Machine Learning Algorithms as an Early Predictor of Alzhemier’s disease

Marek Kociński

Voss seminar
20.06.2022

Alzheimer's disease

Loss of autonomy in day-to-day functioning

Managing everyday life activities such as:

- finances,
- medication,
- running errands,
- preparing meals,
- maintaining interests,

is one of the criteria differentiating between mild cognitive impairment (MCI) and Alzheimer’s disease (AD).

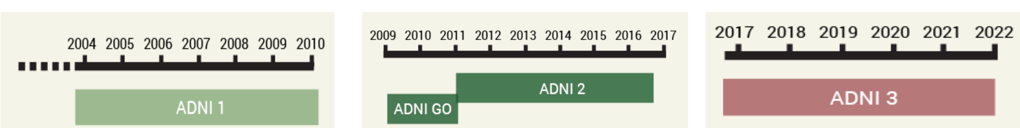
The goal of the project: To find an early predictor(s) of AD

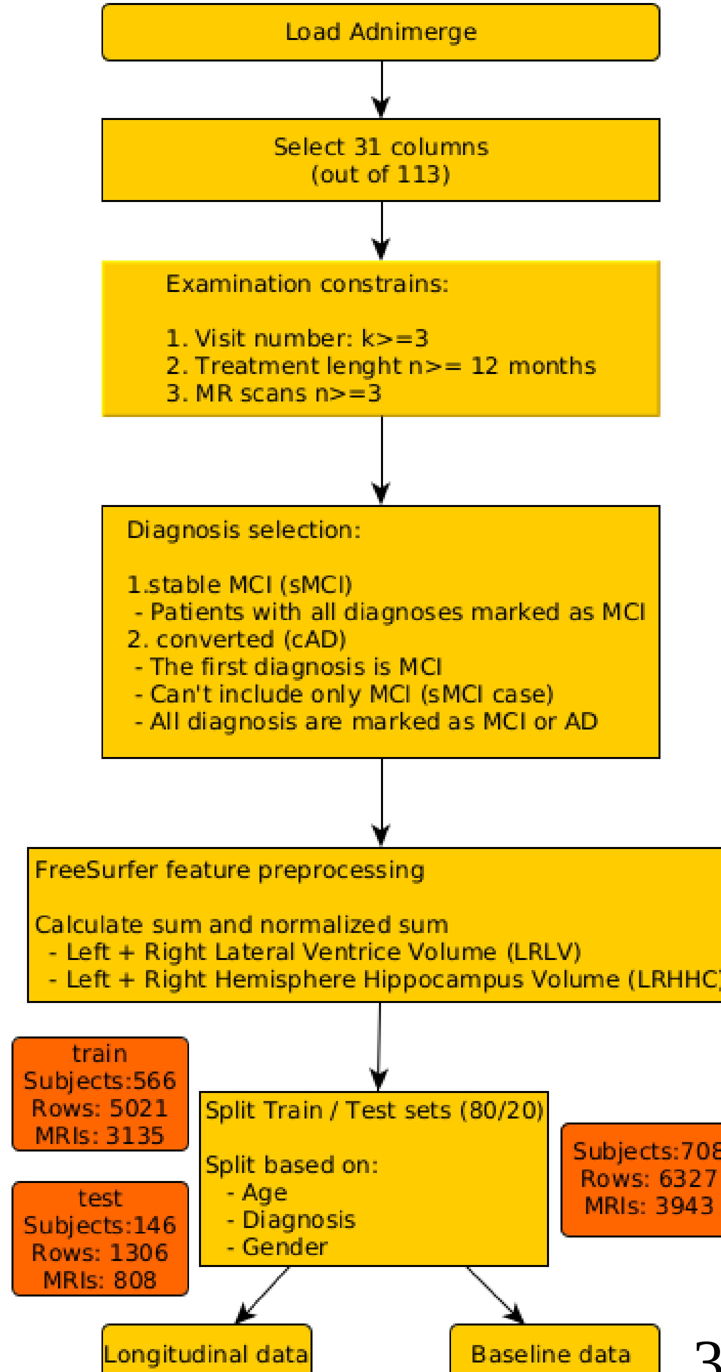
DATA

The ADNI clinical dataset comprises clinical **longitudinal** information about each subject including:

- recruitment,
- demographics,
- physical examinations,
- and cognitive assessment data.

