Towards an MRI-based Prediction of Neurofibrillary Tangles

Saifullah K[1], Tazwar M[1], Evia AM[2], Tamhane AA[2], Bennett DA[2], Schneider JA[2], Arfanakis K[1,2]

[1]Department of Biomedical Engineering, Illinois Institute of Technology, Chicago, IL, USA

[2]Rush Alzheimer's Disease Center, Rush University Medical Center, Chicago, IL, USA

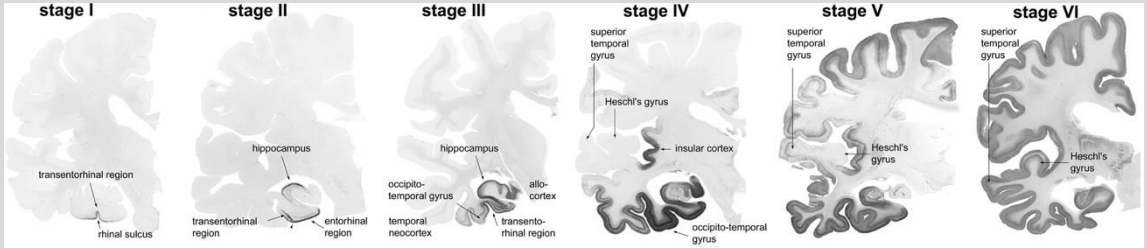
Declaration of Financial Interests or Relationships

Speaker Name: Khalid Saifullah

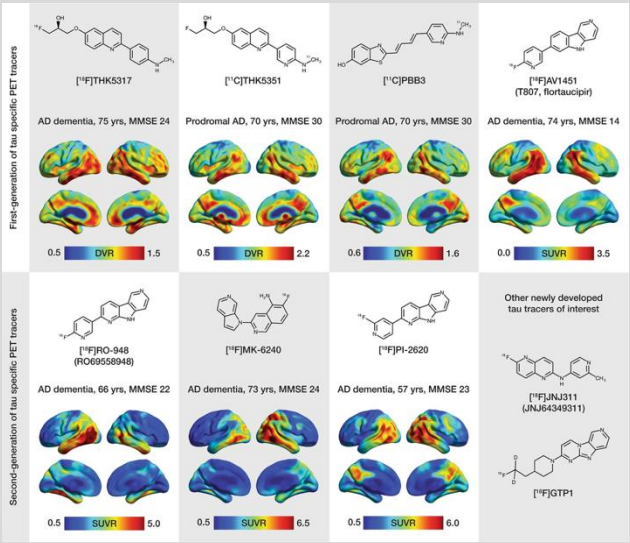
I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

Introduction

- Alzheimer's disease is the most common cause of dementia
- Neurofibrillary tangles (NFT) are associated with brain atrophy and cognitive decline
- NFT deposition follows a well-defined trajectory



Braak et al. Acta Neuropathol 2006



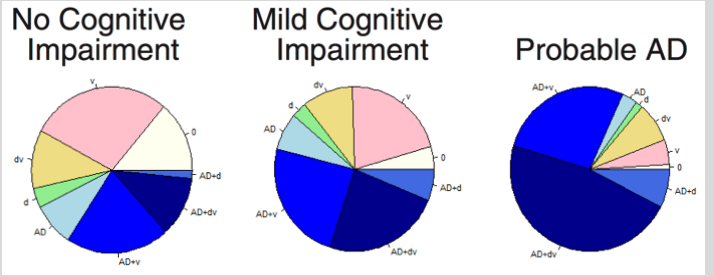
Leuzy et al. Mol Psychiatry 2019

- NFT detection:
  - Tau PET: current state of the art, ionizing radiation, expensive, not widely available.
  - Blood-based markers: similar accuracy to PET, no ionizing radiation, easy to use, cheap (Janelidze et al. Nat Med 2020)

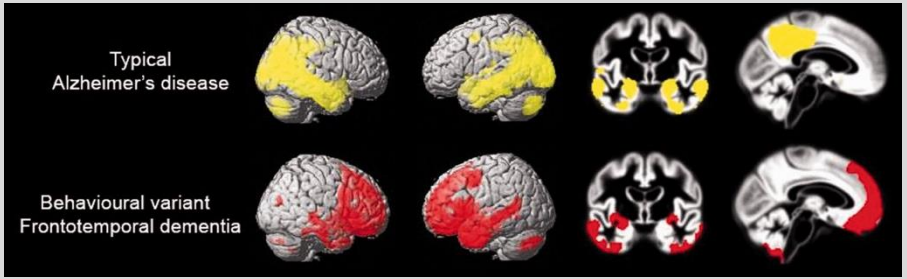
What is the role of MRI in NFT detection?

