Table S1. Summary of Biomarkers Investigated in Remote Ischemic Conditioning for Cerebrovascular Disease.

Biomarker Category	Specific Biomarker	Sample Type	Disease Context	Effect of RIC	Key Clinical Correlation
NEURONAL INJURY MARKERS	S100B	Serum	AIS, sICAS	↓	Correlates with stroke severity and 90-day mRS; reduced in RIC groups
	NSE	Serum	AIS	↔	Correlates with infarct volume; inconsistent RIC effects
INFLAMMATORY CYTOKINES	IL-6	Serum/CSF	AIS, sICAS, cSVD	↓ in sICAS/cSVD	Reduced after prolonged RIC; no change in acute stroke
	IL-10	Serum/CSF	AIS	N/A	Low levels linked to poor outcomes
	TNFα	Serum/CSF	AIS, cSVD	Brief ↓	Short-lived reduction; variable in chronic disease
	IL-1β	Serum/CSF	AIS	N/A	Rises in CSF days 2-3 post-stroke
	CRP	Serum	sICAS, cSVD	↓	Reduced after 30 days RIC in sICAS
CELL ADHESION MOLECULES	ICAM-1	Serum	AIS, sICAS	↓	Reduced after 6 months; correlates with perfusion
	ICAM-3	Serum	General inflammation	↓	Reduced in RIC-treated periodontitis patients
	P-selectin	Serum	AIS	Variable	Inconsistent clinical results
MATRIX METALLOPROTEINASES	MMP-9	Serum	AIS, sICAS	↓ in sICAS	Significant reduction after 6 months in sICAS; variable in AIS
TRANSCRIPTION FACTORS	NF-κB	Serum	AIS	↓	Reduced after 8 weeks RIC
	TLR4	Serum	AIS	↓	Reduced after 8 weeks; inversely correlates with collaterals
HEAT SHOCK PROTEINS	HSP27 (total)	Serum	AIS	↑	Increased after 4 days RIC
	HSP27 (phosphorylated)	Serum	AIS	↑	Increased after 4 days; associated with better outcomes
	HSP70	Serum	AIS	↑	Upregulated in conditioning response
ANGIOGENIC FACTORS	VEGF	Serum	AIS, sICAS	↑	Elevated after RIC in both AIS and sICAS
	bFGF	Serum	AIS, sICAS	Variable	Increased in sICAS; unchanged in AIS
	EGF	Serum	AIS	↑	Correlates with motor recovery
	PDGF	Serum	AIS	↔	No change observed
NEUROTROPHIC FACTORS	BDNF	Serum	AIS, sICAS	↑ in chronic	Increased after 6 months in sICAS; no acute change
VASCULAR MARKERS	Endothelin-1	Serum	AIS	↓	Reduced after 6 months; correlates with perfusion
	Homocysteine	Serum	cSVD	↓	Reduced after 1 year; linked to WMH improvement
COAGULATION & PLATELET FUNCTION	Fibrinogen	Serum	sICAS, cSVD	↓ in sICAS	Reduced in sICAS; no change in cSVD
	TPA	Serum	sICAS	↑	Increased fibrinolytic activity
	PAI-1	Serum	sICAS	↓	Reduced after 30 days RIC
	Platelet aggregation rate	Whole blood	sICAS	↓	Decreased aggregation
	D-dimer	Serum	Lacunar stroke	↔	No significant change
	Fractal dimension (df)	Whole blood	Lacunar stroke	↑	Increased clot density (paradoxical finding)

Biomarker Category	Specific Biomarker	Sample Type	Disease Context	Effect of RIC	Key Clinical Correlation
HAEMORHEOLOGICAL MARKERS	Erythrocyte aggregation	Whole blood	AIS	↓	Reduced aggregation improves microvascular flow
	RBC deformability	Whole blood	AIS	↔	No change with RIC
	Intracellular NO	RBC	AIS	↔	No change with RIC
	Whole-blood nitrite	Whole blood	AIS	↔	No change with RIC
CELL COUNT-DERIVED INDICES	White blood cell count	Whole blood	sICAS	↓	Reduced after 30 days RIC
	PNR (Platelet-to-Neutrophil Ratio)	Whole blood	AIS	N/A	Low PNR (<30.98) predicts better RIC response
LIPID MARKERS	Total cholesterol	Serum	cSVD	↓	Reduced after 1 year RIC
	LDL cholesterol	Serum	cSVD	↓	Reduced after 1 year RIC
	Triglycerides	Serum	cSVD	↓	Reduced after 1 year RIC
	Lipoprotein(a)	Serum	sICAS	↔	No change but levels >17.4 mg/dL predict RIC benefit
CEREBRAL PERFUSION (IMAGING)	CBF	MRI/CT perfusion	AIS, cSVD	↑	Increased at 90 days post-stroke
	MTT	MRI/CT perfusion	AIS	↓	Decreased at 90 days
	CBV	MRI/CT perfusion	AIS	N/A	Measured but not primary endpoint
	Blood flow velocity (MCA, ACA, PCA, vertebral, basilar)	TCD ultrasound	AIS, sICAS	↑	Improved velocities at 6 months across all vessels
	MCA pulsatility index	TCD ultrasound	cSVD	↓	Reduced after 1 year RIC
	Brachial artery pulsatility index	Doppler ultrasound	cSVD	↓	Reduced after 1 year RIC
STRUCTURAL IMAGING	WMH volume	MRI (FLAIR/T2)	cSVD	↓	Significantly reduced after 1 year RIC
ENDOTHELIAL FUNCTION	BA-FMD (%)	Ultrasound	Chronic stroke, lacunar	Variable	Improved in chronic stroke; variable in acute SVD
EPIGENETIC & RNA MARKERS	DNA methylation patterns	Whole blood	aSAH	Altered	Widespread changes in gene expression
	miRNA let-7a	Serum	Stroke (preclinical)	Normalized	Elevated post-stroke; restored by RIC
	miRNA-143	Serum	Stroke (preclinical)	Normalized	Elevated post-stroke; restored by RIC
RETINAL IMAGING	Retinal vessel density	OCTA	Stroke, cSVD	N/A	Reduced in patients; RIC effects not yet studied
EMERGING BIOMARKERS (PRECLINICAL/PROPOSED)	Kallistatin	Serum	Preclinical	↑	Protects against vascular damage in animal models
	SDF-1α	Serum	Preclinical	↑	Promotes regeneration in stroke models
	GLP-1	Serum	Preclinical	N/A	Neuroprotective; increases CBF in animal models
	Neurofilament light (NF-L)	CSF	cSVD	N/A	Proposed for future RIC trials

Abbreviations: AIS = Acute Ischemic Stroke; sICAS = Symptomatic Intracranial Arterial Stenosis; cSVD = Cerebral Small Vessel Disease; aSAH = Aneurysmal Subarachnoid Hemorrhage; MRI = Magnetic Resonance Imaging; CT = Computed Tomography; TCD = Transcranial Doppler; OCTA = Optical Coherence Tomography Angiography; CSF = Cerebrospinal Fluid; RBC = Red Blood Cell; NO = Nitric Oxide; MCA = Middle Cerebral Artery; ACA = Anterior Cerebral Artery; PCA = Posterior Cerebral Artery; WMH = White Matter Hyperintensities; BA-FMD = Brachial Artery Flow-Mediated Dilation; ↑ = Increased; ↓ = Decreased; ↔ = No change; N/A = Not assessed in clinical RIC trials.

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