

Supplemental Online Content

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eFigure 1. Measurement of the Hemi-Intercadate Distance (h-ICD) and Inner Table Width (ITW)

eFigure 2. Structural Equation Models Including Different Latent Variables as Possible Mediator, MRI Only (n = 568)

eTable 1. Imaging Core Laboratory Members

eTable 2. Effect Estimates for Each Pathway in the Mediation Models, MRI Only (N = 568)

This supplemental material has been provided by the authors to give readers additional information about their work.

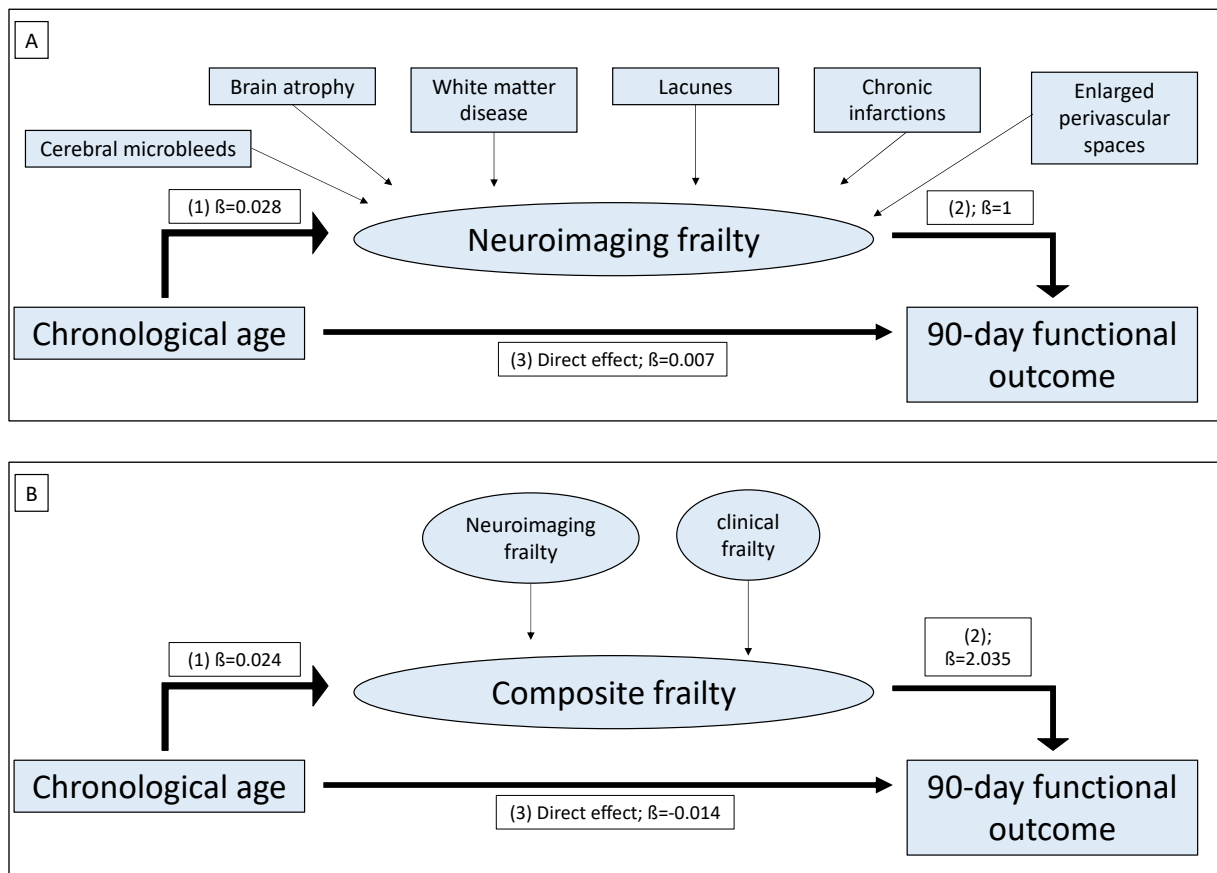
eFigure 1. Measurement of the Hemi-Intercaudate Distance (h-ICD) and Inner Table Width (ITW)



eFigure 1. Non-Contrast CT (NCCT) is shown in the sagittal plane (top) and axial plane (bottom). Measurements of the h-ICD are performed on the contralateral side to the AIS to account for any ischemic areas or hemorrhages associated with potential edema. To determine the h-ICD, the distance in mm between the septum pellucidum and the caudate head is measured (green line). In a second step, the h-ICD is multiplied by 2 to obtain the ICD. The ITW in mm is measured on the same sectional plane (turquoise line). Measurements are done with multiplanar reconstruction (MPR), to assure an accurate anterior-posterior commissural (APC) line (purple line). Finally, the intercaudate distance to inner table width ratio (CC/IT) is automatically calculated.

eFigure 2. Structural Equation Models Including Different Latent Variables As Possible

Mediator, MRI Only (n = 568)



eFigure 2. Shown are 2 causal diagrams including a latent variable (brain-frailty) as possible mediator for the association of chronological age and 90-day functional outcome. Each model includes a different latent variable: (A) shows imaging-based brain frailty, (B) shows a total construct of brain frailty. Adjustments for all models were made for the administration of Nerinetide, Alteplase, Onset to puncture time, NIHSS at baseline and ASPECTS at baseline.

eTable 1. Imaging Core Laboratory Members

Name	Subspecialty	Stroke imaging experience, years	Role in the core lab
Faysal Benali	Neuroradiology (diagnostic)	4	Cortical atrophy, subcortical atrophy and WMD burden assessments
Johanna Ospel	General radiology	5	FIV delineations
Fouzi Bala	Neuroradiology (diagnostic & interventional)	7	Cortical atrophy, subcortical atrophy and WMD burden assessments
Joachim Fladt	Stroke neurology	7	Cortical atrophy, subcortical atrophy and WMD burden assessments
Nishita Singh	Stroke neurology	7	Cortical atrophy, subcortical atrophy and WMD burden assessments
Aravind Ganesh	Stroke neurology	10	Cortical atrophy, subcortical atrophy and WMD burden assessments *

* In case of ≥ 2 grade disagreements.

eTable 2. Effect Estimates for Each Pathway in the Mediation Models, MRI Only (N = 568)

Neuroimaging frailty	β -coefficient	P-value	95% CI
Direct effect	0.007	0.59	-0.017; 0.030
Indirect effect	0.028	0.01	0.007-0.050
Total effect	0.035	<0.001	0.025-0.045
Relative proportion of indirect effect		80%	
Composite frailty	β -coefficient	P-value	95% CI
Direct effect	-0.014	0.34	-0.042; 0.015
Indirect effect	0.049	<0.001	0.022-0.076
Total effect	0.035	<0.001	0.025-0.045
Relative proportion of indirect effect		~100%	