- Less specific
- No ionizing radiation, cheaper than PET, more widely available than PET
- Rich information
- **AD path is mixed most of the time with other neurodegenerative and vascular path**
- **MRI is part of the ATN framework**

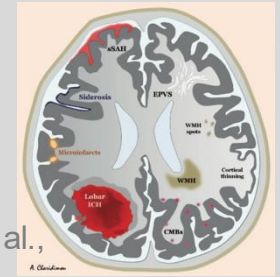
MRI is indispensable in AD research, clinical trials, and diagnosis



Kapasi et al., Acta Neuropathol. 2017



Ossenkoppele et al., Brain 2015



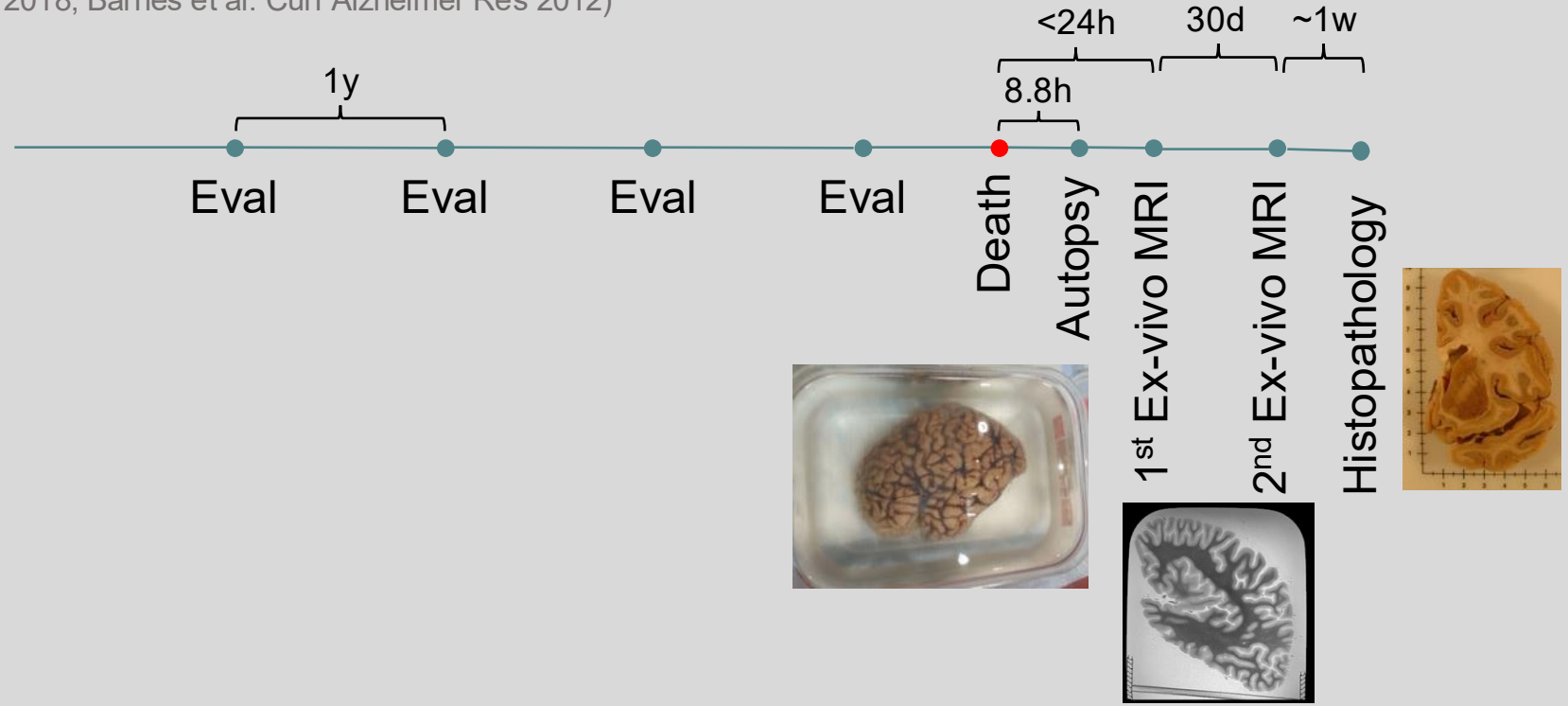
Charidimou et al., Brain 2017

Purpose: Develop an MRI-based classifier of NFTs by combining ex-vivo MRI and neuropathology in a large number of community-based older adults

