



2014 Neurosonology update

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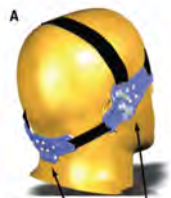
- Carotid stent and microemboli (*Stroke*)
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CLOTBUST-Hands Free

Initial Safety Testing of a Novel Operator-Independent Ultrasound Device in Stroke-Free Volunteers

Stroke 2013;44:1641-46

- To evaluate safety and tolerability of a new ultrasound device in healthy volunteer
- Headframe containing 18 ultrasound transducer
- 2 hour insonation
- Neurological examination and pre-and post MRI to see blood brain barrier damage



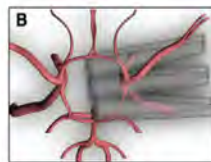
Suboccipital array

각각 6개 transducer

Transtemporal arrays



No neurological dysfunction, no blood brain barrier damage



CLOTBUST-Hands Free

Pilot Safety Study of a Novel Operator-Independent Ultrasound Device in Patients With Acute Ischemic Stroke

Stroke 2013;44:3376-81

- Subject: acute ischemic stroke with proximal intracranial occlusion
- Method: standard dose IV tPA, subsequent CLOTBUST-HF device for 2 hours (2-MHz pulsed wave)
- Primary outcome: symptomatic intracerebral hemorrhage
- Results
 - 20 patients: MCA 14, terminal ICA 3, VA 3
 - No symptomatic intracerebral hemorrhage
 - Recanalization rate: 40% complete, 20% partial
 - 25% good outcome at 3 months

- CLOTBUST-ER trial ongoing
- Phase 3 randomized placebo-controlled trial to evaluate the efficacy and safety of transcranial ultrasound device adjuvant to IV tPA



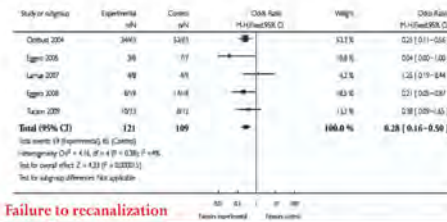
Cochrane Corner

Section Editor: Peter A. Samuels, MA, DM, FRCPE, FMedSci

Stroke 2013;44:e6-7

Sonothrombolysis for Acute Ischemic Stroke

- Significant increase in recanalization rate, with nonsignificant increase of hemorrhagic transformation
- Significant clinical improvement at 3 month follow up



- Insufficient evidence to establish the effectiveness and safety in routine clinical practice
- There is a clear need for a new multicenter randomized trial
- CLOTBUST-ER trial

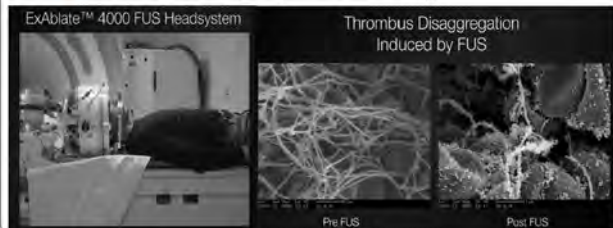
Neuroimaging

MR-Guided Focused Ultrasound for Acute Stroke

A Rabbit Model

Stroke 2013;44:3376-81

- Transcranial focused ultrasound
- Clot lysis within second without tPA
- Need further trial (safety issue and efficacy)



Cerebral Vasomotor Reactivity and Risk of Mortality The Rotterdam Study

Stroke 2014;45:42-7

- Investigate whether cerebral vasomotor reactivity is associated with the risk of mortality, focusing particularly on cardiovascular mortality independent from stroke
- Rotterdam population based cohort study
- TCD study during 1997-1999
 - 1695 person
 - measure vasomotor reactivity
 - average follow up 10 years
- 557 participants died, of whom 181 due to a cardiovascular cause.

