Sonothrombolysis

Background:

Intravenous tissue plasminogen activator (rt-tPA) therapy can be monitored with 2 MHz transcranial Doppler (TCD). Transcranial Doppler ultrasonography (2 MHz) that is aimed at (residual) obstructive intracranial blood flow may help expose thrombi to tissue plasminogen activator (t-PA). Gaseous microspheres, initially developed as ultrasound contrast agents, can further increase the effectiveness of rt-PA. Latest research focusses on tPA-loaded microbubbles (MB) to improve efficiency.

Literature:

Outcomes following sonothrombolysis in severe acute ischemic stroke: subgroup analysis of the CLOTBUST trial.

Author	Barlinn K[1], Tsivgoulis G, Barreto AD, Alleman J, Molina CA, Mikulik R, Saqqur M, Demchuk AM, Schellinger PD, Howard G, Alexandrov AV.
Content/Summary Abstract	**BACKGROUND:** Sonothrombolysis is safe and may increase the likelihood of early recanalization in acute ischemic stroke patients. **AIMS:** In preparation of a phase III clinical trial, we contrast the likelihood of achieving a sustained recanalization and functional independence in a post hoc subgroup analysis of patients randomized to transcranial Doppler monitoring plus intravenous tissue plasminogen activator (sonothrombolysis) compared with intravenous tissue plasminogen activator alone in the CLOTBUST trial. **METHODS:** We analyzed the data from all randomized acute ischemic stroke patients with pretreatment National Institutes of Health Stroke Scale scores ≥ 10 points and proximal intracranial occlusions in the CLOTBUST trial. We compared sustained complete recanalization rate (Thrombolysis in Brain Ischemia flow grades 4-5) and functional independence (modified Rankin Scale 0-1) at 90 days. Safety was evaluated by the rate of symptomatic intracranial hemorrhage within 72 h of stroke onset. **RESULTS:** Of 126 patients, a total of 85 acute ischemic stroke patients met our inclusion criteria: mean age 71 ± 11years, 56% men, median National Institutes of Health Stroke Scale 17 (interquartile range 14-20). Of these patients, 41 (48%) and 44 (52%) were randomized to intravenous tissue plasminogen activator alone and sonothrombolysis, respectively. More patients achieved sustained complete recanalization in the sonothrombolysis than in the intravenous tissue plasminogen activator alone group (38·6% vs. 17·1%; P = 0·032). Functional independence at

	90 days was more frequently achieved in the sonothrombolysis than in the intravenous tissue plasminogen activator alone group (37·2% vs. 15·8%; P = 0·045). Symptomatic intracranial hemorrhage rate was similar in both groups (4·9% vs. 4·6%; P = 1·00).
Comment	High number of patients
Doppler-device	Not known
Quantification	Author results point to a signal of efficacy and provide information to guide the subsequent phase III randomized trial of sonothrombolysis in patients with severe ischemic strokes.

Thrombolytic efficacy of tissue plasminogen activator-loaded echogenic liposomes in a rabbit thrombus model.

Author	(Laing u. a., 2011)
Content/Summary	All treatments showed thrombolysis, but tPA-loaded ELIP (0 echogenic liposome) was the most efficacious regimen. Both US treatment strategies enhanced thrombolytic activity over control conditions.
Comment	Clots were exposed to transabdominal color Doppler US (6MHz) for 30 minutes at a low mechanical index (MI=0.2) to induce sustained bubble activity (acoustically-driven diffusion), or for 2 minutes at an MI of 0.4 to cause ELIP fragmentation.
Doppler-device	Rabbit examination
Quantification	The thrombolytic efficacy of tPA-loaded ELIP is comparable to other clinically described effective treatment protocols, while offering the advantages of US monitoring and enhanced thrombolysis from a site-specific delivery agent.

The preparation of a new self-made microbubble-loading (MB) urokinase (uPA) and its thrombolysis combined with low-frequency ultrasound in vitro.

Author	(Ren u. a., 2011)
Content/Summary	
Comment	In vitro examination
Doppler-device	Not known
Quantification	uPA-MBs combined with US can decrease the in vitro dosage of uPA for thrombolysis.

Quantification of Target Population for Ultrasound Enhanced Thrombolysis in Acute Ischemic Stroke.

