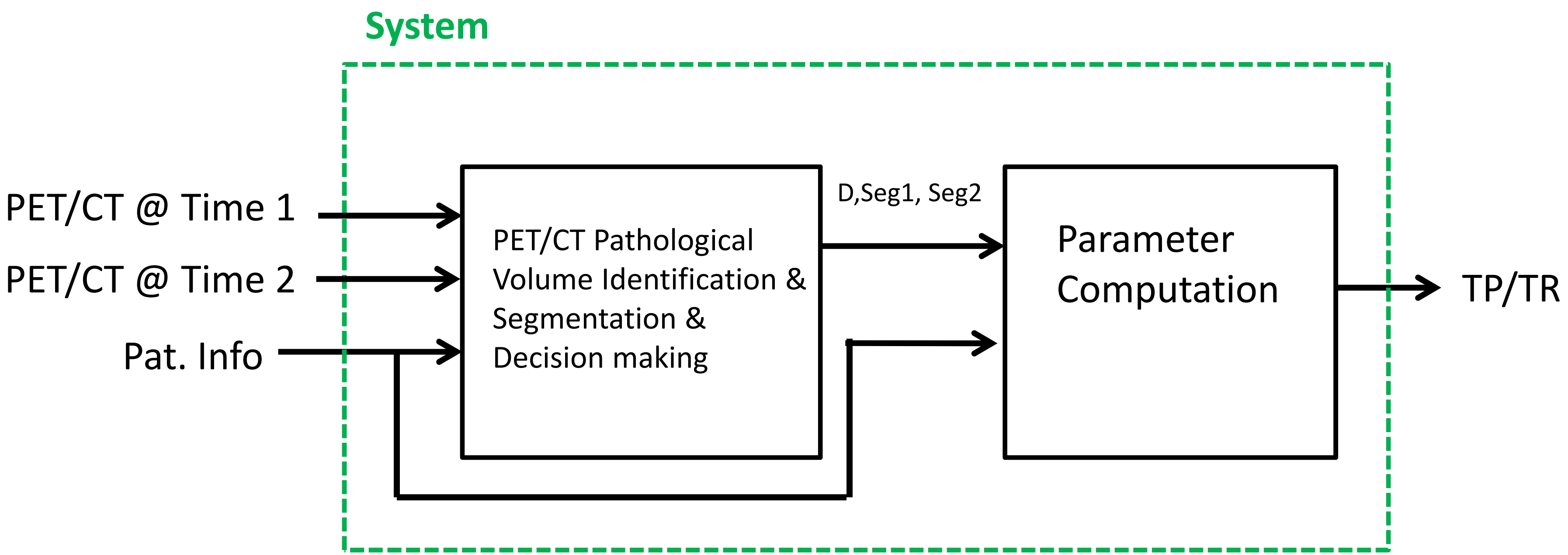
Oncological PET/CT: Tumor response or progression(TR/TP) quantification

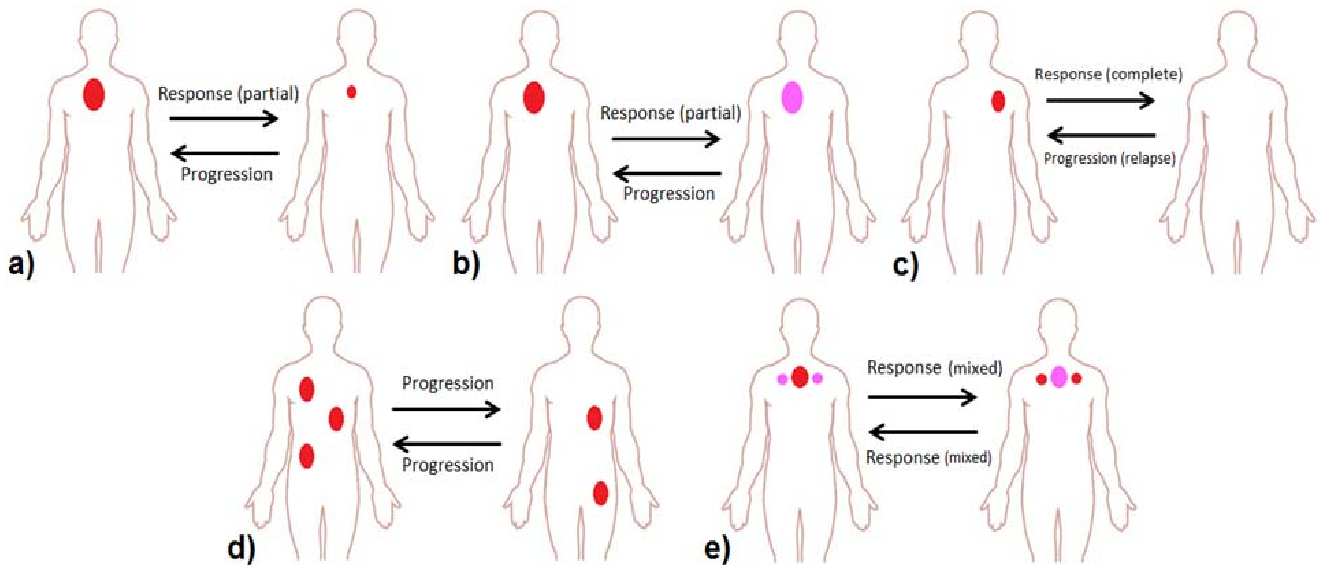


TP/TR computation system

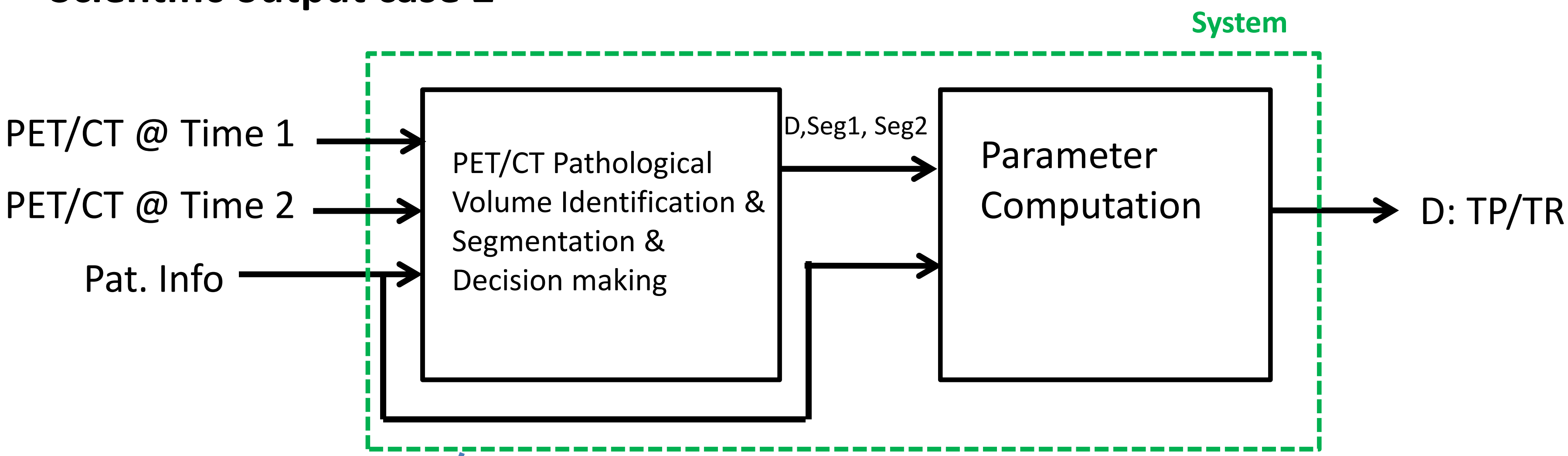


TP/TR computation system





Scientific output case 2



- State of the art classification strategies
- Automatic decision making
- Knowledge codification (feature design)