STUDY CHARACTERISTICS	ADNI-1	ADNI-GO (Grand Opportunities)	ADNI-2	ADNI-3
Primary goal	Develop biomarkers as outcome measures for clinical trials	Examine biomarkers in earlier stages of disease	Develop biomarkers as predictors of cognitive decline, and as outcome measures	Study the use of tau PET and functional imaging techniques in clinical trials
Funding	$40 million federal (NIA), $27 million industry and foundation	$24 million American Recovery Act funds	$40 million federal (NIA), $27 million industry and foundation	$ 40 million federal (NIA), up to $20 million industry and foundation
Duration/start date	5 years/October 2004	2 years/September 2009	5 years/September 2011	5 years/September 2016
Cohort	200 elderly controls 400 MCI 200 AD	Existing ADNI-1 + 200 early MCI	Existing ADNI-1 and ADNI-GO + 150 elderly controls100 early MCI 150 late MCI 150 AD	Existing ADNI-1, ADNI-GO, ADNI-2 + 133 elderly controls 151 MCI 87 AD





RESEARCH

Functional activity level reported by an informant is an early predictor of Alzheimer's disease.

Alexandra Vik[1*], Marek Kocinski[1,3], Ingrid Rye[2], Astri J Lundervold[2], Alexander S Lundervold[1,4] and for the Alzheimer's Disease Neuroimaging Initiative[5]
Vik et al.

BMC Part of Springer Nature

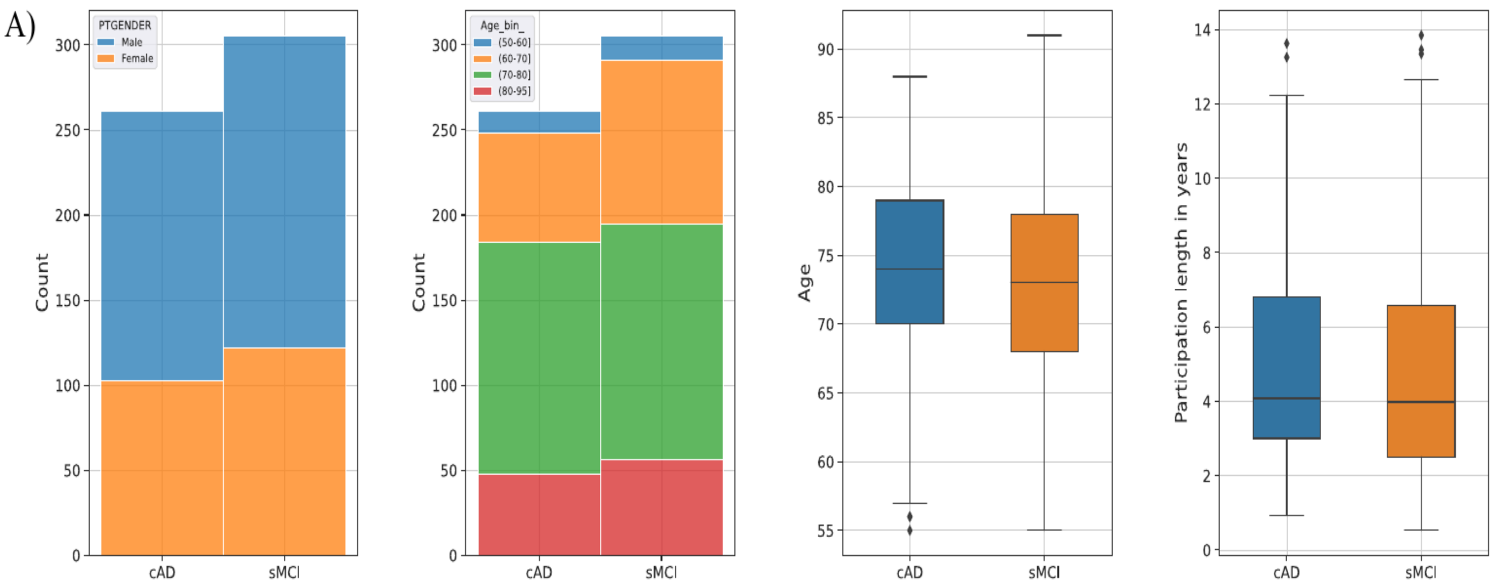
BMC Geriatrics

Home About Articles Submission Guidelines Collections

Citation Impact
3.921 - 2-year Impact Factor
4.878 - 5-year Impact Factor
1.758 - Source Normalized Impact per Paper (SNIP)
1.414 - SCImago Journal Rank (SJR)

Loss of autonomy in day-to-day functioning may be noticed by relatives subtle changes in ordinary life situations long before these changes are given medical diagnosis.