Author	(Nolte u. a., 2011)
Content/Summary	MCA occlusions were detected in 39% of patients (N= 69) with 48 (27%) occlusions in the proximal M1-segment and 21 (12%) in a distal M2-segment. Arterial occlusions others than MCA were seen in an additional 9% (N= 16). TCCS (without contrast agent) revealed sufficient bone windows in 70% of patients with MCA occlusions (N= 48) corresponding to 27% of all patients treated with thrombolysis.
Comment	One-hundred and seventy-nine patients (age [years], median [IQR]= 75 [65-83]; 42% female; NIH Stroke Scale [NIHSS], median [IQR]= 10 [6-17]) were analyzed.
Doppler-device	Not known
Quantification	Conventional sonothrombolysis is restricted to a minority of stroke patients suitable for intravenous thrombolysis.

Microbubble-augmented ultrasound sonothrombolysis decreases intracranial hemorrhage in a rabbit model of acute ischemic stroke.

Author	(Flores u. a., 2011)
Content/Summary	Percentage of rabbits having ICH outside the infarct area was significantly decreased ($P = 0.004$) for MB + US (19%) rabbits compared with tPA + US (73%), US only (56%), tPA (48%), tPA + MB + US (36%), and control (36%) rabbits. Incidence and severity of ICH within the infarct did not differ ($P > 0.39$). Infarct volume was significantly greater ($P = 0.002$) for rabbits receiving US (0.97% ± 0.17%) than for MB + US (0.20% ± 0.14%)
Comment	Rabbits (n = 158) received a 1.0-mm clot, angiographically injected into the internal carotid artery causing infarcts. US groups received pulsed wave US (1 MHz, 0.8 W/cm) for 1 hour; rabbits with tPA received intravenous tPA (0.9 mg/kg) over 1 hour. Rabbits with MB received intravenous MB (0.16 mg/kg) given over 30 minutes.
Doppler-device	Not known
Quantification	Treatment with MB + US after embolization decreased the incidence of ICH and efficacy was similar to tPA in reducing infarct volume.

Platelet-targeted microbubbles inhibit re-occlusion after thrombolysis with transcutaneous ultrasound and microbubbles.

Author	(X. B. Zhou u. a., 2011)
Content/Summary	
Comment	Rabbit examination
Doppler-device	Not known
Quantification	These results indicated that platelet-targeted microbubbles were beneficial in preventing re-thrombosis in vivo and microbubbles served as good carrier of thrombolytic and anticoagulation drugs.

Microbubbles improve sonothrombolysis in vitro and decrease hemorrhage in vivo in a rabbit stroke model.

Author	(Brown u. a., 2011)
Content/Summary	Combining tPA and MB yielded effective loss of clot with very low dose or even no dose tPA, and infarct volumes and ICH were reduced in acute strokes in rabbits.
Comment	In vitro + rabbit examination
Doppler-device	Not known
Quantification	The ability of MBs to reduce tPA requirements may lead to lower rates of hemorrhage in human stroke treatment.

Sonothrombolysis for the treatment of acute stroke: current concepts and future directions.

Author	(Amaral-Silva u. a., 2011)
Content/Summary	This article reviews the present status of sonothrombolysis in acute stroke treatment, highlighting both experimental and clinical studies addressing this issue, and discusses its future regarding both efficacy and safety.
Comment	Review
Doppler-device	Not known
Quantification	Latest review on sonothrobolysis

Reperfusion therapies for acute ischemic stroke: current pharmacological and mechanical approaches.

Author	(Carlos A Molina, 2011)
Content/Summary	About CLOTBUST-Trial: Among 126 patients randomized to tPA plus 2-hour transcranial Doppler monitoring (target group) or tPA alone (control group), symptomatic intracerebral hemorrhage occurred in 4.8% of target and 4.8% of control patients. Complete recanalization or dramatic clinical recovery at 2 hours after tPA bolus was observed in 49% of target and 29% of control patients (P=0.02). Moreover, trends toward better clinical outcomes at 24 hours and long term were noted in sonothrombolysis patients. Enhancement of enzymatic thrombolysis by ultrasound may allow testing regimens with low-dose tPA to reduce the risk of intracerebral hemorrhage. The capability of microbubbles to further accelerate ultrasound-enhanced lysis ...
Comment	Review
Doppler-device	Not known
Quantification	Summary of recent treatments

Pharmacological and non-pharmacological recanalization strategies in acute ischemic stroke.

Author	(Frendl und Csiba, 2011)
Content/Summary	
Comment	Review
Doppler-device	Not known
Quantification	Current review an recanalization. Very positive estimation on sonothrombolysis.

Ultrasound-assisted thrombolysis for stroke therapy: better thrombus break-up with bubbles.