- Tumor's Spread Change Computational Modeling
- Image Processing
- Combination of TP/TR indicators

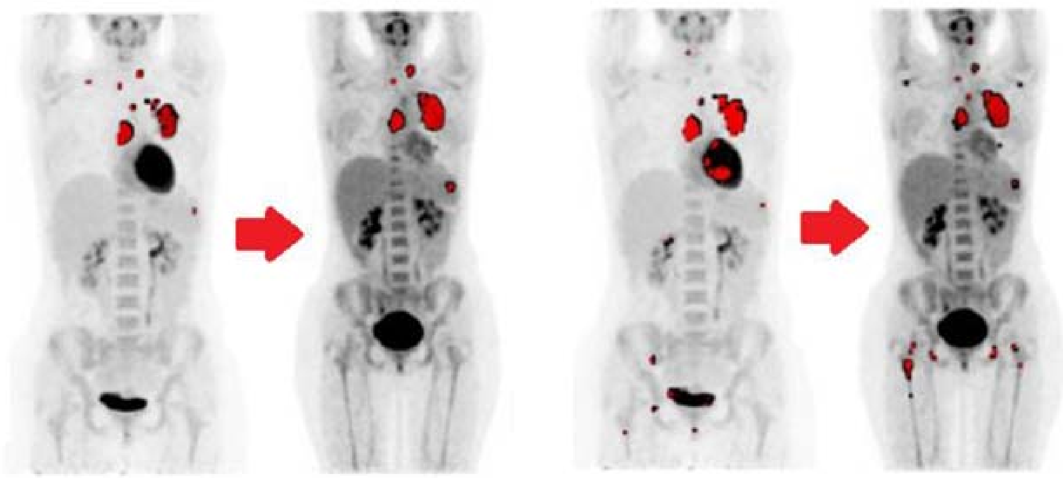
- Sampedro et al. A computational framework for cancer response assessment based on oncological PET-CT scans. Computers in Biology and Medicine. 2014.

- Sampedro et al. Deriving global quantitative tumor response parameters from 18F-FDG PET-CT scans in patients with non-Hodgkin Lymphoma. Nuclear Medicine Communications. 2014.

Illustrative results

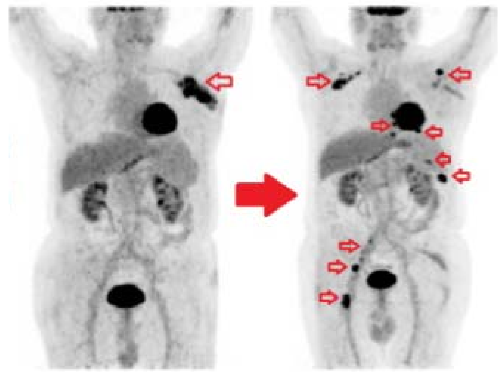
Manual Segmentation **Automatic Segmentation**

70% accuracy at **automatically classifying** response from progression scenarios (**90%** when using **expert-guided** tumor segmentations)



Unable to detect subtle cases given the limitation of the automatic segmentation system

Correlation (%)	ΔWBMTV	ΔSUV_{mean}	ΔSUV_{max}	ΔSUV_{peak}	ΔTLG
Progression	32.3	5.7	4.2	13.8	30.7
Partial Response	76.9	48.1	59.6	43.7	73.8
Mixed Response	8.3	20.0	13.3	26.7	25.0
Relapse	100	54.8	90.5	78.6	90.5
Complete Response	88.5	44.0	64.8	80.8	83.5

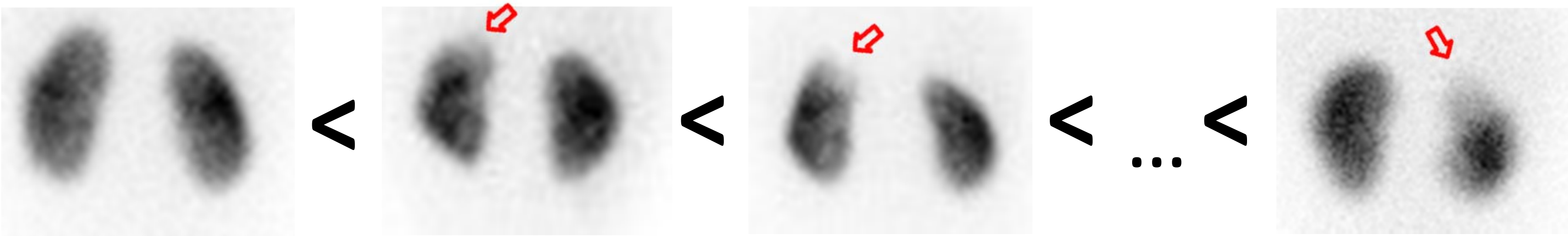


	Indicator	Correlation(%)	Correlation(%): Auto. Seg.
Progression	ΔWBMTV * Vn * nSNTL	80.2	18.1
Partial Response	ΔWBMTV * (1+ |ΔNCC|)	77.1	32.2
Mixed Response	A_N / ΔWBMTV	68.3	28.3
Relapse	ΔWBMTV	100	45.2
Complete Response	ΔNCC	88.5	41.2

Main conclusion: Completely automatic evaluation and quantification of the tumor response in time from a pair of PET-CT scans has important computational limitations and therefore remains unpractical. Quantitative tumor response indicators that take into consideration the tumor's spread change in time offer higher performance properties at modeling the underlying tumor evolution.

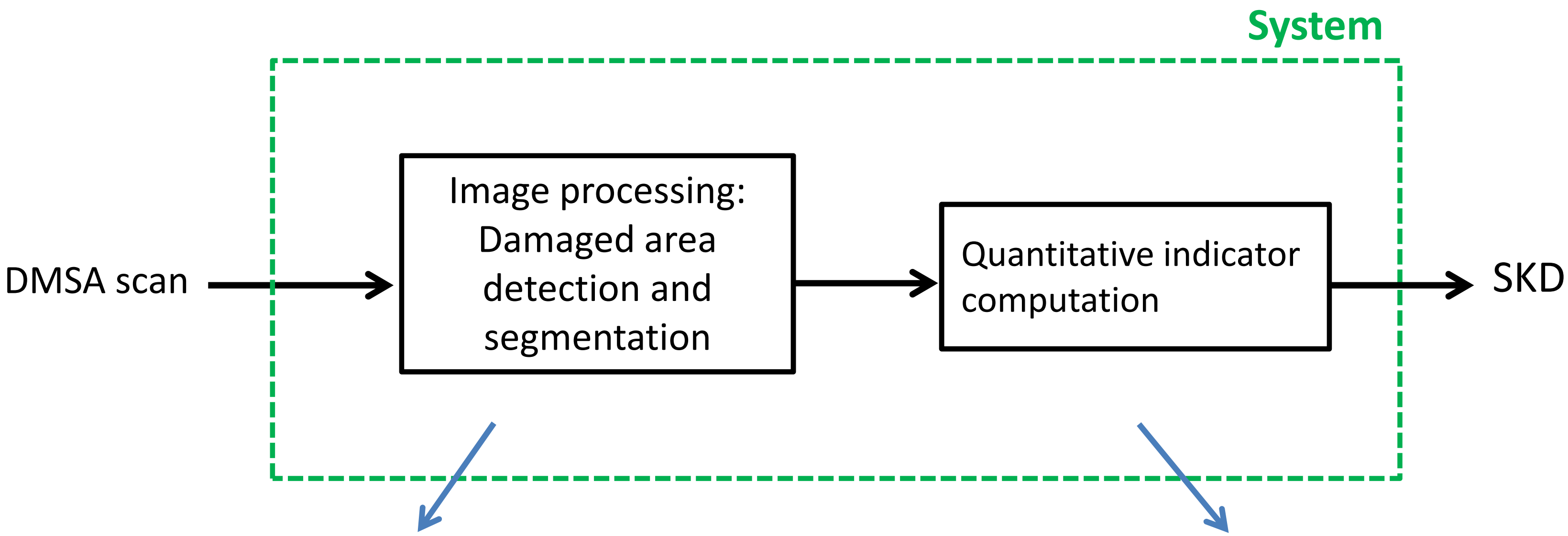
Scenario 3

DMSA quantification of structural kidney damage (SKD)