In this study we ask if: even such subtle changes should be given weight as an early predictor of AD, by including report scales like the functional activity questionnaire (FAQ).



Data balance for: gender, age bins, age and length of participation

Methods and Results

Demographics	sMCI (360) Train (285)/Test (75)	cAD (320) Train (255)/Test (65)
Sex (F:M)	114:171/32:43	99:156/25:40
Age at inclusion [years]: mean (SD)	73.9 (7.4)/72.7(7.3)	73.9 (7.7)/73.9 (6.9)
Age at inclusion [years]: range	55-91/57.8-87.8	55.2-88.3/55-88.4
Education [years]: mean (SD)	15.8 (2.9)/16.2(2.9)	15.8 (2.9)/16.2(2.9)
Participation length [years]: mean (SD)	4.6 (2.8)/4.5(2.7)	5.0 (2.7)/5.5(2.8)

Demographics of the included subsample extracted from the ADNI cohort.
sMCI – stable mild cognitive impairment, cAD – converting Alzheimer's Disease

Eleven neurocognitive features were used as input in a **Random Forest binary classifier** (sMCI vs. cAD) model

Results for RF classifier:

accuracy = 73%

Confusion Matrix

Observed (true) Outcome \ Predicted Outcome	sMCI	cAD
sMCI	**N = 58 (41%-TN)** Age: 72, Sex: 25:33 FAQ ≥ 9: 3, 1.8 (3.7) GDS ≥ 5: 3, 1.9 (1.4) RAVLT-Im: 39.1 (8.7) TMTB: 93 (36) HC: 0.0046 LVV: 0.023	**N = 17 (12%-FP)** Age: 76, Sex: 7:10 FAQ ≥ 9: 3, 4.4 (4.8) GDS ≥ 5: 0, 1.6 (0.9) RAVLT-Im: 29.1 (6.2) TMTB: 131 (56) HC: 0.0037 LVV: 0.030
cAD	**N = 20 (14%-FN)** Age: 74, Sex: 8:12 FAQ ≥ 9: 0, 1.8 (2.3) GDS ≥ 5: 0, 1.5 (1.2) RAVLT-Im: 37.2 (6.7) TMTB: 115 (82) HC: 0.0045 LVV: 0.025	**N = 45 (32%-TP)** Age: 74, Sex: 17:28 FAQ ≥ 9: 10, 5.7 (4.8) GDS ≥ 5: 0, 1.4 (1.2) RAVLT-Im: 27.8 (4.8) TMTB: 140 (80) HC: 0.0038 LVV: 0.030

Predicting conversion to Alzheimer's Disease in individuals with Mild Cognitive Impairment using clinically transferable features

Ingrid Rye[1,+], Alexandra Vik[2+], Marek Kocinski[2,3,4+], Alexander S. Lundervold[2,5], Astri J. Lundervold[1], and for the Alzheimer's Disease Neuroimaging Initiative[**]

scientific reports

Explore content ⌄ About the journal ⌄ Publish with us ⌄

Journal metrics 2021

- 2-year impact factor: 4.380
- 5-year impact factor: 5.134
- Immediacy index: 0.783
- Eigenfactor® score: 1.23250
- Article influence score: 1.285
- 2 year median: 3

Longitudinal data that identify two groups of patients who were diagnosed with MCI at a **baseline clinical examination**: one group including patients who were diagnosed with AD and one group retaining their MCI diagnosis during the observation period.

Selected features included **demographic data**, **information from neuropsychological** and **MRI** examinations and **genetic information** about APOE status.