Data collection

Participants

- 878 older adults participating in the Rush Memory and Aging Project (MAP), Religious Orders Study (ROS), Minority Aging Research Study (MARS) (Bennett et al. J Alzheimer's Disease 2018; Barnes et al. Curr Alzheimer Res 2012)



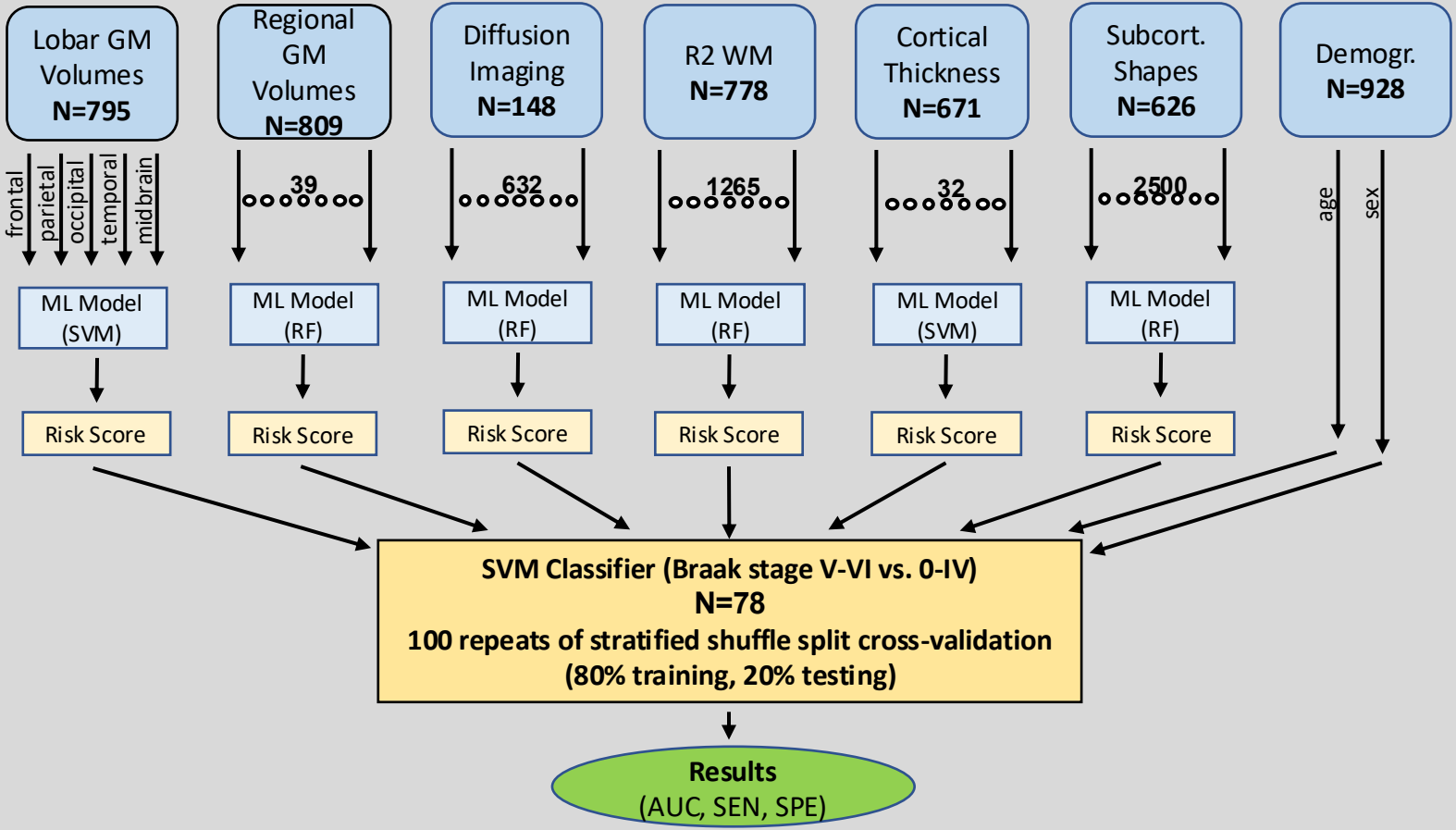
Demographic, clinical, neuropathologic characteristics