0 < SKD_1 < SKD_2 < … < SKD_N

SKD computation system

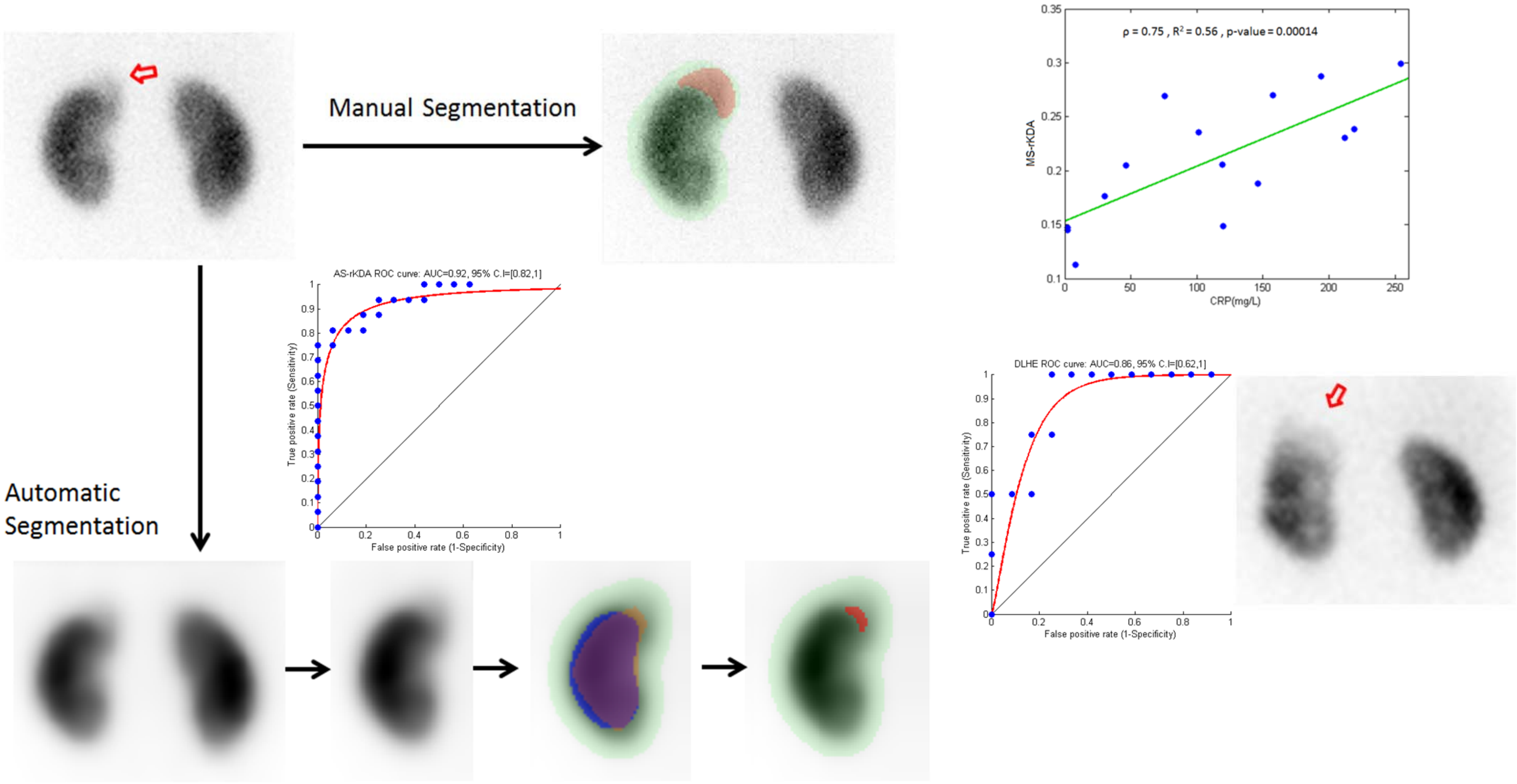


- Anisotropic filtering (Perona & Malik)
- Kidney segmentation (gradient search+LRBAS)
- Lesion detection (ad-hoc iterative erosion)

- Relative damaged area
- Relative damaged area tracer uptake

Sampedro et al. Computing quantitative indicators of structural renal damage in pediatric DMSA scans. Revista Española de Medicina Nuclear e Imagen Molecular. 2016.

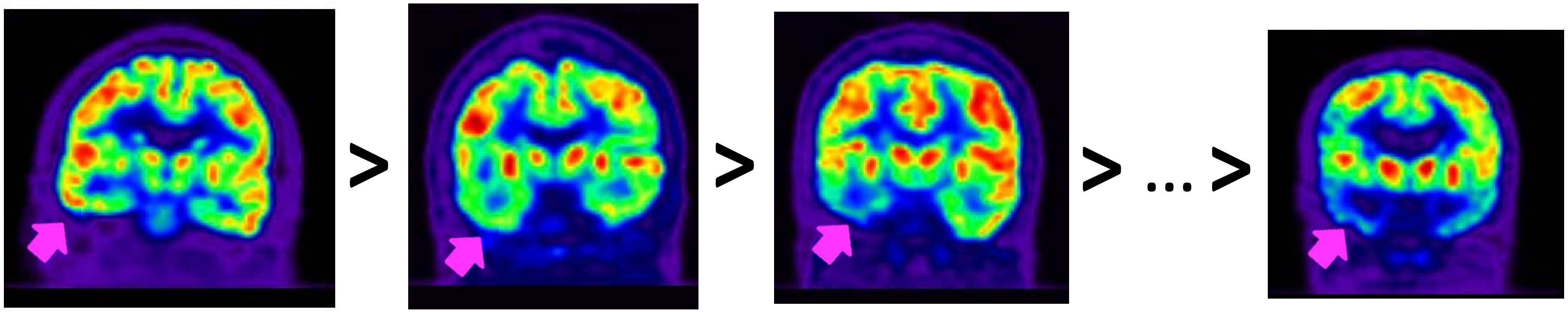
Illustrative results



Main conclusion: Automatic structural kidney damage detection in DMSA scans can successfully distinguish pathological from control scans. Quantitative indicators derived from the properties of the damaged area correlate with other clinical variables relevant in this scenario. These results suggest a promising potential of this technology to complement visual diagnosis and to contribute to the understanding of the disease pathophysiology.