Author	(Hitchcock und Holland, 2010)
Content/Summary	
Comment	Summary on MB-enhancement of thrombolysis
Doppler-device	Not known
Quantification	Ultrasound-driven stable cavitation nucleated by an infusion of an echo contrast agent facilitates recombinant tissue plasminogen activator thrombolysis. Optimization of this gently effervescent phenomenon has the potential to reduce the morbidity and mortality of victims of ischemic stroke.

Intra-arterial administration of microbubbles and continuous 2-MHz ultrasound insonation to enhance intra-arterial thrombolysis.

Author	(Marc Ribo u. a., 2010)
Content/Summary	In-procedure recanalization was observed in 78% (n= 7): complete-TICI3 in 22% (n= 2).
Comment	Of the 18 included patients (mean age 72), 16 received standard iv-tPA (.9 mg/kg). Nine patients were recanalized during tPA infusion and 9 patients underwent IA (intra-arterial)-rescue procedures.
Doppler-device	PMD-100 Spencer
Quantification	The combination of ultrasound and intra arterial MB and tPA may be a strategy to enhance the thrombolytic effect and increase recanalization rates.

Construction of thrombus-targeted microbubbles carrying tissue plasminogen activator and their in vitro thrombolysis efficacy: a primary research.

Author	(Hua u. a., 2010)
Content/Summary	The results showed that the microbubbles were suitable for intravenous injection The drug-loaded microbubbles plus ultrasound irradiation got higher thrombolysis with the lowest dosage
Comment	We tried to develop a new type of ultrasound microbubbles carrying thrombolytics and simultaneously targeting to thrombus, which could bind with thrombus specifically and release the encapsulated drug locally under the ultrasound exposure Microbubbles carrying tissue plasminogen activator (tPA) and Arg-Gly-Asp-Ser tetrapeptide (RGDS) were prepared by lyopyilization.
Doppler-device	In vitro
Quantification	The tPA-loaded microbubbles targeting to thrombus can be prepared by lyopyilization, which will bring out a novel way for the targeting drug-released thrombolysis therapy.

Effects of ultrasound-induced inertial cavitation on enzymatic thrombolysis.

Author	(Chuang u. a., 2010)
Content/Summary	Microscopically, enzymatic thrombolysis effects manifest as multiple large cavities within the clot that are uniformly distributed on the side exposed to ultrasound. This suggests that inertial cavitation plays an important role in producing cavities, while microjetting of the microbubbles induces pits on the clot surface.
Comment	summary
Doppler-device	Not known
Quantification	These observations preliminarily demonstrate the clinical potential of sonothrombolysis. The use of the differential inertial cavitation dose as an indicator of blood clot weight loss for controlled sonothrombolysis is also possible and will be further explored.

Safety and efficacy of ultrasound-enhanced thrombolysis: a comprehensive review and meta-analysis of randomized and nonrandomized studies.

Author	(Tsivgoulis u. a., 2010)
Content/Summary	The rates of symptomatic intracerebral hemorrhage in randomized studies were as follows: tPA+TCD, 3.8% (95% CI, 0%-11.2%); tPA+TCCD, 11.1% (95% CI, 0%-28.9%); tPA+low-frequency ultrasound, 35.7% (95% CI, 16.2%- 61.4%); and tPA alone, 2.9% (95% CI, 0%-8.4%). Complete recanalization rates were higher in patients receiving combination of TCD with tPA 37.2% (95% CI, 26.5%- 47.9%) compared with patients treated with tPA alone 17.2% (95% CI, 9.5%-24.9%) In 8 trials of high-frequency (TCD/TCCD) ultrasound-enhanced thrombolysis, tPA+TCD/TCCD+/-microS was associated with a higher likelihood of complete recanalization (pooled OR, 2.99; 95% CI, 1.70-5.25; P=0.0001) when compared to tPA alone. High-frequency ultrasound-enhanced thrombolysis was not associated with an increased risk of symptomatic intracerebral hemorrhage (pooled OR, 1.26; 95% CI, 0.44-3.60; P=0.67).
Comment	Metaanalysis: A total of 6 randomized (n=224) and 3 nonrandomized (n=192).
Doppler-device	Not known
Quantification	Very important and postive metaanalysis!

Current and future recanalization strategies for acute ischemic stroke.

