SUPPLEMENTAL MATERIAL

SUPPLEMENTAL METHODS

Inclusion/Exlusion Criteria: Patients were included when they met the following criteria at the time of consent: (1) age between 18 and 90 years; (2) experienced an ischemic stroke resulting in unilateral upper extremity motor weakness as defined by a score of ≥1 on the NIH Stroke Scale arm motor drift questions (5A or 5B); and (3) ability to follow simple commands in English. Participants with a history of developmental, neurologic, or major psychiatric disorders resulting in functional disability as well as those with visual or auditory disorders limiting their ability to participate in testing procedures were excluded.

Methods for Spatial Normalization of Stroke Lesions: Diffusion images were skull stripped using BET (FSL) and spatially normalized to the 2mm T1-weighted Montreal Neurological Institute (MNI) brain template using Advanced Normalization Tools (ANTs, Philadelphia, PA). For scans with stroke lesions above the level of the brainstem, co-registration included center-of mass alignment, rigid, similarity, and fully affine linear transformations. For scans with stroke lesions within the brainstem, an additional non-linear (symmetric diffeomorphic) transformation was added to ensure accurate co-registration in this region. The resulting transformation matrices were applied to the stroke masks using ANTS to bring them into the MNI space.[1] The anatomic accuracy of each stroke mask in template space was visually verified by two-board certified neurologists (DJL and SBS).

Distinguishing Proportional from Limited Recoverers: Proportional recovery predicts that most patients will achieve 70% of their recovery potential:[2]

$$\Delta FM_{Predicted} = 0.7 \times FM_{Potential}$$

The residual from the proportional recovery model was calculated as:

$$FM_{Residual} = \Delta FM_{Predicted} - \Delta FM_{Actual}$$

Proportional recoverers were distinguished from limited recoverers by achieving a residual of < 10 points from predicted FM proportional recovery. The cutoff of 10 points was determined by (1) the minimally-clinically important difference (MCID) of the FM as defined by a prior study in subacute stroke patients[3] and (2) visual inspection of the plot of FM residuals verifying that two clear subgroups separated by a cutoff of 10 FM points. Hierarchical clustering based on Mahalanobis distances was also performed (Supplemental Figure I).[4, 5] We ultimately chose to use the MCID cutoff of residuals from the proportional recovery model to distinguish proportional recoverers versus limited recoverers because of the clinical relevance of this approach.

SUPPLEMENTAL FIGURES

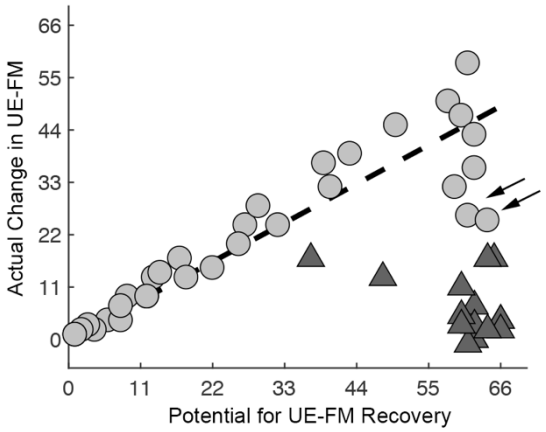

Figure I. Hierarchical clustering by Mahalanobis distances of potential for FM recovery (66 – FM_{Init}) versus actual change in FM (FM_{3mo} – FM_{Init}). Light gray circles show participants classified as proportional recoverers and dark gray triangles show those classified as limited recoverers. Participants were classified into the same groups based on clustering as classification based on a residual cutoff of 10 points from the proportional recovery model except for two patients indicated by arrows who were classified as proportional recoverers using clustering but limited recoverers using cutoff method.