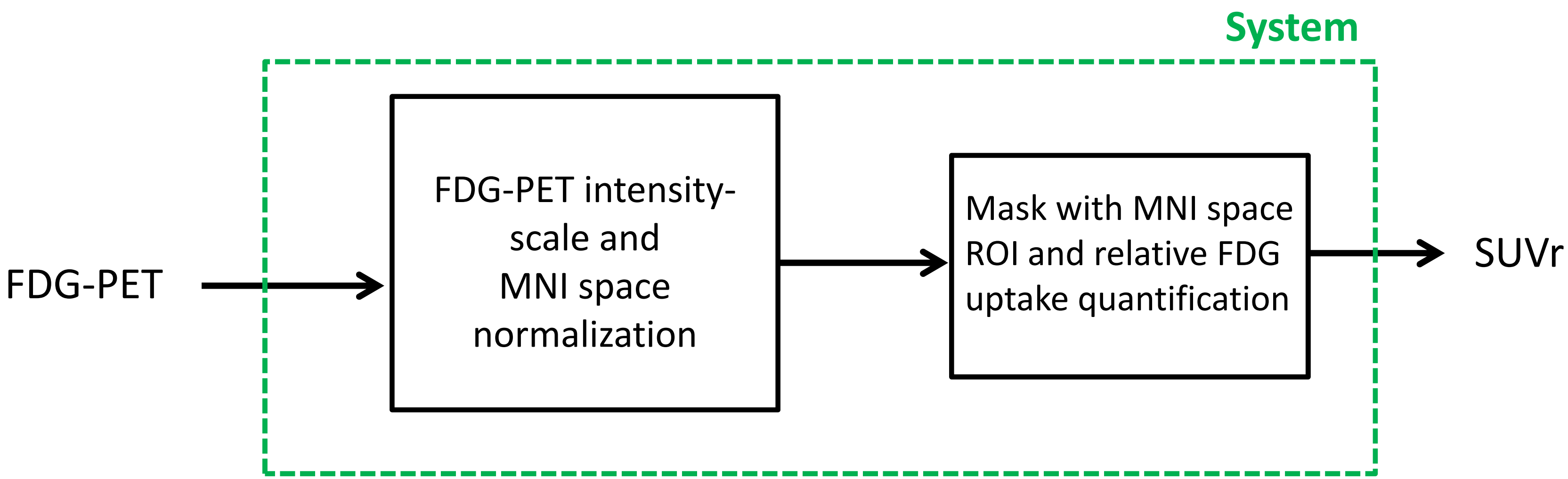
Scenario 4

Cerebral ^{18}F-FDG PET: Brain metabolism quantification (SUVr)



$SUVr_1 > SUVr_2 > SUVr_3 > \ldots > SUVr_N$

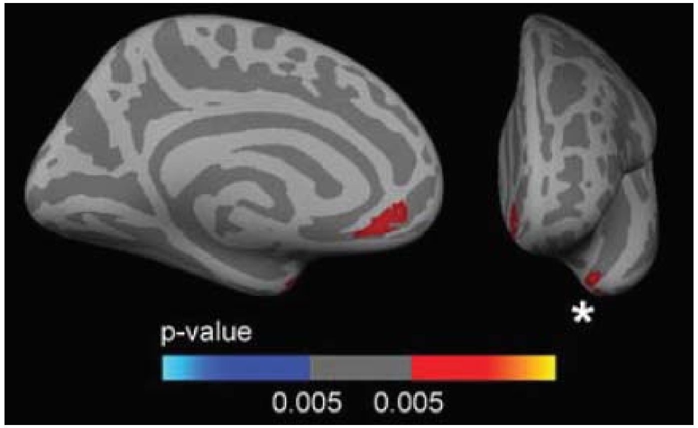
SUVr computation system

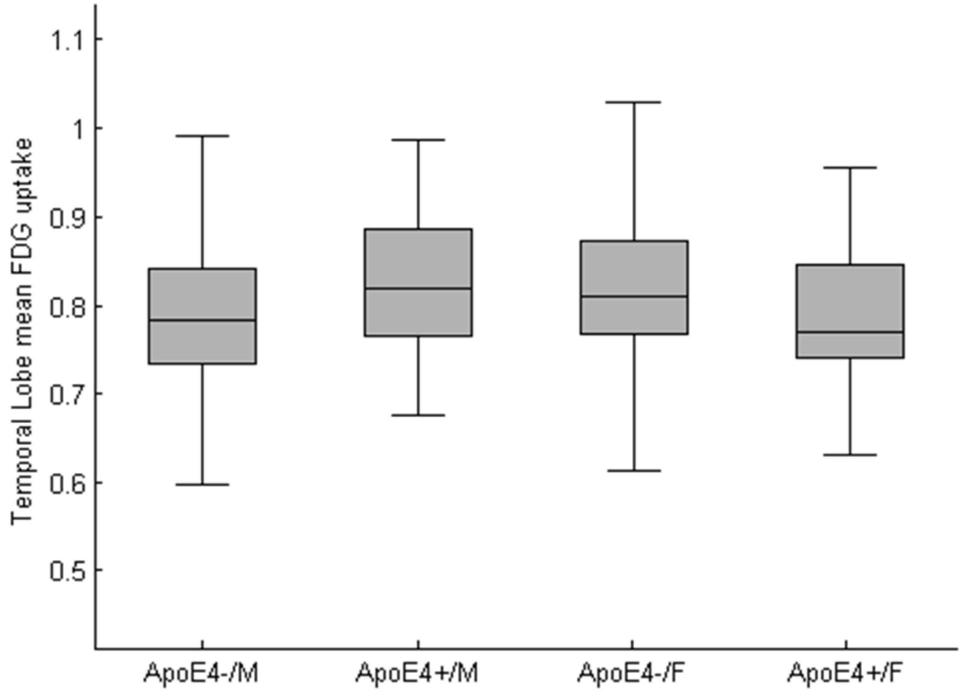


- APOE4: Strongest genetic risk factor for Alzheimer's Disease (AD)
- Clinical observation: Female APOE4+ → higher risk of developing (AD)
- Known association: AD -> Temporal Lobe hypometabolism
- **Relationship between SUVr in Temporal love, APOE status and gender?**

Sampedro et al. APOE-by-sex Interactions on Brain Structure and Metabolism in Healthy Elderly Controls. Oncortarget. 2015.

Illustrative results

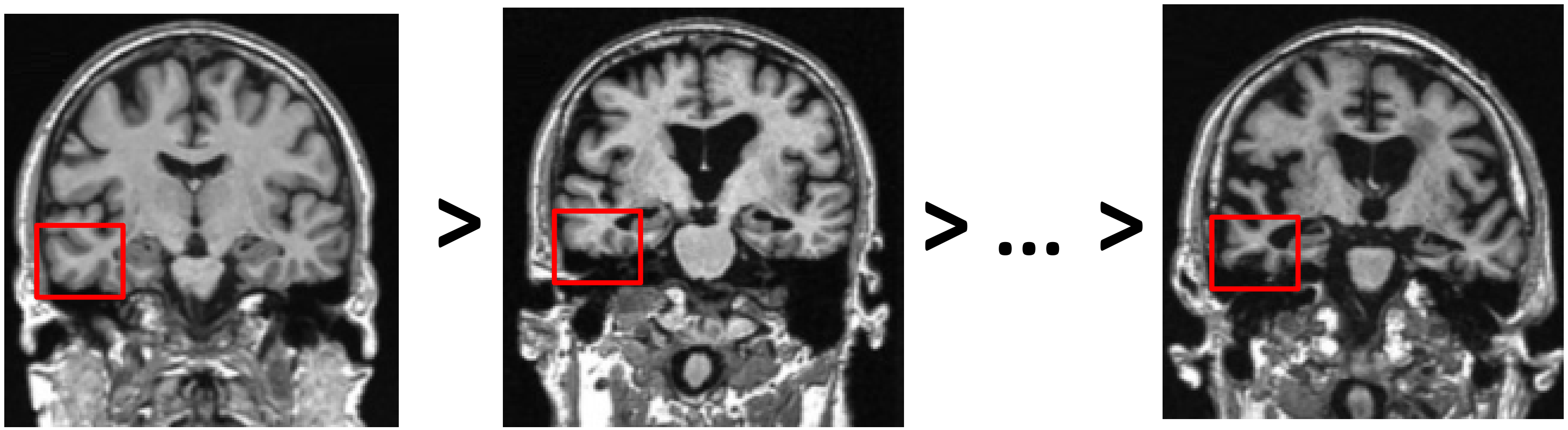




Main conclusion: The brain metabolism in key areas of dementia is altered by the APOE4 genotype but in a different manner depending on the gender. APOE4+ females show stronger hypometabolism than APOE4+ males. This finding contributes to explain the clinically observed APOE4+ women's higher risk of developing Alzheimer's Disease.