Table 2. Vasomotor Reactivity and Risk of All-Cause Mortality

Vasomotor Reactivity*	n/N	Model 1†, HR (95% CI)	Model 2†, HR (95% CI)
Quartile 1	182/423	1.40 (1.10-1.80)	1.30 (1.01-1.67)
Quartile 2	154/424	1.36 (1.06-1.74)	1.33 (1.03-1.71)
Quartile 3	117/424	1.04 (0.79-1.35)	1.07 (0.82-1.40)
Quartile 4	104/424	1 (reference)	1 (reference)
Per SD decrease	557/1695	1.12 (1.03-1.21)	1.10 (1.01-1.19)

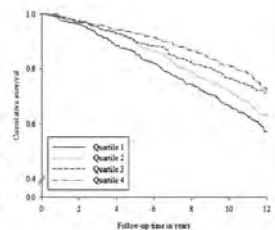


Table 5. Vasomotor Reactivity and Risk of Mortality, After Censoring for Incident Stroke

Vasomotor Reactivity*	n/N	All-Cause Mortality, HR (95% CI)	Cardiovascular Mortality, HR (95% CI)
Quartile 1	150/423	1.49 (1.13-1.96)	1.76 (1.01-3.07)
Quartile 2	128/424	1.39 (1.05-1.83)	2.07 (1.20-3.56)
Quartile 3	103/424	1.13 (0.85-1.51)	1.32 (0.74-2.38)
Quartile 4	84/424	1 (reference)	1 (reference)
Per SD decrease	465/1695	1.12 (1.03-1.22)	1.20 (1.03-1.40)

- Loss of cerebral vasomotor reactivity is associated with an increased risk of mortality, especially cardiovascular mortality, independent of stroke.
- This suggests that impaired cerebral vasomotor reactivity reflects a systemically impaired vascular system.

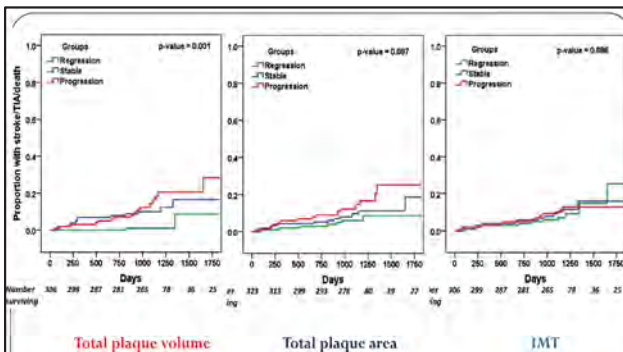
Progression of Carotid Plaque Volume Predicts Cardiovascular Events

Stroke 2013;44:1859-65

- Carotid intima-media thickness (IMT) is used for risk stratification and evaluation of antiatherosclerotic therapy.
- Compare IMT, total plaque area, total plaque volume as predictors of cardiovascular outcomes
- 349 patients performed carotid duplex and follow up (median 3.17yrs) for outcome event. 323 patients performed 1year follow up examination

Results

- Progression of total plaque volume predicted stroke/death/TIA, stroke/death/MI, and stroke/death/TIA/MI
- Progression of total plaque area weakly predicted stroke/death/TIA, but not stroke/death/MI or stroke/death/TIA/MI
- IMT did not predict any event



For assessment of response to antiatherosclerotic therapy, measurement of total plaque volume is superior to both IMT and total plaque area

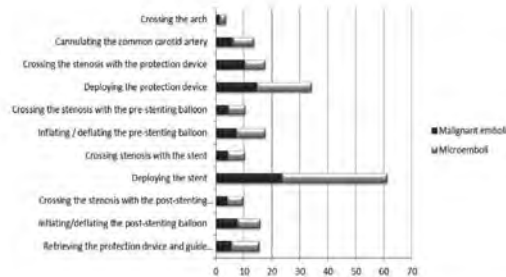
Malignant Emboli on Transcranial Doppler During Carotid Stenting Predict Postprocedure Diffusion-Weighted Imaging Lesions

Stroke 2013;44:1317-22

- Evaluation of CAS safety by correlating the findings of procedural transcranial Doppler with post-stent diffusion-weighted imaging lesions.
- 11 CAS steps
- Microemboli / malignant macroembolus
- Post-stent diffusion-weighted MRI

Results

- median embolic signal count : 212.5
- Stent deployment phase : highest embolic signal count
- 80% had new diffusion lesion
- 6.7% had new or worsening clinical deficits post-CAS
- malignant emboli had a significant association with DWI lesions count.