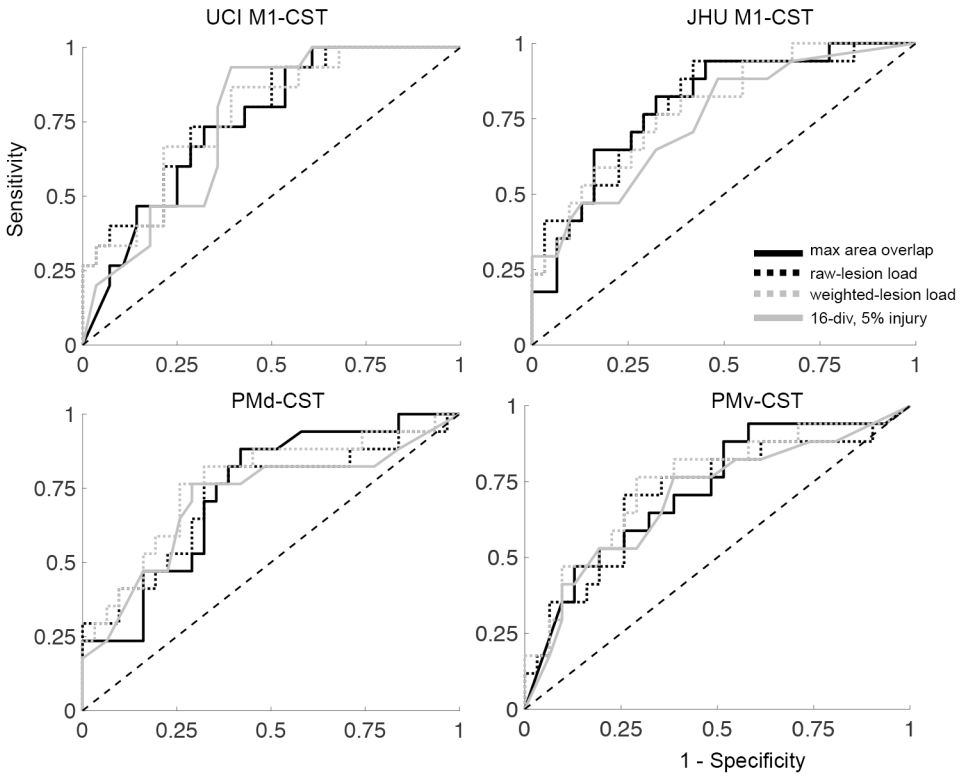

Figure II. Receiver Operating Curves (ROC) curves using amount of CST injury with different methods and different tract templates (UCI M1-CST left top, JHU M1-CST right top, PMd-CST left bottom, PMv-CST left bottom) as classifier for distinguishing limited recoverers from proportional recoverers. Dotted line shows chance prediction. Max area overlap, black solid; raw-lesion load, black dotted; weighted-lesion load, gray dotted; 16-div 5% injury, gray solid.

SUPPLEMENTAL TABLES

Age	Gender	Ethnicity	Dominant Hand	Affected Arm	PreMorbid mRS*	Prior Stroke	tPA⁺	EVT‡	Infarct Location	Initial NIHSS	FM_{Init}	FM_{3mo}	Recovery Status
68	Male	White	Right	Right	0	0	1	0	Left MCA deep (corona radiata / posterior limb)	5	4	40	p
58	Male	White	Right	Right	2	1	0	0	Left MCA deep (thalamocapsular)	6	54	63	p
68	Female	White	Right	Right	0	1	0	0	Left MCA Deep (corona radiata)	1	60	64	p
56	Male	White	Right	Right	0	0	1	1	L MCA Deep (corona radiata / basal ganglia)	5	53	66	p
85	Female	White	Right	Right	0	0	0	0	Left MCA Deep (corona radiata / basal ganglia)	4	62	64	p
72	Male	White	Right	Right	0	1	1	0	Left MCA Cortical (frontal - motor / premotor)	4	44	59	p
62	Female	White	Right	Left	0	0	0	0	Right MCA / PCA (Frontal + Occipital)	7	27	64	p
66	Male	White	Right	Right	1	1	1	1	Left MCA / PCA Cortical + Deep	10	29	46	p
75	Male	White	Right	Right	0	0	0	0	Left MCA Deep (corona radiata, watershed)	4	39	63	p
68	Male	Black	Left	Left	2	0	0	0	Right PCA (Occipital + Thalamus)	13	7	39	p
74	Female	White	Right	Right	0	1	0	0	Left MCA (cortical + deep (caudate))	7	37	65	p
64	Male	White	Right	Right	0	0	0	0	Left MCA (cortical + deep)	10	8	58	p
68	Female	White	Right	Left	0	0	1	0	Right MCA (temporal tip + basal ganglia)	4	34	58	p
77	Female	White	Right	Left	1	0	1	1	Right MCA (thalamocapsular + temporal tip)	5	63	66	p
56	Male	White	Left	Right	1	0	0	0	Left MCA (cortical)	8	52	66	p
57	Male	White	Right	Left	0	0	0	0	Right Brainstem (pons) + Left cerebellum	7	6	33	p