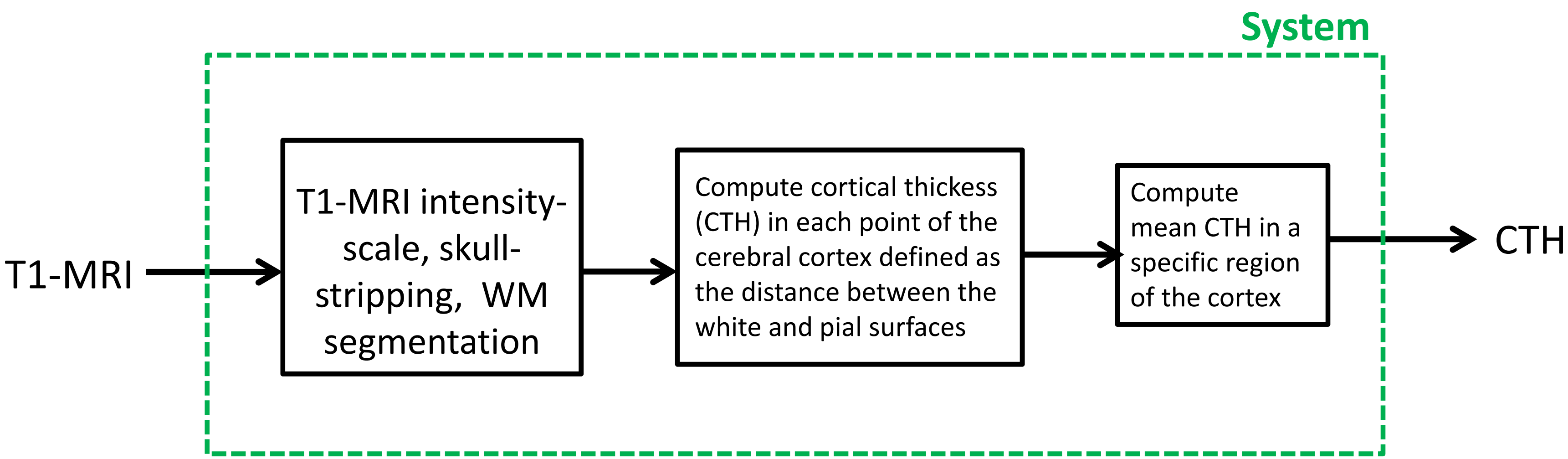
Scenario 5

Cortical thickness(CTH) quantification from T1 MRI images



CTH_1 > CTH_2 > … > CTH_N

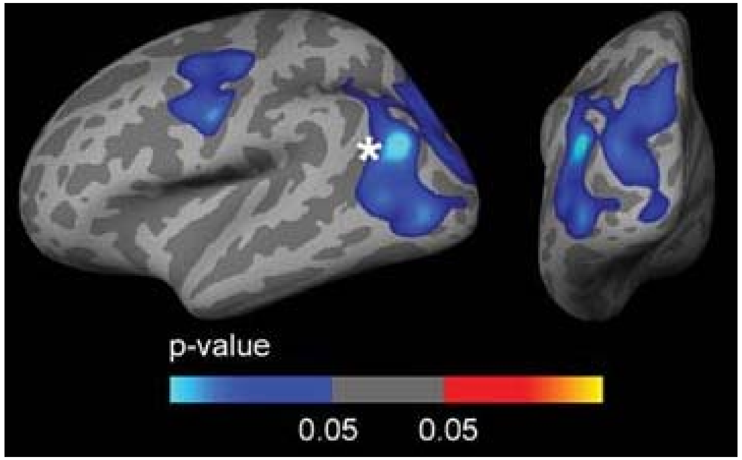
CTH computation system

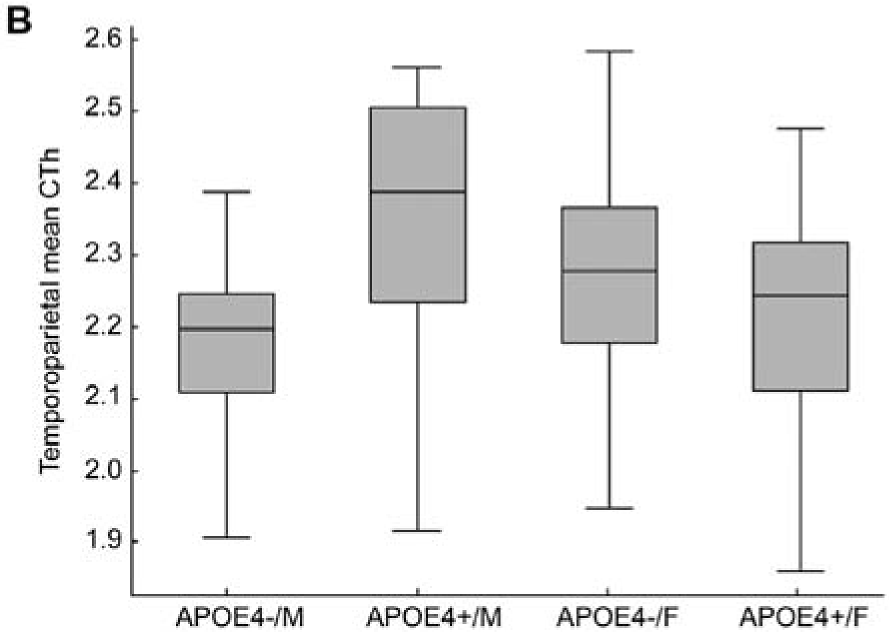


- APOE4: Strongest genetic risk factor for Alzheimer's Disease (AD)
- Clinical observation: Female APOE4+ → higher risk of developing (AD)
- Known association: AD -> Parieto-temporal atrophy
- **Relationship between CTH in parieto-temporal area, APOE status and gender?**

Sampedro et al. APOE-by-sex Interactions on Brain Structure and Metabolism in Healthy Elderly Controls. Oncortarget. 2015.

Illustrative results

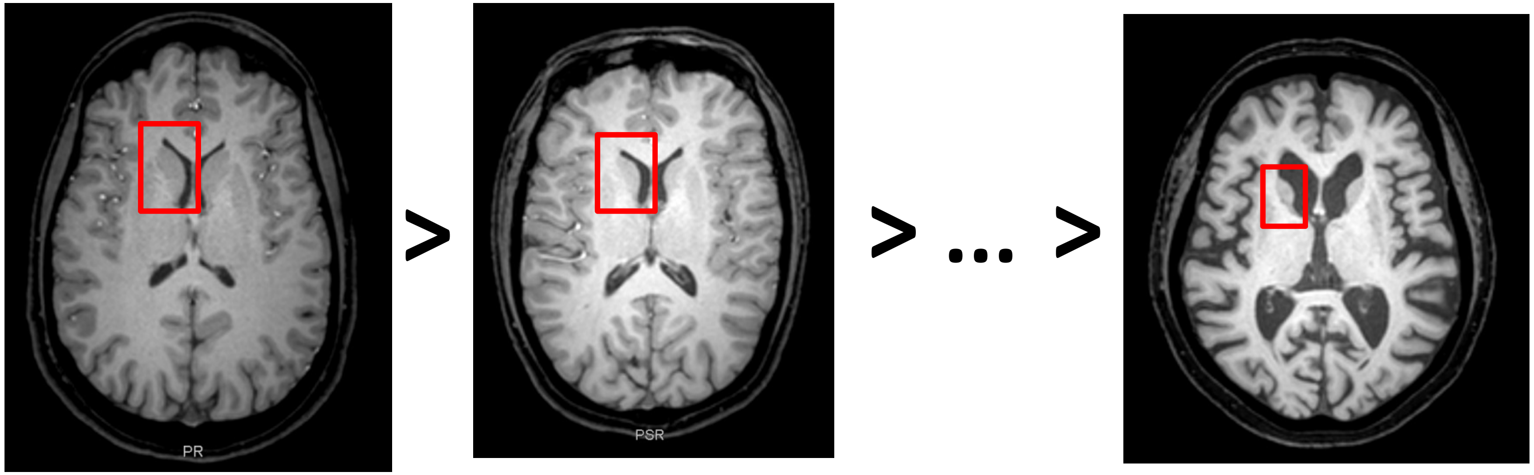




Main conclusion: Brain atrophy in key areas of dementia is altered by the APOE4 genotype but in a different manner depending on the gender. APOE4+ females show stronger atrophy than APOE4+ males. This finding contributes to explain the clinically observed APOE4+ women’s higher risk of developing Alzheimer’s Disease.