Review of Transcranial Doppler Ultrasound to Detect Microemboli during Orthopedic Surgery

AJNR 2013

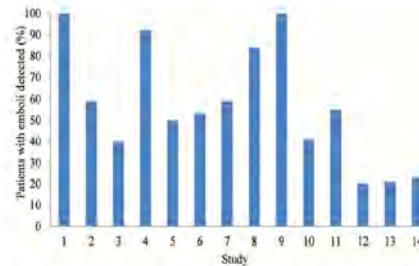
- In orthopedic surgery, TCD is introduced to detect fat embolism in the venous system after long bone fracture and subsequently to detect microemboli in the middle cerebral artery.

Table 1: Criteria for identification of high-intensity transient signals

Criteria
1) Doppler microembolic signal is transient, usually lasting <300 ms
2) The amplitude is usually at least 3 dB higher than the background blood flow
3) A signal is unidirectional within the Doppler velocity spectrum
4) Microembolic signal is accompanied by an audible output

Table 2: Recommended parameters to be reported for transcranial Doppler ultrasound

Parameters
1) Ultrasound device
2) Transducer type
3) Insonated artery
4) Insonation depth
5) Algorithms for signal-intensity measurement
6) Scale settings
7) Detection threshold
8) Axial extension of sample volume
9) Fast Fourier transformation size (no. of points used)
10) Fast Fourier transformation length (time)
11) Fast Fourier transformation overlap
12) Transmitted ultrasound frequency
13) High-pass filter settings
14) Recording time



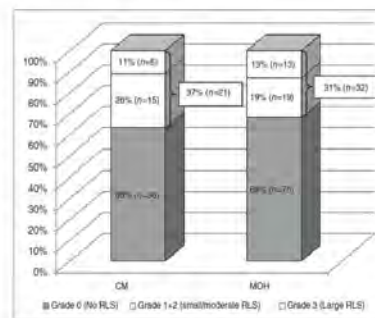
- Emboli were detected in all studies, occurring in 20%–100% of patients.
- No study identified an association between postoperative cognitive function and embolic count
- Higher counts were found in the presence of arteriovenous shunts.

Prevalence of right-to-left shunts on transcranial Doppler in chronic migraine and medication-overuse headache

Cephalalgia 2014

- Right-to-left shunt may be highly prevalent in chronic migraine indicating patent foramen ovale might be an aggravating and chronifying factor of migraine.
- Determine the prevalence and grade of RLS in patients suffering from chronic migraine and medication overuse headache.
- Air-contrast transcranial Doppler was conducted in 159 patients with CM (n=57) or MOH (n=102)

- Prevalence of RLS in CM was 37% (11% large shunts) and in MOH patients 31% (13% large shunts). There was no difference between the two groups (p=0.49).



Clinical implications

- The prevalence of right-to-left shunts (RLS) is not different between chronic migraine and medication overuse headache and is within the upper range of those reported in the general population.
- PFO is unlikely to have a significant causal role in chronic migraine and medication overuse headache

Transcranial Doppler Velocities in a Large, Healthy Population

J Neuroimaging 2013: 466-72

- To define normal TCD values in a healthy population, 364 healthy subjects, ages 18-80 years have a complete, nonimaging TCD examination

Factor		Average \pm SD	Percentage (Range)
Age		44.7 \pm 6.5	(18-80)
Sex	Men	101	28.5
	Women	253	71.5
Race	Caucasian	297	83.9
	Non-Caucasian	57	16.1
BMI		26.4 \pm 5.8	(17.2-57.2)
Systolic BP		128.4 \pm 14	(96-170)
Diastolic BP		73.2 \pm 9.7	(40-108)
MAP		91.6 \pm 10.1	(63.7-126.0)
Handedness	Right	318	89.8
	Left	36	10.2