Author	(A V Alexandrov, 2010)
Content/Summary	This review focuses on the following strategies available to clinicians now or being tested in clinical trials: (a) faster initiation of tPA infusion; (b) sonothrombolysis; (c) intra-arterial revascularization, bridging intravenous and intra-arterial thrombolysis, mechanical thrombectomy and aspiration; and (d) novel experimental approaches
Comment	Review
Doppler-device	Not known
Quantification	Another review of Alexandrov

Ultrasound- and microspheres-enhanced thrombolysis for stroke treatment: state of the art.

Author	(Balucani und Andrei V Alexandrov, 2010)
Content/Summary	A recent microsphere dose-escalation study called TUCSON showed sustained complete recanalization rates of 67% in patients receiving TCD monitoring with a 1.4-mL perflutren-lipid microsphere dose compared with controls receiving rt-PA alone with no increase in hemorrhage rate.
Comment	Review
Doppler-device	Not known
Quantification	A 2-MHz pulsed-wave monitoring can at least double the chance of early complete arterial recanalization at no increase in the risk of symptomatic intracerebral hemorrhage. Gaseous microspheres, initially developed as ultrasound contrast agents, can further increase the effectiveness of rt-PA.

Sonothrombolysis in the management of acute ischemic stroke.

Author	(Marta Rubiera und Andrei V Alexandrov, 2010)
Content/Summary	Operator-independent devices, different MB-related techniques, and other ultrasound parameters for improving and spreading sonothrombolysis are being tested.
Comment	
Doppler-device	Not known
Quantification	Another Review of Alexandrov

Reperfusion after stroke sonothrombolysis with microbubbles may predict intracranial bleeding.

Author	(Dinia u. a., 2009)
Content/Summary	Recanalization rates were higher in the MB compared with the control group at 1, 2, 6, and 12 hours ($p < 0.05$) MB administration was associated with an increased risk of hemorrhagic infarction (HI)1-HI2 (21% vs 12%, $p = 0.026$) and a higher degree of clinical improvement at 24 hours (54.9% vs 31.1%, $p = 0.004$)
Comment	296 patients
Doppler-device	DWL Multi-Dop X4 or Spencer Technologies, Seattle, WA
Quantification	This hypothesis-generating study shows that microbubble administration was associated with early recanalization and a high rate of hemorrhagic transformation but does not seem to increase the risk of symptomatic intracranial hemorrhage. However, definitive conclusions cannot be made based on these data.

Ultrasound-enhanced thrombolysis with tPA-loaded echogenic liposomes.

Author	(Shaw u. a., 2009)
Content/Summary	The fractional clot loss FCL was 31% (95% CI: 26-37%) and 71% (56-86%) for clots exposed to tPA alone or tPA with 120 kHz ultrasound. Similarly, FCL was 48% (31-64%) and 89% (76-100%) for clots exposed to t-ELIP without or with ultrasound.
Comment	In vitro
Doppler-device	120 kHz ultrasound exposures used an unfocused transducer (Sonic Concepts, Inc., Woodburn, WA)
Quantification	The lytic efficacy of tPA containing echogenic liposomes is comparable to that of tPA alone. The addition of 120 kHz ultrasound significantly enhanced lytic treatment efficacy for both tPA and t-ELIP. Liposomes loaded with tPA may be a useful adjunct in lytic treatment with tPA.

Transcranial ultrasound in clinical sonothrombolysis (TUCSON) trial.

Author	(Carlos A Molina u. a., 2009)
Content/Summary	Among 35 patients (Cohort 1 = 12, Cohort 2 = 11, controls = 12) no sICH occurred in Cohort 1 and controls, whereas 3 (27%, 2 fatal) sICHs occurred in Cohort 2 (p = 0.028). Sustained complete recanalization/clinical recovery rates (end of TCD monitoring/3 month) were 67%/75% for Cohort 1, 46%/50% for Cohort 2, and 33%/36% for controls (p = 0.255/0.167). The median time to any recanalization tended to be shorter in Cohort 1 (30 min; interquartile range [IQR], 6) and Cohort 2 (30 min; IQR, 69) compared to controls (60 min; IQR, 5; p = 0.054).
Comment	Stroke patients receiving 0.9mg/kg tissue plasminogen activator (tPA) with pretreatment proximal intracranial occlusions on transcranial Doppler (TCD) were randomized (2:1 ratio) to microS (MRX-801) infusion over 90 minutes (Cohort 1, 1.4ml; Cohort 2, 2.8ml) with continuous TCD insonation, whereas controls received tPA and brief TCD assessments.
Doppler-device	TOC Neurovision, Multigon, Yonkers, NY
Quantification	Perflutren lipid microS can be safely combined with systemic tPA and ultrasound at a dose of 1.4ml. In both dose tiers, sonothrombolysis with microS and tPA shows a trend toward higher early recanalization and clinical recovery rates compared to standard intravenous tPA therapy.