N	878
Age at death, y (SD)	91 (6.4)
Male, n (%)	247 (28)
Education, y (SD)	16 (3.6)
MMSE, mean (SD)	19.9 (9.6)
Antemortem clinical diagnosis, n (%)	
NCI	278 (32)
MCI	208 (24)
Dementia	392 (45)

BRAAK stages, n (%)	
Stage 0	7 (1)
Stage 1 & 2	119 (14)
Stage 3 & 4	476 (54)
Stage 5 & 6	276 (31)
TDP-43, n (%)	
Stage 0	385 (44)
Stage 1	159 (18)
Stage 2	103 (12)
Stage 3	231 (26)
Gross infarcts, n (%)	383 (44)
Microscopic infarcts, n (%)	349 (40)

Lewy Bodies, n (%)	262 (30)
Hippocampal sclerosis, n (%)	97 (11)
CAA, n (%)	
None	191 (22)
Mild	369 (42)
Moderate	212 (24)
Severe	106 (12)
Atherosclerosis, n (%)	
None	201 (23)
Mild	460 (52)
Moderate	171 (20)
Severe	46 (5)
Arteriolosclerosis, n (%)	
None	310 (35)
Mild	330 (38)
Moderate	185 (21)
Severe	53 (6)

Ex-vivo classifier model



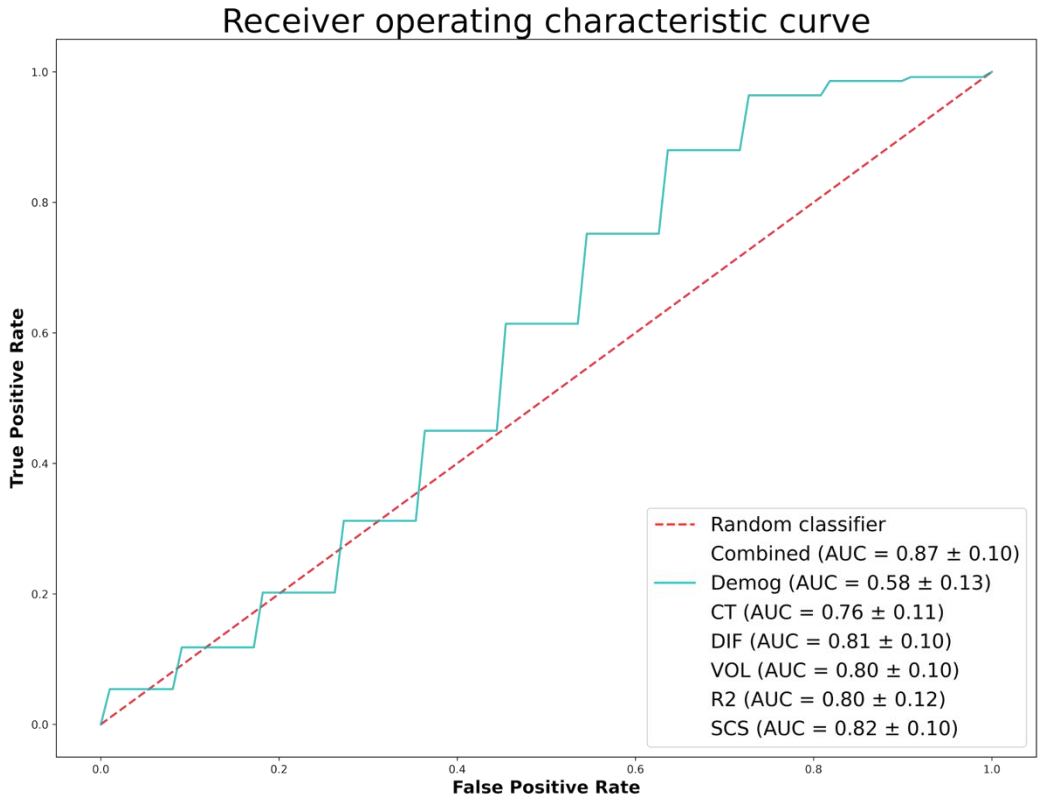
Results

Features

Demographics

AUC=0.58

(SEN 86.0%, SPE 38.2%)