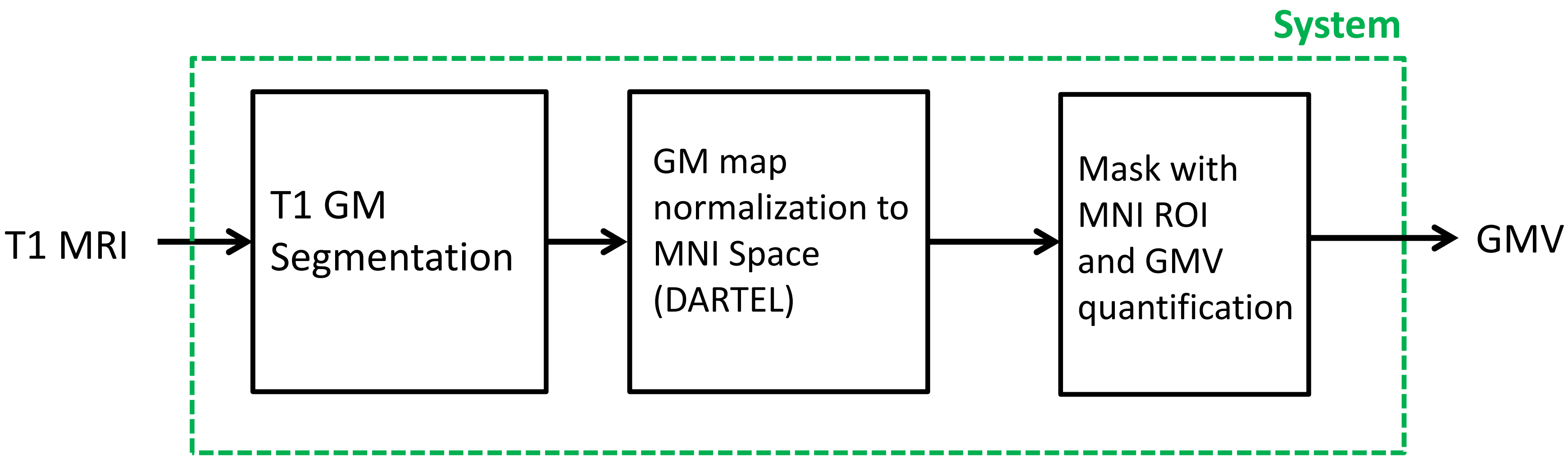
<u>Scenario 6</u>

Gray matter volume (GMV) quantification from T1 MRI images



GMV_1 > GMV_2 > … > GMV_N

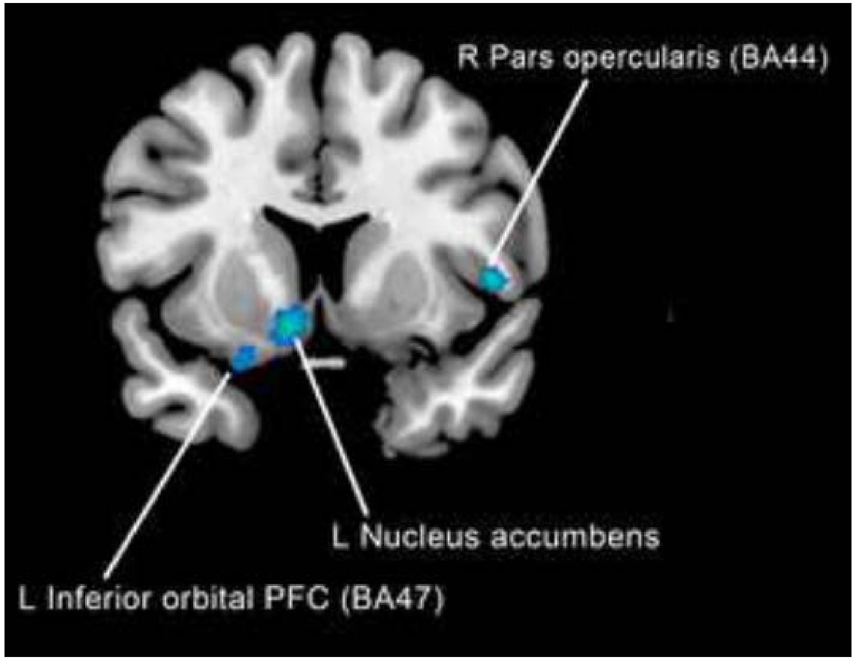
GMV computation system

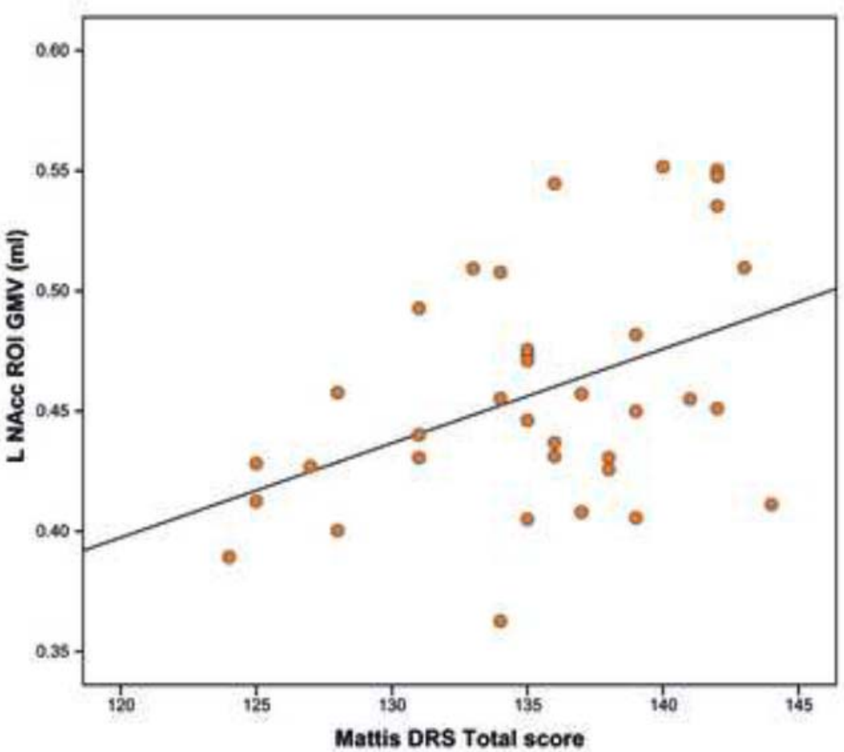


- Apathy in Parkinson's Disease (PD): a common symptom
- Clinical observation: Apathy in PD → higher risk of developing dementia
- Known association: Apathy -> Brain Reward's circuit -> Nucleus Accumbens (NAcc)
- **Relationship between GMV in NAcc, apathy and dementia in PD?**

Martínez-Horta&<u>Sampedro</u> et al. Non-demented Parkinson's disease patients with apathy show decreased grey matter volume in key executive and reward-related nodes. Brain Imaging and Behaviour. 2016.