Simulation of intracranial acoustic fields in clinical trials of sonothrombolysis.

Author	(Baron u. a., 2009)
Content/Summary	
Comment	
Doppler-device	Not known
Quantification	Simulating the pressure field of ultrasound protocols for clinical trials of sonothrombolysis may help explain mechanisms of adverse effects. Such simulations could prove useful in the initial design and optimization of future protocols for this promising therapy of ischemic stroke.

Ultrasound enhancement of fibrinolysis.

Author	(Andrei V Alexandrov, 2009)
Content/Summary	In the CLOTBUST trial, 83% of patients achieved any recanalization (46% complete, 27% partial) with tPA+transcranial Doppler vs 50% (17% complete, 33% partial) with tPA alone within 2 hours of treatment (P<0.001) A recent meta-analysis of 6 randomized and 3 nonrandomized clinical studies of sonothrombolysis showed that any diagnostic ultrasound monitoring can at least double the chance of early complete arterial recanalization at no increase in the risk of symptomatic intracerebral hemorrhage Catheter-based ultrasound delivery to arterial thrombi and intraventricular clots is the subject of ongoing clinical trials Transcranial ultrasound delivery in an operator-independent and dose-controlled manner is being tested in a clinical trial.
Comment	Review
Doppler-device	Not known
Quantification	Another review of Alexandrov

Safety and dose-escalation study design of Transcranial Ultrasound in Clinical SONolysis for acute ischemic stroke: the TUCSON Trial.

Author	(Barreto u. a., 2009)
Content/Summary	
Comment	
Doppler-device	Not known
Quantification	TUCSON study design

Residual flow at the site of intracranial occlusion on transcranial Doppler predicts response to intravenous thrombolysis: a multi-center study.

Author	(Saqqur u. a., 2009)
Content/Summary	The pretreatment residual flow at intracranial occlusion predicts the likelihood of complete recanalization, time of recanalization and long-term outcome. No detectable residual flow indicates the least chance to achieve recanalization and recovery with systemic thrombolysis and may support an early decision for combined endovascular rescue.
Comment	Results of CLOTBUST
Doppler-device	Not known
Quantification	Initial TCD findings help to predict outcome.

Microbubbles for thrombolysis of acute ischemic stroke.

Author	(Meairs und Culp, 2009)
Content/Summary	Recent results suggest that ultrasound and microbubbles may be effective in clot lysis of ischemic stroke without additional thrombolytic drugs. Moreover, targeting thrombus with specific immunobubbles may improve the efficacy of sonothrombolysis.
Comment	Review
Doppler-device	Not known
Quantification	Safety remains a major concern in the further development of ultrasound-enhanced thrombolysis and extensive animal work is required to define the most promising methods to translate into human application.

Do bubble characteristics affect recanalization in stroke patients treated with microbubble-enhanced sonothrombolysis?

Author	(Rubiera u. a., 2008)
Content/Summary	MB administration during sonothrombolysis is associated with a high recanalisation (RE) rate. However, RE rates, clinical course and long-term outcome are comparable when administering galactose-based air-filled MB (Levovist) or sulphur hexafluoride-filled MB (Sonovue).
Comment	Ninety-one patients received Levovist (LV) and 47 received Sonovue (SV).
Doppler-device	Not known
Quantification	No difference in using Levovist or Sonovue.

Characterization of ultrasound propagation through ex-vivo human temporal bone

Author	(Ammi u. a., 2008)
Content/Summary	
Comment	to perform intracranial measurements of the acoustic pressure field generated by 0.12, 1.03 and 2.00-MHz ultrasound transducers to identify optimal ultrasound parameters that would maximize penetration and minimize aberration of the beam.
Doppler-device	Not known
Quantification	This work provides needed information on ultrasound beam shapes inside the human skull, which is a necessary first step for the development of an optimal transcranial ultrasound-enhanced thrombolysis device.

Ultrasound-induced thermal elevation in clotted blood and cranial bone.