61	Male	White	Left	Right	0	1	1	0	Left MCA (cortical + white matter)	4	49	66	p
71	Male	White	Right	Left	1	1	0	0	Brainstem (Right medial anterior pons)	5	48	61	p
76	Female	White	Right	Right	0	0	0	0	Brainstem (Left anterior pons)	9	4	47	p
65	Female	White	Right	Left	2	0	0	0	Right MCA (corona radiata)	6	58	62	p
57	Male	White	Right	Right	0	0	0	0	Left MCA (corona radiata)	2	64	66	p
80	Male	White	Right	Right	1	1	0	0	Bilateral cortical (L peri-central sulcus, R posterior parietal)	2	57	66	p
73	Male	White	Right	Left	0	0	0	0	Right MCA (scattered, cortical + deep)	1	40	60	p
67	Male	White	Right	Left	0	0	0	0	Right MCA (cortical, precentral gyrus)	2	65	66	p
71	Female	White	Right	Right	0	0	1	0	Left corona radiata	6	23	62	p
50	Male	White	Left	Left	0	0	1	1	Right MCA (cortical + deep)	3	65	66	p
56	Female	White	Right	Right	0	0	1	0	Left MCA (deep, basal ganglia)	4	54	63	p
47	Female	White	Right	Left	0	0	1	1	Right MCA (cortical + deep)	10	5	63	p
66	Female	Black	Right	Left	0	0	1	1	Right MCA (cortical + deep)	9	26	58	p
57	Male	Black	Right	Left	0	0	0	0	Right Midbrain + R thalamus + corpus callosum	9	16	61	p
63	Male	White	Right	Left	0	0	0	0	Right MCA (cortical + deep)	3	58	65	p
74	Female	White	Right	Right	1	1	0	0	Left Brainstem (pons) + Bilateral Cerebellum	13	0	4	1
72	Male	White	Right	Left	0	0	0	0	Right MCA / PCA (occipital, medial temporal, thalamocapsular)	16	0	4	1

62	Female	Hispanic	Left	Right	2	0	1	0	Left MCA Deep (globus pallidus / internal capsule)	9	4	11	1
82	Female	White	Right	Left	0	0	1	1	Right MCA Cortical + Deep (frontal / temporal / basal ganglia)	21	4	4	1
66	Female	White	Right	Right	0	0	0	0	Left MCA deep (corona radiata / external capsule)	8	5	31	1
88	Female	White	Right	Left	2	0	1	1	Multifocal, Bilateral MCA (Right cortical + basal ganglia / L frontal)	17	4	4	1
21	Female	White	Right	Left	3	0	0	0	Right MCA Cortical + Deep (frontal / parietal / temporal / BG)	15	1	18	1
70	Female	White	Left	Right	2	0	0	0	Left MCA (Cortical + Deep)	21	5	4	1
58	Male	White	Left	Left	0	1	0	0	Right MCA Deep (corona radiata + thalamocapsular)	6	18	31	1
51	Male	White	Right	Left	0	0	0	0	Right MCA Deep (corona radiata + posterior putamen)	11	6	17	1
80	Female	White	Right	Left	2	0	0	0	Left corpus callosum + Brainstem (Medulla)	9	0	2	1
71	Female	White	Left	Left	0	0	0	0	Right MCA (cortical)	16	4	7	1
48	Male	White	Left	Right	0	0	1	0	Left MCA (cortical + deep)	17	2	27	1
55	Male	Male	Right	Right	0	0	0	0	Left PCA (thalamus + midbrain)	20	2	4	1
57	Female	White	Right	Left	0	0	0	0	Right MCA deep	13	6	11	1
60	Female	White	Right	Left	2	0	0	1	Right MCA cortical + deep	10	2	19	1
62	Male	Male	Right	Left	0	1	0	1	Right MCA (cortical + deep, scattered)	11	6	9	1

Table I. Baseline participant and stroke characteristics grouped by proportional (p, top) versus limited (l, bottom) recoverer status.
*mRS = modified Rankin Scale
+tPA = alteplase