Illustrative results



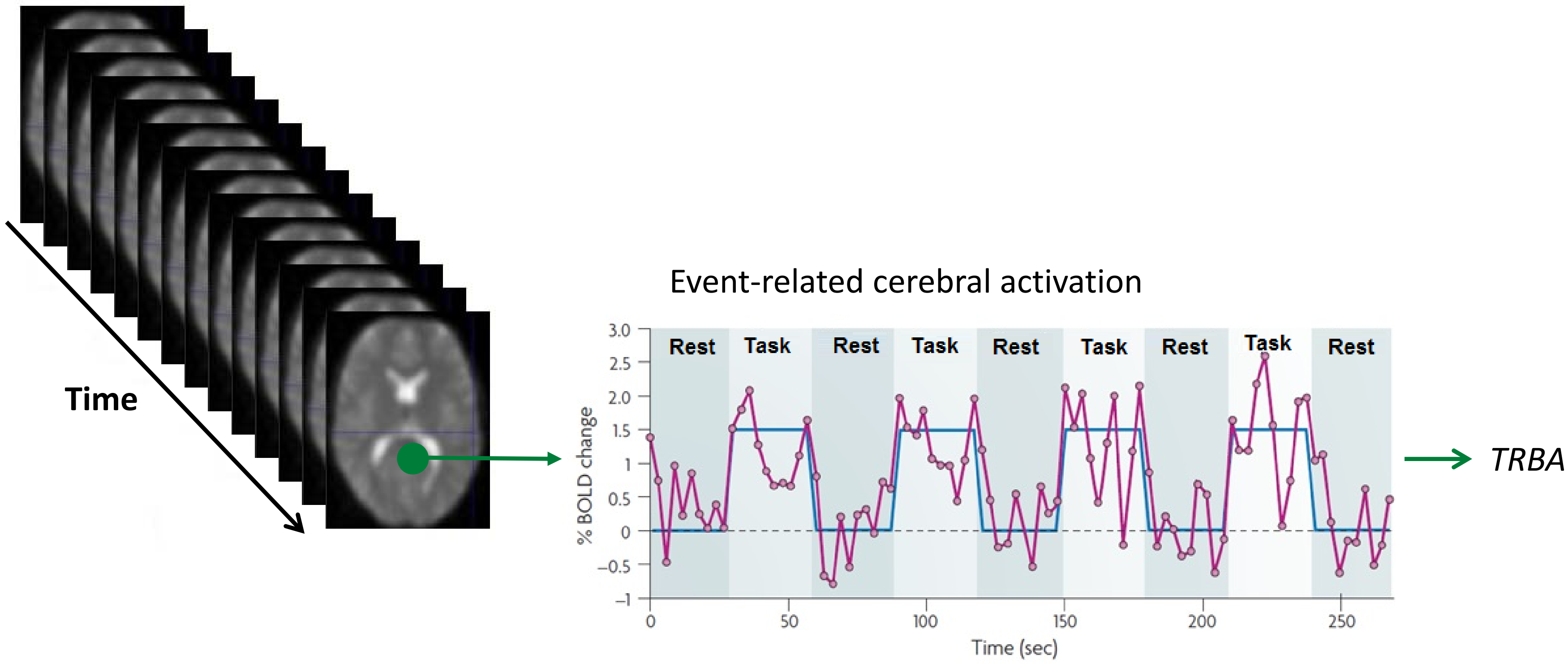


Main conclusion: Gray matter volume of the Nucleus Accumbens is reduced in apathetic Parkinson's Disease patients and correlate with cognitive status. These results suggest apathy as a marker of more widespread brain degeneration in Parkinson's disease.