Results

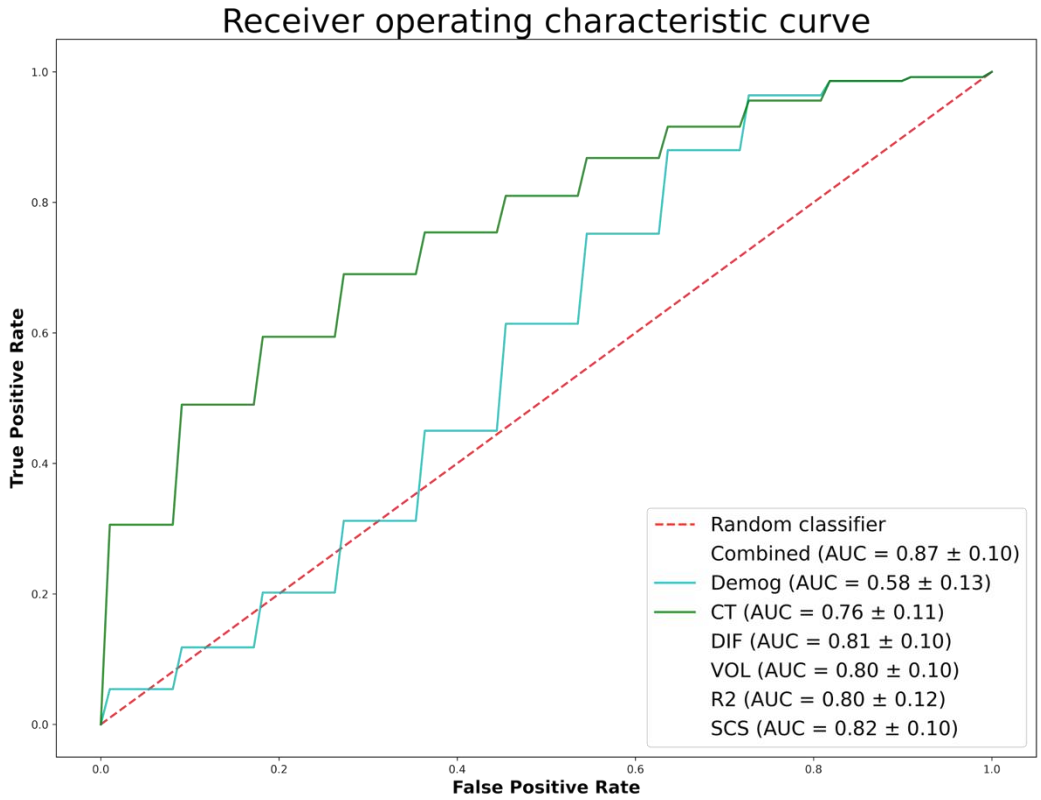
Features

Cortical thickness

Demographics

AUC=0.76

(SEN 69.2%, SPE 58.8%)