‡EVT = endovascular therapy
§p = proportional recover, l = limited recoverer

		UCI-M1 CST				JHU M1-CST				PMd-CST				PMv-CST		
		Max Area	RLL	WLL	16/5	Max Area	RLL	WLL	16/5	Max Area	RLL	WLL	16/5	Max Area	RLL	WLL
UCI M1-CST	Max Area															
	RLL	0.79														
	WLL	0.80	0.97													
	16/5	0.89	0.78	0.77												
JHU M1-CST	Max Area	0.89	0.83	0.80	0.85											
	RLL	0.75	0.90	0.90	0.76	0.86										
	WLL	0.76	0.91	0.91	0.77	0.86	1.0									
	16/5	0.80	0.88	0.86	0.83	0.88	0.92	0.91								
PMd-CST	Max Area	0.93	0.84	0.81	0.90	0.94	0.81	0.81	0.89							
	RLL	0.75	0.95	0.91	0.79	0.81	0.87	0.88	0.89	0.85						
	WLL	0.75	0.94	0.90	0.78	0.81	0.86	0.85	0.88	0.84	0.99					
	16/5	0.82	0.80	0.76	0.92	0.83	0.74	0.75	0.87	0.92	0.84	0.84				
PMv-CST	Max Area	0.73	0.66	0.68	0.67	0.65	0.62	0.63	0.69	0.77	0.71	0.68	0.68			
	RLL	0.70	0.92	0.87	0.68	0.75	0.79	0.79	0.79	0.78	0.94	0.92	0.71	0.73		
	WLL	0.71	0.91	0.87	0.67	0.75	0.77	0.77	0.79	0.78	0.94	0.93	0.72	0.74	0.99	
	16/5	0.80	0.76	0.75	0.81	0.74	0.68	0.69	0.77	0.83	0.79	0.77	0.83	0.87	0.79	0.79

Table II. Correlation matrix showing correlations between CST injury values estimated by different methods (max area overlap, raw lesion-load, weighted lesion-load, and 16-Div, 5% injury) and on different CSTs (UCI M1-CST, JHU M1-CST, PMd-CST, PMv-CST).

	UCI M1-CST				JHU M1-CST			
	AUC	Thr	Sens	Spec	AUC	Thr	Sens	Spec
Max area overlap	0.75	0.94	0.47	0.86	0.80	0.63	0.65	0.84
Raw lesion load	0.77	2.18	0.4	0.93	0.80	0.71	0.41	0.97
Weighted lesion load	0.77	5.69	0.27	1	0.79	1.0	0.53	0.87
16 Div, 5% Injury	0.75	0.56	0.93	0.61	0.75	0.81	0.29	1

	PMd-CST				PMv-CST			
	AUC	Thr	Sens	Spec	AUC	Thr	Sens	Spec
Max area overlap	0.74	0.94	0.24	1	0.72	0.85	0.47	0.87
Raw lesion load	0.72	3.43	0.29	1	0.71	0.86	0.71	0.74
Weighted lesion load	0.77	2.37	0.77	0.74	0.75	2.41	0.47	0.90
16 Div, 5% Injury	0.71	0.56	0.76	0.71	0.70	0.88	0.41	0.90

Table III. Area under the curve (AUC), optimal threshold values (Thr), and sensitivity (Sens) and specificity (Spec) for performance of threshold injury values for classifying limited recoverers versus proportional recoverers using CSTs from M1 (top) and PMd/PMv (bottom) seed regions.

CST Injury	Total # Patients	# Proportional Recoverers (n=31)	# Limited Recoverers (n=17)
0 – 25%	13	12	1
26 – 50%	15	11	4
51 – 75%	11	5	6
76 – 100%	9	3	6

Table IV. Proportional and limited recoverers grouped by percent CST injury. CST Injury values were determined here using the maximum cross-sectional area method on the JHU M1-CST tract. These are the same data as presented in the ROC AUC figure (Supplemental Figure II) and table (Supplemental Table III) above, but here presented in quartiles for clearer impact.

	Model 1			Model 2			Model 3		
	Beta	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**	**Beta**	**95% CI**	**p-value**
CST Injury	-0.65	-0.98, -0.31	<0.001	-0.65	-0.99, -0.31	<0.001	-0.43	-0.94, 0.08	0.10
M1-pM injury	-	-	-	0.007	-0.18, 0.20	0.94	0.18	-0.18, 0.55	0.32
CST * M1-pM injury	-	-	-	-	-	-	-0.38	-1.07, 0.30	0.26
Overall Model R^2	R^2=0.25	-	<0.001	R^2=0.25	-	0.002	R^2=0.27	-	0.003
R^2 Change	-	-	-	ΔR^2=0	-	0.94	ΔR^2=.021	-	0.26

Table V. Hierarchical linear regression including CST injury (Model 1), CST Injury + M1-pM injury (Model 2), and CST injury + M1-pM + interaction term (Model 3). CI=Confidence Interval

SUPPLEMENTAL REFERENCES

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