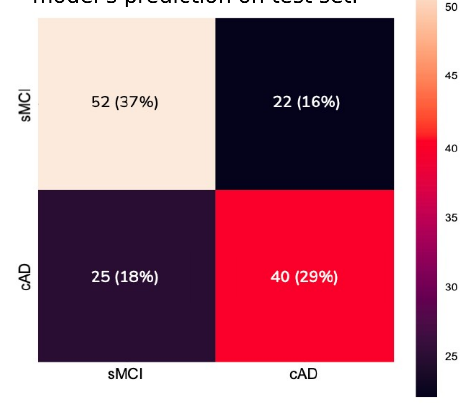
We train two different supervised learning algorithms:

- an ensemble-based model constructed by combining five different models
- a Random Forest (RF) model

	sMCI (N = 357) Mean (SD)	cAD (N = 321) Mean (SD)
Demographics		
Age	73.1 (7.45)	73.9 (7.11)
Gender (%F)	41.2	38.9
Cognitive Function		
RAVLT-Im	36.9 (10.5)	29.3 (7.7)
RAVLT-Delay	4.88 (3.93)	2.05 (2.67)
RAVLT-Recog	11.26 (3.16)	9.42 (3.56)
TMTA	39.2 (15.6)	44.7 (21.5)
TMTB	108.1 (56.9)	133.8 (73.9)
CFT animals	17.8 (5.17)	15.8 (4.75)
GDS: mean (SD)	1.71 (1.44)	1.65 (1.38)
ANART Total errors	12.9 (9.3)	13.3 (9.6)
Biological measures		
Hippocampus volume	0.00451 ($7.6*10^{-4}$)	0.00398 ($6.8*10^{-4}$)
APOE (%positive)	42.3	64.2

Demographics of the included subsample extracted from the ADNI cohort.
sMCI – stable mild cognitive impairment, cAD – converting Alzheimer's Disease

Confusion matrix for Random Forest model's prediction on test set.

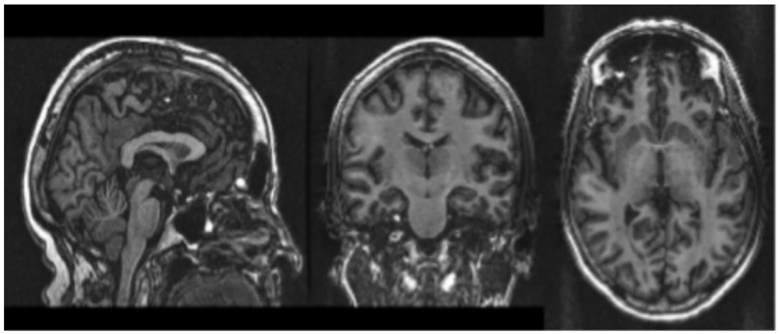


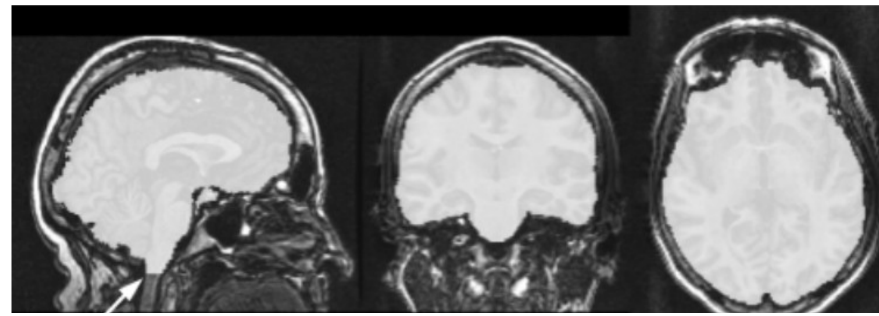
Results for RF classifier:

accuracy = 66%

2D and 3D U-Nets for skull stripping in large and heterogeneous set of head MRI using *fastai**



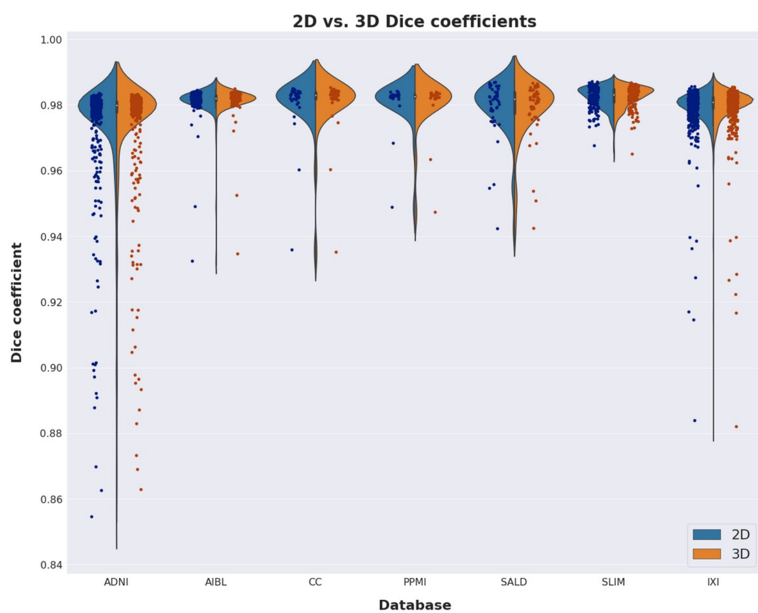




* - Sathiesh's presentation "*Deep learning for medical image analysis: fastai + MONAI*"; tomorrow 11:30-11:45