Results

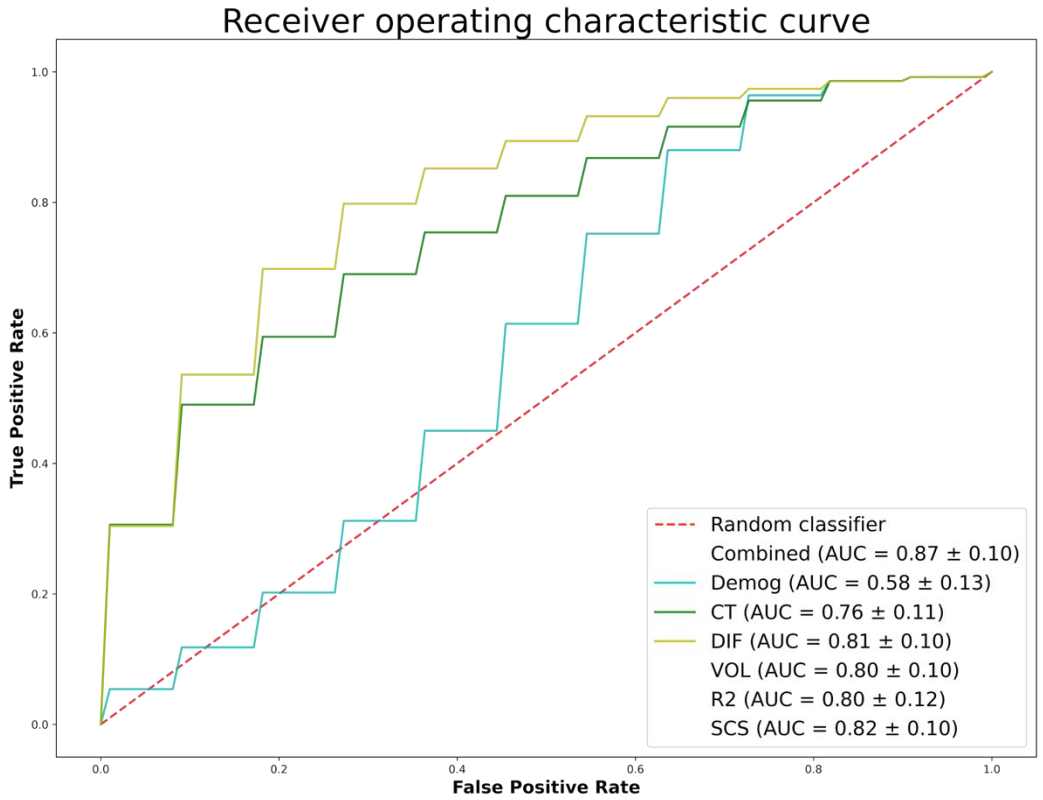
Features

Diffusion imaging

Demographics

AUC=0.81

(SEN 87.4%, SPE 62.5%)



Results

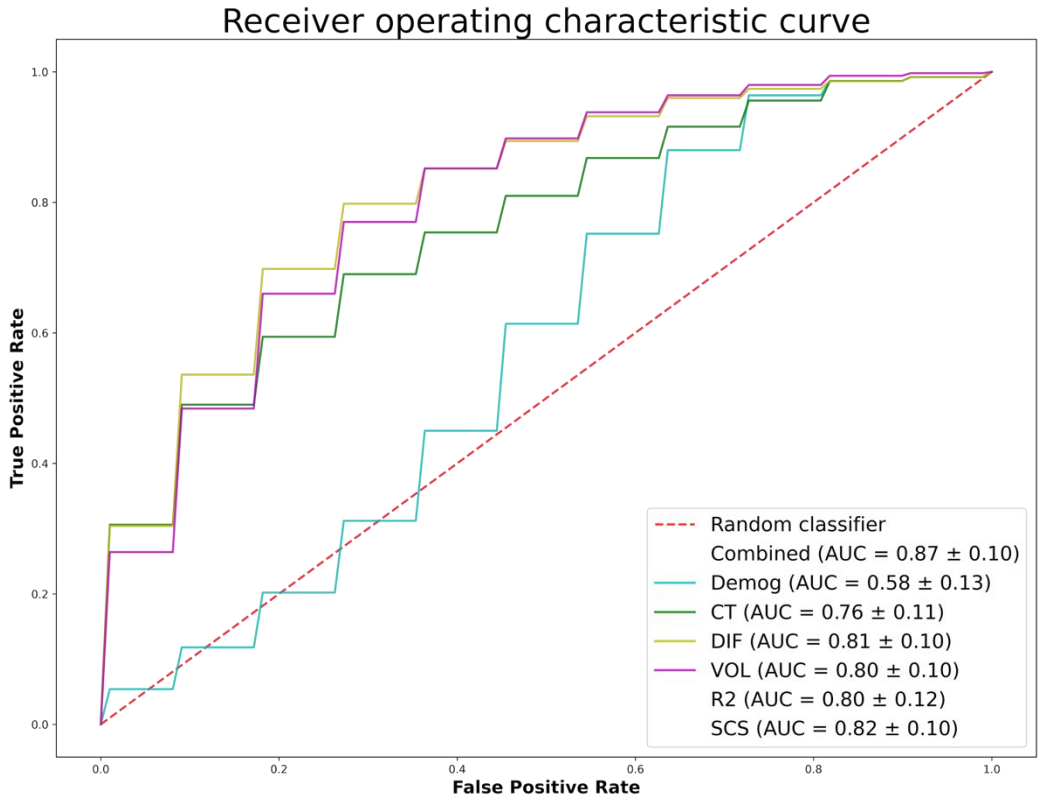
Features

Volumes

Demographics

AUC=0.80

(SEN 72.4%, SPE 71.9%)