Table 2. Mean Flow Velocity and Yield by Arterial Segment

Segment	Flow Velocity						Yield (%)
	Men		Women		Combined		
	Mean	SD	Mean	SD	Mean	SD	
A1	47.1	9.8	51.9	9.8	50.5	10.0	95.3
BA-distal	38.1	10.5	45.1	10.9	43.1	11.2	99.1
BA-mid	35.8	9.1	43.7	10.7	41.4	10.9	99.7
BA-proximal	34.5	8.6	41.7	10.3	39.7	10.4	99.4
C1	35.4	8.2	37.2	9.7	36.5	9.4	94.9
C2	20.8	7.1	23.1	8.9	22.5	8.6	88.2
C4	25.0	6.2	28.2	7.5	27.3	7.3	98.7
MCA-distal	55.7	12.2	62.5	12.1	60.6	12.5	96.7
MCA-proximal	56.4	12.1	61.6	11.8	60.1	12.1	96.6
OA	14.9	3.6	14.6	4.6	14.7	4.3	92.5
P1	27.5	5.2	30.6	6.1	29.7	6.1	94.5
P2	25.7	5.1	28.1	5.5	27.4	5.5	94.3
VA	29.3	7.8	36.2	9.2	34.3	9.4	99.7

- mean blood flow velocities were highest in the MCA and lowest in the PCA
- mean blood flow velocities were higher among women than men
- mean blood flow velocities decreased with advancing age, but this was specific to Caucasian subjects.

Table 3. Mean Flow Velocities by Age (Decade) in Key Vessel Segments: Proximal Middle Cerebral Artery

Age	Combined	Men	Women	Caucasian	Non-Caucasian
	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)	Mean (SD)
<30	66.6(14.4)	62.6(13.6)	70.1(14.3)	67.5(14.9)	62.6(11.4)
30-39	64.6(8.8)	61.2(8.0)	66.2(8.8)	65.2(8.7)	63.2(9.1)
40-49	60.0(11.2)	48.5(7.3)	62.4(10.4)	60.6(11.8)	57.3(7.4)
50-59	56.6(9.4)	52.3(9.4)	57.5(9.2)	56.0(8.4)	63.7(17.4)
60-69	51.2(10.0)	46.7(7.3)	52.8(10.4)	51.3(10.2)	49.6(-)
70-80	49.6(10.5)	47.6(11.1)	50.8(10.5)	49.6(10.5)	NA
P value	<.0001	<.0001	<.0001	<.0001	.3861

Table 9. Pulsatility Index by Age (Decade) in Key Arterial Segments: Proximal Middle Cerebral Artery

Age	Combined Mean (SD)	Men Mean (SD)	Women Mean (SD)	Caucasian Mean (SD)	Non-Caucasian Mean (SD)
<30	.85 (0.13)	.89 (0.13)	.82 (0.13)	.85 (0.13)	.88 (0.13)
30-39	.80 (0.15)	.82 (0.13)	.79 (0.16)	.80 (0.13)	.80 (0.20)
40-49	.76 (0.10)	.80 (0.13)	.75 (0.09)	.77 (0.10)	.71 (0.10)
50-59	.80 (0.10)	.80 (0.08)	.80 (0.10)	.79 (0.09)	.83 (0.21)
60-69	.85 (0.10)	.79 (0.09)	.87 (0.09)	.85 (0.10)	.81 (-)
70-80	.95 (0.17)	.92 (0.23)	.97 (0.13)	.95 (0.17)	NA
P value	<.0001	.0316	<.0001	<.0001	.1644

PI increased with age in all segments for women, but only in some segments for men, and this finding was also specific to Caucasian subjects.

Non imaging based study

Mainly Caucasian - cannot represent non-Caucasian

Needs our own data based on imaging study