

# Sonothrombolysis in Acute Ischemic Stroke

Thesis

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## List of Abbreviations

<b>ACA</b>	:	Anterior cerebral artery
<b>AchA</b>	:	Anterior choroidal artery
<b>AF</b>	:	Atrial fibrillation
<b>AHA</b>	:	American heart association
<b>ASA</b>	:	American stroke association
<b>BHI</b>	:	Breth holding index
<b>BUN</b>	:	Blood urea nitrogen
<b>CBC</b>	:	Complete blood count
<b>CLOTBUST</b>	:	Combined lysis of thrombus in brain ischemia using transcranial ultrasound and systemic TRA
<b>CO<sub>2</sub></b>	:	Cargon dioxide
<b>CT</b>	:	Computed pomography
<b>CTA</b>	:	Computed tomography angiography
<b>C-US</b>	:	Continuous ultrasound
<b>DEFUSE</b>	:	Diffusion weighted imaging for understanding stroke evolution
<b>DIAS</b>	:	Desmoteplase in acute stroke
<b>DWI</b>	:	Diffusion weighted imaging
<b>ECASS</b>	:	European cooperative acute stroke study
<b>ECG</b>	:	Electrocardiography
<b>EMS</b>	:	Emergency management of stroke
<b>ESO</b>	:	European stroke organization



### **List of Abbreviations (Cont.)**

<b>EXTEND</b>	:	Extending the time for thrombolysis in neurological emergency deficit
<b>FBS</b>	:	Fasting blood sugar
<b>FDA</b>	:	Food and Drug administration
<b>HITS</b>	:	High intensity signals
<b>i.e.</b>	:	That is
<b>IA</b>	:	Intraarterial
<b>ICA</b>	:	Internal carotid artery
<b>IMS</b>	:	Interventional management of stroke
<b>IQR</b>	:	Interguartile range
<b>LDL</b>	:	Low density lipoprotein
<b>LFUS</b>	:	Low-frequency ultrasound
<b>M1</b>	:	Proximal segment of middle cerebral artery
<b>M<sub>2</sub></b>	:	Distal segment of middle cerebral artery
<b>M<sub>4</sub></b>	:	Terminal branches of middle cerebral artery
<b>MB</b>	:	Microbubbles
<b>MCA</b>	:	Middle cerebral artery
<b>MES</b>	:	Microenbolic signal
<b>Mets</b>	:	Metabolic syndrome
<b>MFV</b>	:	Mean flow velocity
<b>MHZ</b>	:	Megahertz

### **List of Abbreviations (Cont.)**

<b>MRCI</b>	:	Mechanical embolus removal in cerebral ischemia
<b>MRI</b>	:	Magnetic resonance imaging
<b>N</b>	:	Number
<b>NIHSS</b>	:	NIH stroke scale
<b>NINDs</b>	:	National institute of neurological disorders & stroke
<b>NS</b>	:	Non significant
<b>PCA</b>	:	Posterior cerebral artery
<b>PET</b>	:	Position emission tomography
<b>PFO</b>	:	Patent foramen ovale
<b>PI</b>	:	Pulsatility index
<b>PS</b>	:	Power & sample size
<b>RBS</b>	:	Rabdom blood sugar
<b>r-tPA</b>	:	Recombinant tissue plasminogen activator
<b>S</b>	:	Significant
<b>SBP</b>	:	Systolic blood pressure
<b>SD</b>	:	Standard deviation
<b>SICH</b>	:	Symptomatic intracranial hemorrhage
<b>SPSS</b>	:	Statistical package for social science
<b>Std</b>	:	Standard

### **List of Abbreviations (Cont.)**

<b>TCCD</b>	:	Transcranial color coded duplex
<b>TCD</b>	:	Transcranial Doppler
<b>TIA</b>	:	Transient ischemic attack
<b>TIBI</b>	:	Thrombolysis in brain ischemia
<b>TIMI</b>	:	Thrombolysis in myocardial infarction
<b>TOE</b>	:	Transoesophageal echo
<b>tPA</b>	:	Tissue plasminogen activator
<b>TRUMBI</b>	:	Transcranial low frequency ultrasound mediated thrombolysis in brain ischemia
<b>TUCSON</b>	:	Transcranial ultrasound in clinical sonothrombolysis
<b>UET</b>	:	Ultrasound-enhanced thrombolysis
<b>US</b>	:	Ultrasound

## **Introduction**

Acute ischemic stroke is characterized by the sudden loss of blood circulation to an area of the brain, resulting in sudden onset of a focal neurologic deficit (*Lopez et al., 2006*).

Cerebrovascular disease was the second leading cause of death worldwide in 1990, killing more than 4.3 million people. It was also the fifth leading cause of lost productivity, as measured by disability-adjusted life years (DALYs) (*Flynn et al., 2008*).

Transcranial Doppler (TCD) is a non-invasive, non-ionising, inexpensive, portable and safe technique that measures the velocity of blood flow through the brain's blood vessels (*Sarkar et al., 2007*). So, it is helpful in the diagnosis of acute ischemic stroke as it can provide rapid information about major arterial occlusion or stenosis (especially middle cerebral artery occlusion), and also the hemodynamic status of the cerebral circulation, as well as monitoring of reperfusion and recanalization (*Alexandrov et al., 2009*).

TCD has emerged as a tool to treat ischemic stroke since the last few years. The potential advantage of ultrasound (US) is to decrease the risk of systemic bleeding complications due to its site-specific effect. Moreover, external application is

noninvasive and is readily available. A 2-MHz pulsed-wave diagnostic ultrasound beam provides real-time bedside monitoring of thrombolysis. It can augment residual flow and speed up thrombolysis, allowing patients to recover from stroke more rapidly and completely (*Alexandrov and Mikulik, 2006*).

Some recent researchers studied the effect of combined use of intravenous tissue plasminogen activator (TPA) and TCD ultrasound on recanalization of the occluded intracranial arteries, it shows that thrombolysis with intravenous tissue plasminogen activator (TPA) can be enhanced with ultrasound. Ultrasound delivers mechanical pressure waves to the clot, thus exposing more thrombus surface to circulating drug (*Alexandrov and Tsivgoulis, 2007*).

Low-frequency US with high power has been demonstrated to produce cavitations and fluid motion in the thrombus (*Alexandrov and Molina, 2007*). Some experimental studies use the administration of micro bubbles (MB) (e.g. galactose-based air-filled MB & sulphur hexafluoride-filled MB) as it may augment the effect of ultrasound-enhanced systemic thrombolysis in acute stroke. Bubble structural characteristics may influence the effect of MB on sonothrombolysis (*Rubiera et al., 2008*). Other recent studies suggest that acceleration of thrombolysis using pulsed wave US is effective & can enhance thrombolysis even without rt-PA (*Eggers et al., 2005*). Although some experimental studies and

pilot clinical evidence show that TCD has role in the enhancement of thrombolysis with or even without rt-PA (*Alexandrov and Tsivgoulis, 2007*), yet more studies are needed to evaluate the potential of TCD ultrasound technology to enhance thrombolysis & to study the effect of vascular risk factors (e.g DM, hyperlipidemia) as predictors of recanalization.

## **Aim of the Work**

Our aim is to study the effect of continuous insonation using 2-MHz transcranial Doppler US on the recanalization rate and the short-term outcome of subjects with acute ischemic stroke due to Middle Cerebral Artery (MCA) occlusion.