Results

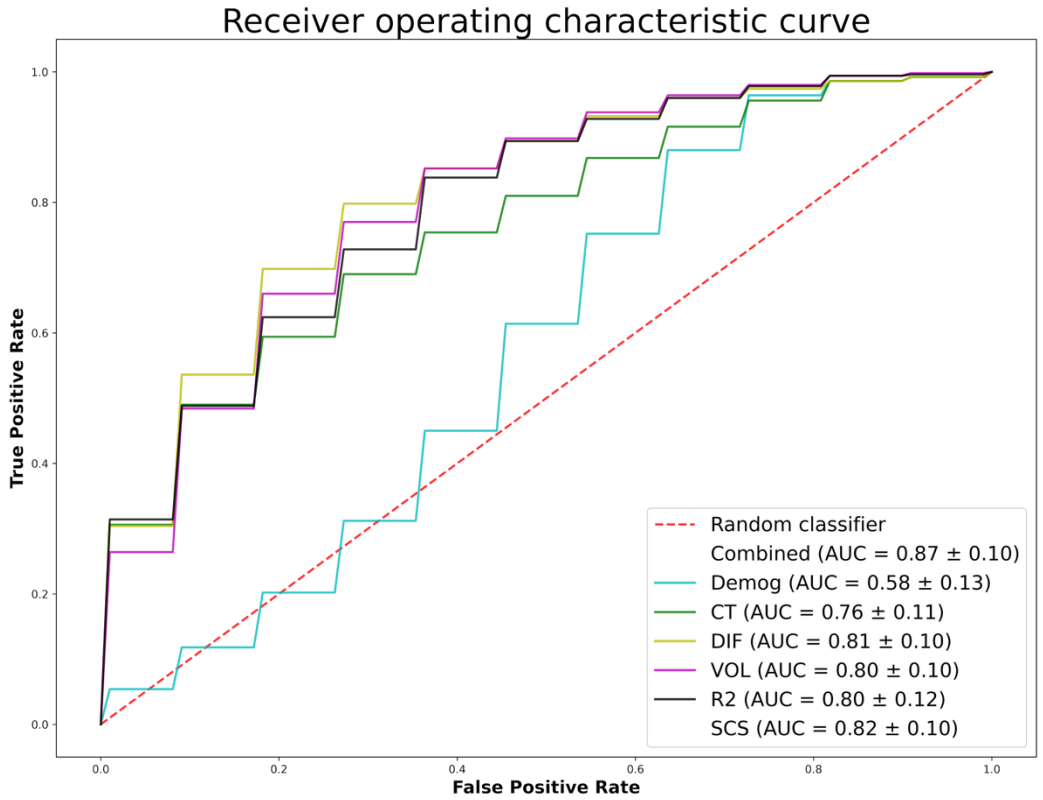
Features

R2

Demographics

AUC=0.80

(SEN 84.4%, SPE 60.4%)