Data sets:
- ADNI
- AIBL
- IXI
- PPMI
- SLIM
- Calgary-Campinas
- SALD

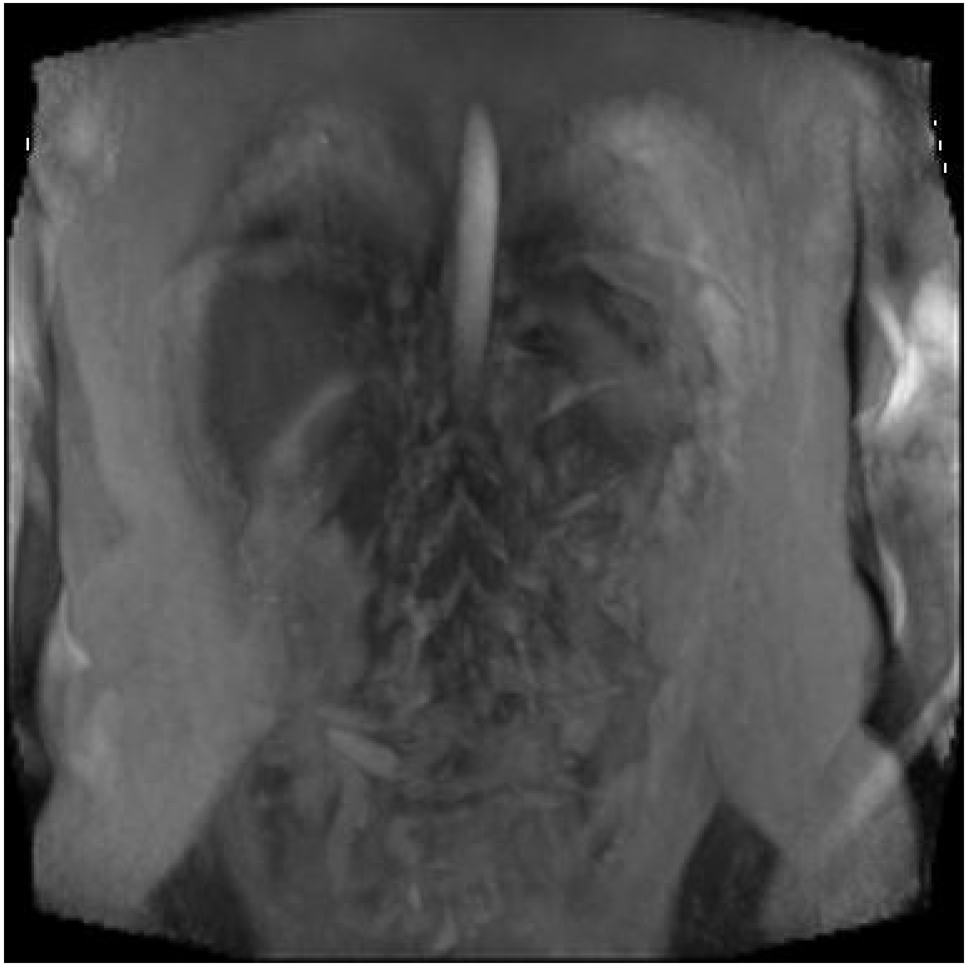
Training test: 2791 3D images
Test sets: 934 + 561 3D images

