Automatic Image Quantification Strategies in Nuclear Medicine and Neuroradiology

PhD Defense Presentation

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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

Observer-independent
Continuous + categorical output.
Capable of handling large 4D datasets

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

Medical Scenario → Image Modality → Image’s Region of Interest (ROI) identification → Quantification of a particular property of interest within the ROI → Image-derived Quantitative Indicator

Conceptual Knowledge → Computational codification → Contribution to the management (dx, px...) or understanding of
**Scenario 1**

Oncological PET/CT: Tumor burden (TB) quantification

\[
\begin{align*}
0 &< TB_1 < TB_2 < TB_3 < \ldots < TB_{N-2} < TB_{N-1} < TB_N \\
\end{align*}
\]
TB computation system
TB computation system

System

PET/CT → PET/CT Tumor Volume Identification & Segmentation → Seg → Parameter Computation → TB

PET/CT: Positron Emission Tomography/Computed Tomography
Pat. Info: Patient Information
Seg: Segmentation
TB: Tumor Burden
TB computation system

System

PET/CT → PET/CT Tumor Volume Identification & Segmentation → Seg → Parameter Computation → TB

PET/CT
Pat. Info

Parameter Computation:
- WBMTV
- SUVmean
- SUVmax
- TLG

...
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 Communications. 2013.**
Illustrative results

<table>
<thead>
<tr>
<th>TB indicator</th>
<th>Man Seg</th>
<th>TB indicator</th>
<th>Man Seg</th>
<th>Auto Seg</th>
</tr>
</thead>
<tbody>
<tr>
<td>SUVmean</td>
<td>48%</td>
<td>nTSUV</td>
<td>80%</td>
<td>58%</td>
</tr>
<tr>
<td>SUVmax</td>
<td>60%</td>
<td>nTSUV*NCC</td>
<td>85%</td>
<td>62%</td>
</tr>
<tr>
<td>WBMTV</td>
<td>80%</td>
<td>nTSUV*aNCC</td>
<td>84%</td>
<td>61%</td>
</tr>
<tr>
<td>TLG</td>
<td>79%</td>
<td>nTSUV*NORG</td>
<td>87%</td>
<td>64%</td>
</tr>
</tbody>
</table>

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

PET/CT @ Time 1

PET/CT @ Time 2

Pat. Info

PET/CT Pathological Volume Identification & Segmentation & Decision making

D, Seg1, Seg2

Parameter Computation

TP/TR
TP/TR computation system

System

PET/CT @ Time 1 → PET/CT Pathological Volume Identification & Segmentation & Decision making → D, Seg1, Seg2 → Parameter Computation → TP/TR

PET/CT @ Time 2 → Pat. Info → PET/CT Pathological Volume Identification & Segmentation & Decision making → D, Seg1, Seg2 → Parameter Computation → TP/TR

Illustrative results

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

<table>
<thead>
<tr>
<th>Correlation (%)</th>
<th>ΔWBMTV</th>
<th>ΔSUV&lt;sub&gt;mean&lt;/sub&gt;</th>
<th>ΔSUV&lt;sub&gt;max&lt;/sub&gt;</th>
<th>ΔSUV&lt;sub&gt;peak&lt;/sub&gt;</th>
<th>ΔTLG</th>
</tr>
</thead>
<tbody>
<tr>
<td>Progression</td>
<td>32.3</td>
<td>5.7</td>
<td>4.2</td>
<td>13.8</td>
<td>30.7</td>
</tr>
<tr>
<td>Partial Response</td>
<td>76.9</td>
<td>48.1</td>
<td>59.6</td>
<td>43.7</td>
<td>73.8</td>
</tr>
<tr>
<td>Mixed Response</td>
<td>8.3</td>
<td>20.0</td>
<td>13.3</td>
<td>25.7</td>
<td>25.0</td>
</tr>
<tr>
<td>Relapse</td>
<td>100</td>
<td>54.8</td>
<td>90.5</td>
<td>78.6</td>
<td>90.5</td>
</tr>
<tr>
<td>Complete Response</td>
<td>88.5</td>
<td>44.0</td>
<td>64.8</td>
<td>80.8</td>
<td>83.5</td>
</tr>
</tbody>
</table>

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 < SKD₁ < SKD₂ < ... < SKDₙ
SKD computation system

Image processing: Damaged area detection and segmentation

DMSA scan → Quantitative indicator computation → SKD

- 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.*
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 computation system

FDG-PET → FDG-PET intensity-scale and MNI space normalization → Mask with MNI space ROI and relative FDG uptake quantification → SUVr

- 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.
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

$\text{CTH}_1 \succ \text{CTH}_2 \succ \ldots \succ \text{CTH}_N$
CTH computation system

T1-MRI intensity-scale, skull-stripping, WM segmentation → Compute cortical thickness (CTH) in each point of the cerebral cortex defined as the distance between the white and pial surfaces → Compute mean CTH in a specific region of the cortex → CTH

- 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.
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.
Scenario 6

Gray matter volume (GMV) quantification from T1 MRI images
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?

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
**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.
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


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.


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.
Acknowledgments

• Dr Carrió

• Dr Escalera, Dr Riba

• A totes aquelles persones amb les que he tingut el plaer de col·laborar durant aquests anys.