Results

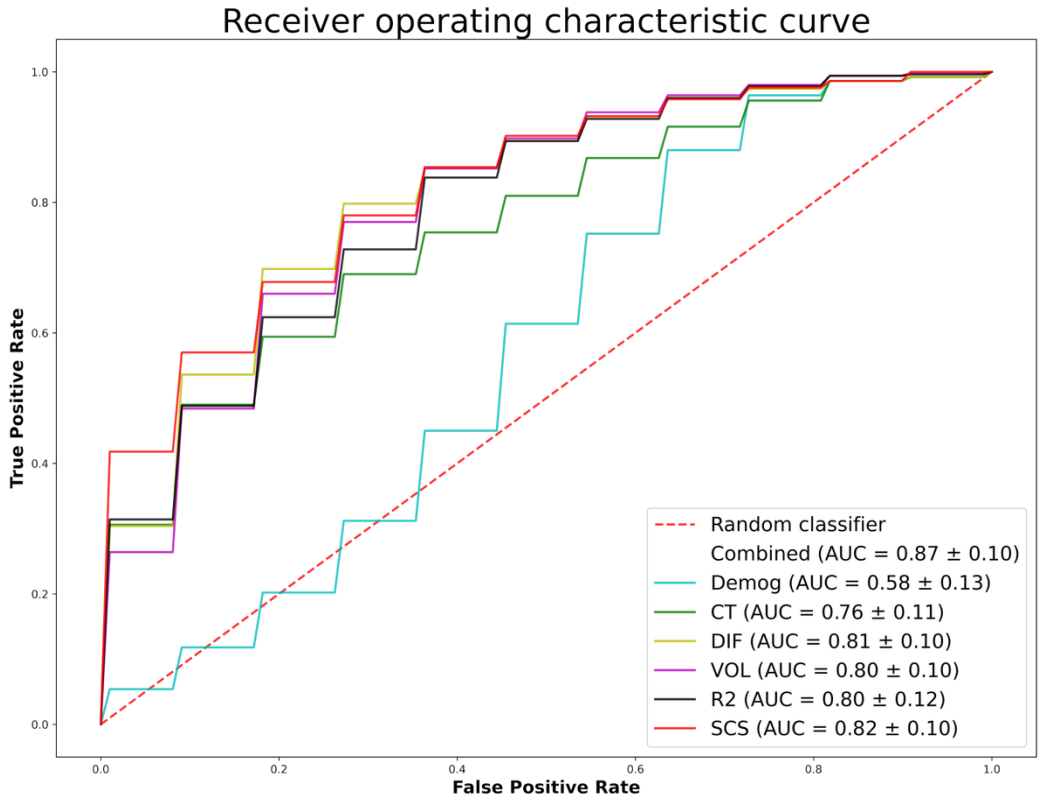
Features

Subcortical shapes

Demographics

AUC=0.82

(SEN 82.4%, SPE 65.3%)



Results

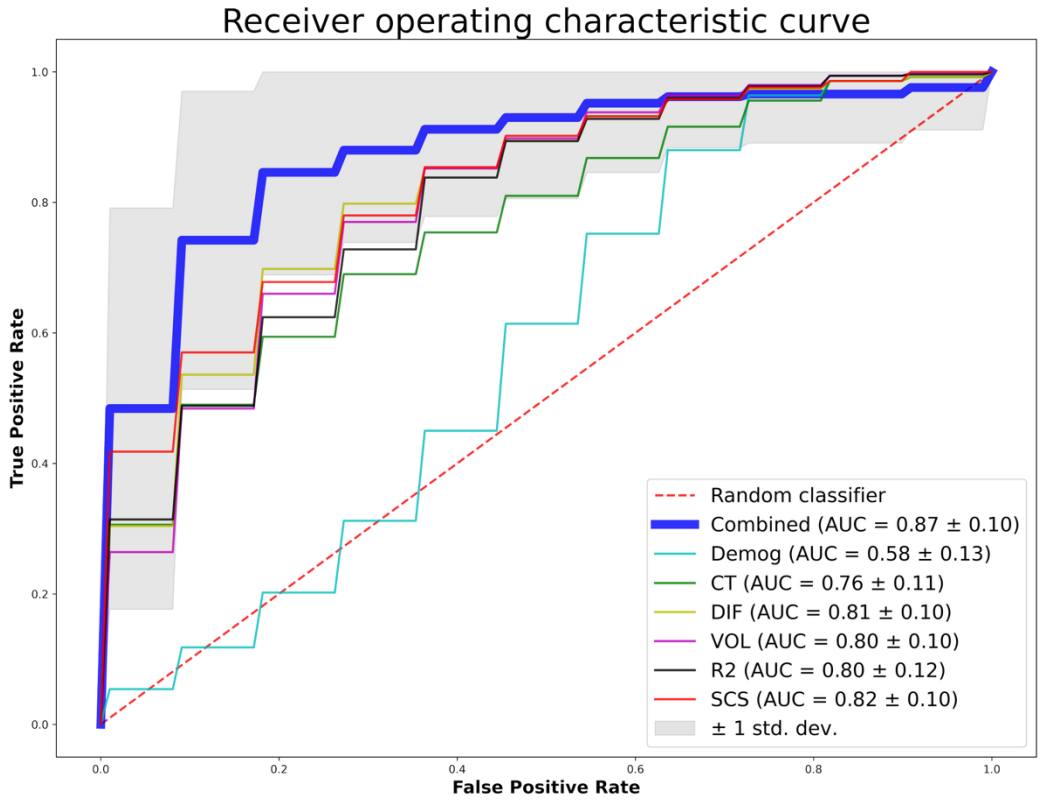
Features

All MRI features

Demographics

AUC=0.87

(SEN 83.6%, SPE 77.3%)



Conclusions

- Developed an ex-vivo MRI-based classifier of Braak stage V-VI vs. 0-IV
  - Mean AUC=0.87 (83.6% SEN and 77.3% SPE)
- Recently published in-vivo MRI-based classifier of Braak stage V-VI vs. 0-III reported mean AUC=0.69 (Dallaire-Théroux et. al. Alzheimers Dement 2019)
- Potential value in MRI-based prediction of NFTs

Future Work

- Translate the ex-vivo classifier to in-vivo
- Other groupings of Braak stages
- Increase N
- Test association of classifier score with cognitive decline

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