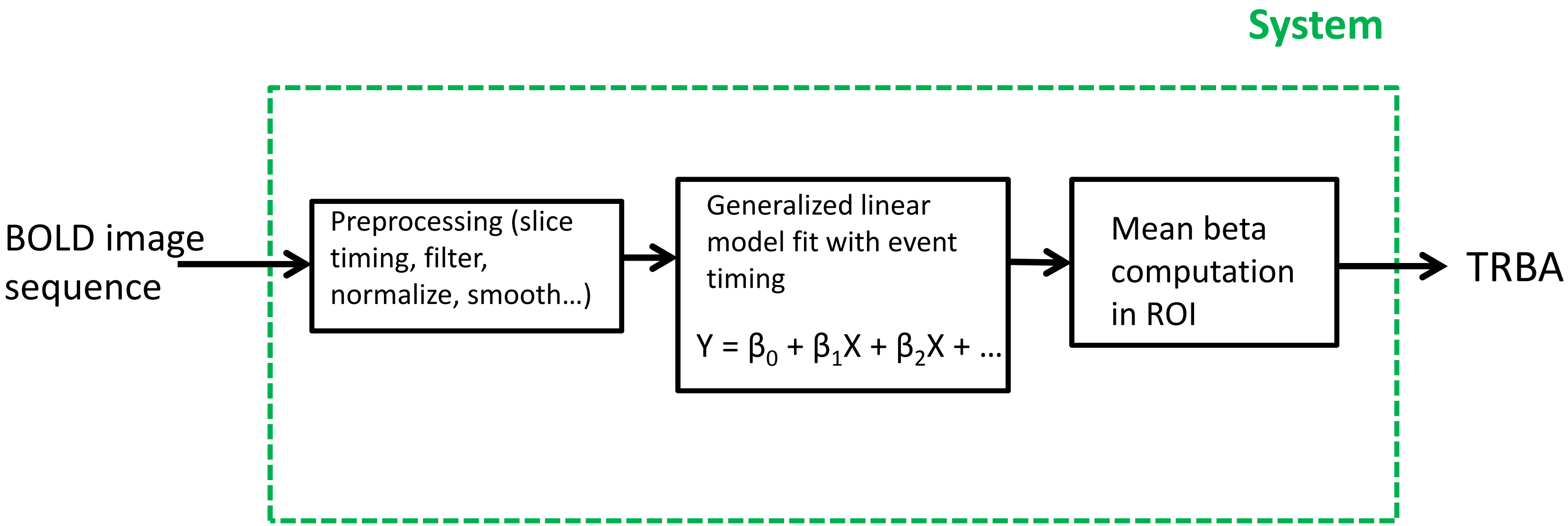
Scenario 7

Task-related brain activation (TRBA) in fMRI

fMRI images



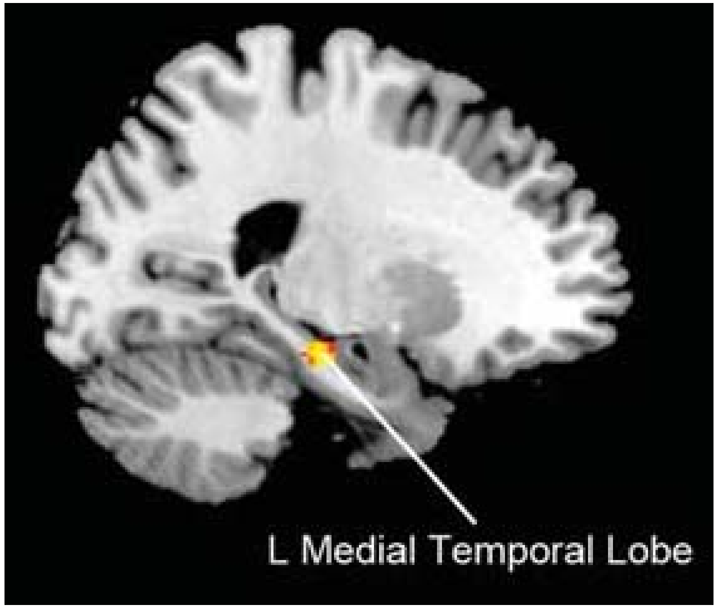
TRBA activation computation system

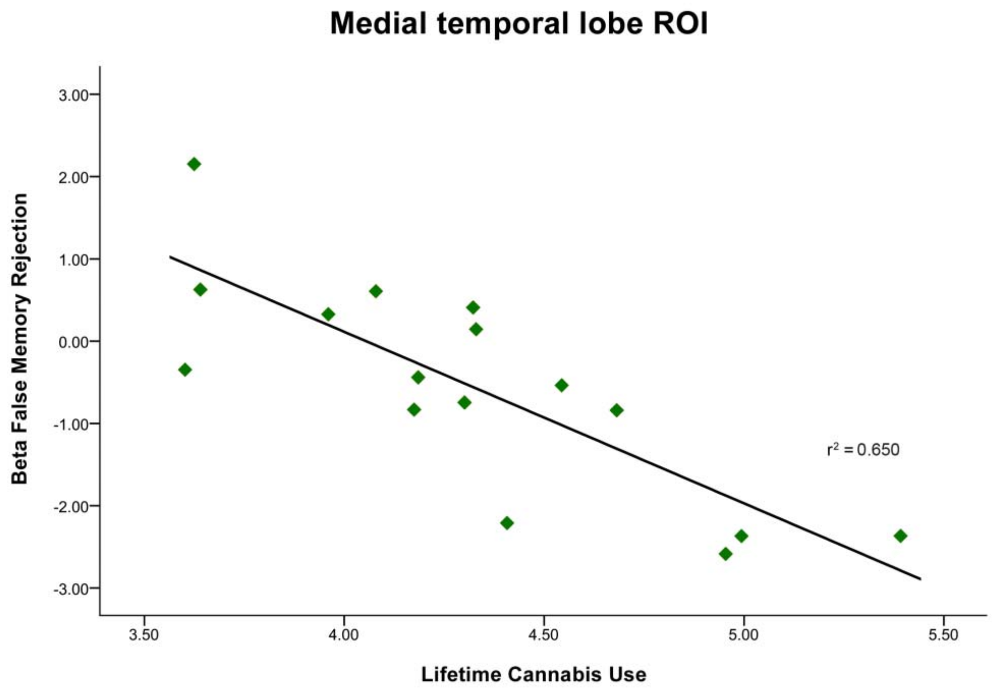


- Memory deficits in drug-free cannabis users: Controversial and contradictory results
- False memories task (FM): more cognitively demanding than classical tests “hielo, congelador, frio → nevera”
- Known association: Memory deficit -> Medial temporal Lobe (MTL) -> Hippocampus
- **Study of the Hippocampal TRBA in a FM task in drug-free cannabis users and a control group**

Riba, Sampedro&Valle et al. Telling true from false: Cannabis users show increased susceptibility to false memories. Molecular Psychiatry. 2014.

Illustrative results





Main conclusion: Hippocampal activation during a false memory task was lower in drug-free cannabis users than in controls. This activation inversely correlated with lifetime cannabis use. These findings indicate that cannabis users have an increased susceptibility to memory distortions even when abstinent and drug-free.

Video_papercannabis.mp4

Other contributions in the field

1: **Frederic Sampedro**, Sergio Escalera, Spatial codification of label predictions in Multi-scale Stacked Sequential Learning: A case study on multi-class medical volume segmentation, IET Computer Vision, pp 1-8. 2014.

2: **Frederic Sampedro**, Sergio Escalera, Anna Puig, Iterative multi-class multi-scale stacked sequential learning: Definition and application to medical volume segmentation, Pattern Recognition Letters, Volume 46, 1 September 2014, Pages 1-10, ISSN 0167-8655.

3: **Frederic Sampedro**, Anna Domenech, and Sergio Escalera, I.Carrio.Static and dynamic computational cancer spread quantification in whole body FDG-PET/CT scans, Journal of Medical Imaging and Health Informatics, Vol 4, 1-7. 2014.

4. **Frederic Sampedro**, M. Revenga, M. Valle, N. Roberto, E. Domínguez-Clavé, M. Elices , E. Luna A. Crippa , J. Hallak , D. Araújo ,P. Friedlander , S. Barker , E.Álvarez , J. Soler , J.Pascual,A. Feilding J. Riba. Assessing the psychedelic "after-glow": Ayahuasca-induced post-acute neurometabolic and functional connectivity changes are associated with enhanced mindfulness capacities. International Journal of Neuropsychopharmacology. 2017. In Press.

5: López-Mora DA, Camacho V, Pérez-Pérez J, Martínez-Horta S, Fernández A, **Sampedro F**, Montes A, Lozano-Martínez GA, Gómez-Anson B, Kulisevsky J, Carrió I. Striatal hypometabolism in premanifest and manifest Huntington's disease patients. Eur J Nucl Med Mol Imaging. 2016 Jun 28. [Epub ahead of print] PubMed PMID: 27349245.

6: Martinez-Horta S, Perez-Perez J, van Duijn E, Fernandez-Bobadilla R, Carceller M, Pagonabarraga J, Pascual-Sedano B, Campolongo A, Ruiz-Idiago J, **Sampedro F**, Landwehrmeyer GB; Spanish REGISTRY investigators of the European Huntington's Disease Network, Kulisevsky J. Neuropsychiatric symptoms are very common in premanifest and early stage Huntington's Disease. Parkinsonism Relat Disord. 2016 Apr;25:58-64. doi: 10.1016/j.parkreldis.2016.02.008. Epub 2016 Feb 11. PubMed
PMID: 26898966.

7: Vaquero L, Cámara E, **Sampedro F**, Pérez de Los Cobos J, Batlle F, Fabregas JM, Sales JA, Cervantes M, Ferrer X, Lazcano G, Rodríguez-Fornells A, Riba J. Cocaine addiction is associated with abnormal prefrontal function, increased striatal connectivity and sensitivity to monetary incentives, and decreased connectivity outside the human reward circuit. Addict Biol. 2016 Jan 19. doi: 10.1111/adb.12356. [Epub ahead of print] PubMed PMID: 26786150.

8: Carmona-Iragui M, Fernández-Arcos A, Alcolea D, Piazza F, Morenas-Rodriguez E, Antón-Aguirre S, Sala I, Clarimon J, Dols-Icardo O, Camacho V, **Sampedro F**, Munuera J, Nuñez-Marin F, Lleó A, Fortea J, Gómez-Ansón B, Blesa R. Cerebrospinal Fluid Anti-Amyloid-β Autoantibodies and Amyloid PET in Cerebral Amyloid Angiopathy-Related Inflammation. J Alzheimers Dis. 2015;50(1):1-7. doi: 10.3233/JAD-150614. PubMed PMID: 26639966.

9: Dols-Icardo O, Vilaplana E, **Sampedro F**, Alcolea D, Belbin O, Camacho V, Blesa R, Lleó A, Clarimón J, Fortea J; Alzheimer's Disease Neuroimaging Initiative. Effect of REST on brain metabolism in the Alzheimer disease continuum. Ann Neurol. 2015 Oct;78(4):661-2. doi: 10.1002/ana.24484. Epub 2015 Aug 25. PubMed PMID: 26179831.

10: Alcolea D, Vilaplana E, Pegueroles J, Montal V, Sánchez-Juan P, González-Suárez A, Pozueta A, Rodríguez-Rodríguez E, Bartrés-Faz D, Vidal-Piñeiro D, González-Ortiz S, Medrano S, Carmona-Iragui M, Sánchez-Saudinós M, Sala I, Anton-Aguirre S, **Sampedro F**, Morenas-Rodríguez E, Clarimón J, Blesa R, Lleó A, Fortea J. Relationship between cortical thickness and cerebrospinal fluid YKL-40 in predementia stages of Alzheimer's disease. Neurobiol Aging. 2015 Jun;36(6):2018-23. doi: 10.1016/j.neurobiolaging.2015.03.001. Epub 2015 Mar 9. PubMed PMID: 25865441.

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Quantitative summary:

→ 20 articles. Total IF=84.76, 101 citations, h-index=5
→ Contributed to 27 conferences and congresses.
→ Research project participation: TIN, 2 Marató

General conclusions and future work

- Digital medical imaging technology and increasing computational power has led to the development of **quantitative medical image analysis**.
- For each image modality and clinical scenario, the **challenge of finding the best image-derived quantitative and observer-independent indicators** that model the underlying pathology emerge. Automatically-computed indicators that succeed in this task will undoubtedly contribute to the medical field.
- This PhD thesis presented a set of medical image quantification scenarios where the design and implementation of **quantitative indicators** that model a specific **clinical context** of interest **contributed to its understanding or management**.
- **A large number of clinical scenarios remain** where computing image-derived observer-independent and quantitative indicators could improve diagnostic accuracy, prognosis estimation or disease understanding.

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