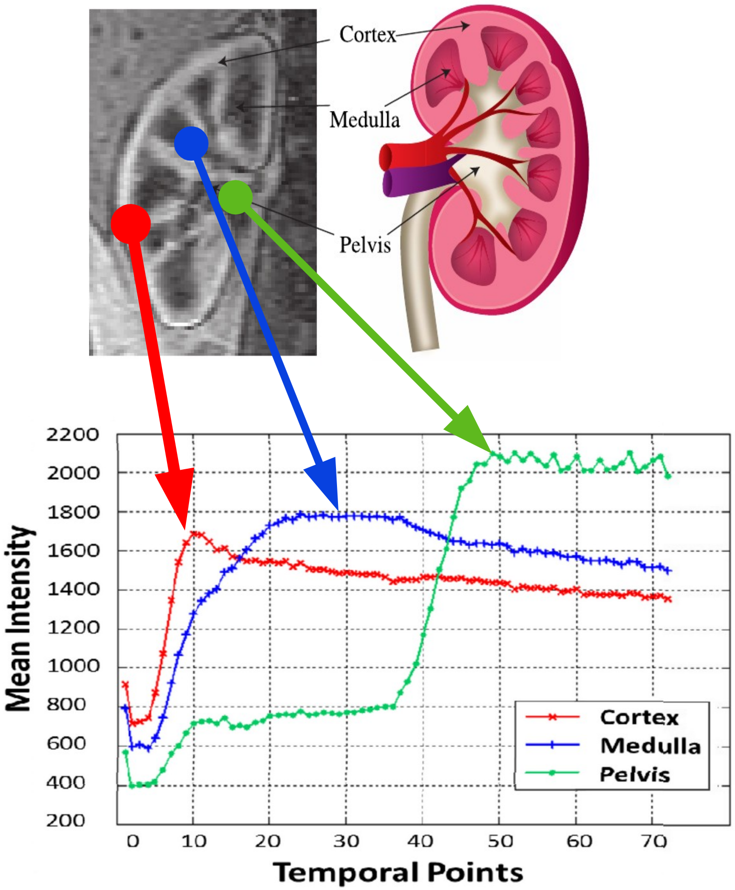


Violin plot of the Dice scores obtained by our models on the test dataset

Dice = 0.978
Jaccard = 0.957

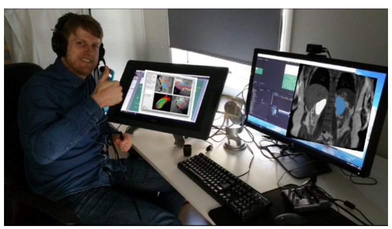
Assessing kidney function from DCE-MRI



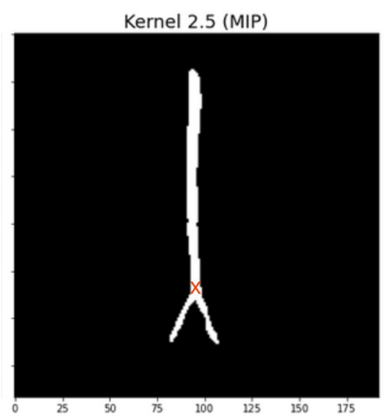


Assessing kidney function from DCE-MRI

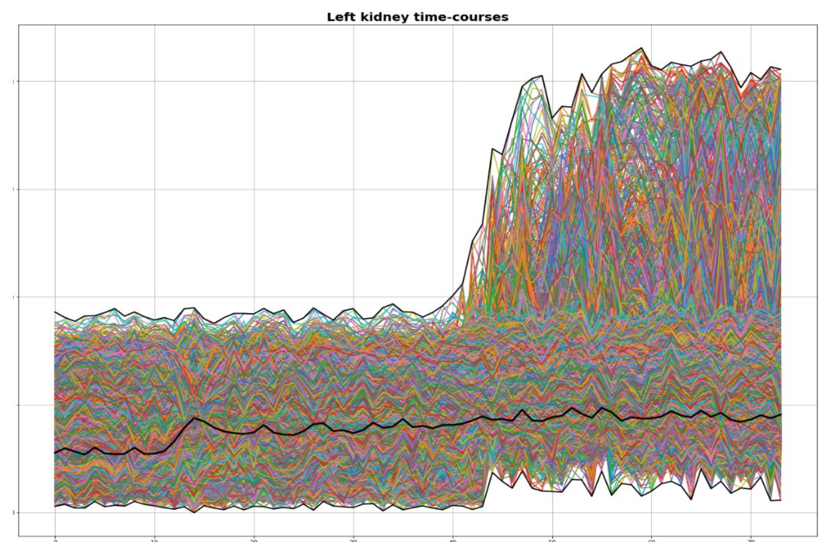
Raw data → Manual labelling → Segmentation model → Time-series extraction → Pharmacokinetic modelling and estimation of filtration



Manual labelling



Automatic aorta segmentation



Time series extraction and modeling