Author	(Nahirnyak u. a., 2007)
Content/Summary	Blood clots exposed to 0.12-MHz pulsed ultrasound exhibited a small temperature increase (0.25 degrees C) and bone exposed to 1.0-MHz pulsed ultrasound exhibited the highest temperature increase (1.0 degrees C).
Comment	A theoretical model is developed to provide an estimate for the worst-case scenario of the temperature increase in blood clots and on the surface of cranial bone exposed to 0.12- to 3.5-MHz ultrasound. Thermal elevation was also assessed experimentally in human temporal bone, human clots and porcine clots exposed to 0.12 to 3.5-MHz pulsed ultrasound in vitro with a peak-to-peak pressure of 0.25 MPa and 80% duty cycle.
Doppler-device	Not known
Quantification	Results show US induced thermal elevation.

Site of arterial occlusion identified by transcranial Doppler predicts the response to intravenous thrombolysis for stroke.

Author	(Saqqur u. a., 2007)
Content/Summary	Clinical response to thrombolysis is influenced by the site of occlusion. Patients with no detectable residual flow signals as well as those with terminal internal carotid artery occlusions are least likely to respond early or long term.
Comment	
Doppler-device	Not known
Quantification	Initial TCD examination may help to guide treatment options.

Microbubble administration accelerates clot lysis during continuous 2-MHz ultrasound monitoring in stroke patients treated with intravenous tissue plasminogen activator.

Author	(Carlos A Molina u. a., 2006)
Content/Summary	Administration of MBs induces further acceleration of US-enhanced thrombolysis in acute stroke, leading to a more complete recanalization and to a trend toward better short- and long-term outcome.
Comment	111 patients with acute stroke attributable to MCA occlusion treated with intravenous tissue plasminogen activator (tPA). Thirty-eight patients were treated with tPA plus continuous 2-hour TCD monitoring plus 3 doses of 2.5 g (400 mg/mL) of galactose-based MBs given at 2, 20, and 40 minutes after tPA bolus (MB group). These patients were compared with 73 patients who were allocated to receive tPA plus continuous 2-hour TCD ultrasound (US) monitoring (tPA/US group) or tPA plus placebo monitoring (tPA group).
Doppler-device	TCD 100, Spencer Technologies, and DWL Multidop X4
Quantification	First article on microbubble induced sonothrombolysis

Ultrasound-enhanced systemic thrombolysis for acute ischemic stroke. (CLOTBUST)

Author	(Andrei V Alexandrov, Carlos A Molina, u. a., 2004)
Content/Summary	Symptomatic intracerebral hemorrhage occurred in three patients in the target group and in three in the control group. Complete recanalization or dramatic clinical recovery within two hours after the administration of a t-PA bolus occurred in 31 patients in the target group (49 percent), as compared with 19 patients in the control group (30 percent; P=0.03).
Comment	New England Journal! 126 patients were randomly assigned to receive continuous ultrasonography (63 patients) or placebo (63 patients).
Doppler-device	All centers had power-motion Doppler units (PMD 100, Spencer Technologies). The use of other portable transcranial Doppler units (EZ-Dop, Multi-Dop T, DWL; 100 M, Multigon; and Companion III, Nicolet) was also permitted.
Quantification	In patients with acute ischemic stroke, continuous transcranial Doppler augments t-PA-induced arterial recanalization, with a nonsignificant trend toward an increased rate of recovery from stroke, as compared with placebo. First randomized trial. All TCD devices were permitted.

CLOTBUST: design of a randomized trial of ultrasound-enhanced thrombolysis for acute ischemic stroke.

Author	(Andrei V Alexandrov, Wojner, u. a., 2004)
Content/Summary	
Comment	
Doppler-device	Not known
Quantification	Design of CLOTBUST trial

Summary:

In patients with acute ischemic stroke, continuous transcranial Doppler augments t-PA-induced arterial recanalization. CLOTBUST trial was the first randomized study, which showed this augmentation. About 40% of patients suffer from MCA-occlusions and can potentially been considered to be treated with US-lysis, which may double the early rate of recannalization and clinical outcome improvement.

ICH rates were similar while treatment with or without 2 MHz TCD (about 3-4%), but higher with TCCD (about 11%). Low frequency US causes high bleeding rates of about 30-35%.
US contrast agents further improve results of US lysis.

New tPA-loaded microbubbles are under latest research and seem to be a promising improvement. uPA-MBs combined with US can decrease the in vitro dosage of uPA for thrombolysis.

Many of pushlished articles are written by Alexandrov. One may say it may be refreshingly independent to read articles from authors despite of Alexandrov and colleagues!

Experts:

Alexandrov
Holland
Molina

Literature

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