



# Clinical Applications Of TCD



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## DISCLOSURES NONE



## Imaging Techniques in CAS 24/7



## Why TCD ?



## Stroke box on ER of CAS







## Special Care Unit, CAS













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## TCD is a useful tool

- Stroke (ischemic)
- Brain trauma
- Brain death
- Subarachnoidal hemorrhage
- Other





## TCD and ischemic stroke





- Responds less to EV rt\_PA
- Worse prognosis
- Frequent worsening in the following hours





## Advantages of TCD



- Low cost
- Does not irradiate
- Bedside test
- ✓ Its performed by the clinician
- Can be repeted as necessary
- Allows monitoring
- Good correlation with DSA y CTA

Site of occlusión	Sensibility	Specificity	VPP	VPN
MCA	93	98	93	98
Distal ICA	81	96	81	96
Proximal ICA	94	97	94	97
Basilar oclussion	60	96	60	96
Vertebral oclussion	55	96	71	92







#### Sensitivity, specificity and LHR of TCD compared with CTA, Clínica Alemana de Santiago

Artery	PLR (95% CI)	NLR (95% CI)	Se (95% CI)	Sp (95% Cl)	Diagnostic Accuracy
Any specific artery	13.7 (5.2–35.9)	0.19 (0.09-0.4)	81.8 (68.7–95.0)	94 (88.3–99.7)	90
MCA	24.6 (8.1–74.7)	0.045 (0.006-0.30)	95.6 (87.3–100)	96.2 (91.7–100)	96
Anterior circulation	18.5 (7.1–48)	0 (0–NA)	100 (100–100)	94.5 (89.4–99.7)	96
Posterior circulation	>1000 (NA–infinity)	0.42 (0.18–1)	57.1 (20.4–93.8)	100 (100–100)	97
Central occlusion	70.3 (10–494.8)	0.08 (0.02-0.3)	91.3 (79.7–100)	98.2 (96.1–100)	97
Any overall artery	15.2 (5.8–38.6)	0.09 (0.03-0.28)	90.9 (81.1–100)	94 (88.3–99.7)	93

Table 2. PLRs, NLRs, Sensitivities, Specificities, and Diagnostic Accuracy for Each Artery With Corresponding 95% Cls

NA indicates not applicable.

#### LHR: Likelihood ratio

Brunser AM.Stroke 2009



#### LMCA occlusion

Marrie Marrie



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# Recanalization with t-PA related to location of obstruction by TCD



Complete recanalization

- MCA M1: 30%
- MCA M2: 44%
- Tandem:27%
- Terminal ICA 6%
- Basilar:33%

Saqqur.Stroke.2007:38;948-954.

## TIBI scale related to Spencer curve





## Initial TIBI scale on TCD and reperfusion with t-PA

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TIBI 2





#### Demchuck.Stroke2001;32:89-93.

35% of complete reperfusion at 2 hours



52% of complete reperfusion at 2 hours



## Científico Docente TCD advantages

- 79 patients
- Evaluated in the first 24 hours
  Brain TC
  - Brain TC
  - Brain CTA
  - DWI
  - TCD blind

Additional information 35% (95% IC 25,7-46,4)

**Change in medical managament 9%**(95% CI 4.3–17.1)

				$D_{-}^{1}$
Brunser	ΑΜ	Cerer	provasc	DS 2010

Table 2. Additional information given by TCD on 28 patients

15 (18.9)
6 (7.6)
3 (3.8)
n = 2
n = 1
2 (2.5)
1 (1.3)
5 (6.3)
2 (2.5)

Data shown as number of patients with percent in parentheses.

## TCD and CTA do complement each other





## Additional Information

# • Ischemic stroke NIHSS 3, frequent fluctuation of symptoms.







# Changes in management caused by TCD in 79 patients with AIS



#### 8.8%, 95% CI 4.3–17.1

	Case	Sex age, years	NIHSS	ASIP findings	TCD findings	Change in management	mRS 3 months after stroke
$\rightarrow$	11	F 18	9	left stroke MCA occlusion	left MCA occlusion, with no recanalization during i.v. rt-PA	DSA angiography and intra-arterial thrombolysis were performed, with recanalization of the occluded artery	0
$\rightarrow$	12	F 84	14	right stroke MCA occlusion	right MCA occlusion that recanalized during diagnostic TCD; NIHSS score decreased from 15 to 4	planned DSA and intra-arterial thrombolysis were not performed	1
	33	M 66	13	right stroke MCA M2 occlusion	right M2 occlusion, with important collateral flow from ipsilateral ACA and PCA	aggressive neurocritical care was started	1
$\Rightarrow$	40	M 66	19	left stroke MCA occlusion	left MCA occlusion, with no recanalization during i.v. rt-PA	DSA and intra-arterial thrombolysis were performed, with recanalization of the artery	0
$\rightarrow$	51	F 69	15	left MCA stroke no occlusion on circle of Willis	post-stenotic left MCA flow signal and inverted ophthalmic artery suggest proximal left carotid artery disease	DSA was performed and ICA stenosis was found; intensive secondary prevention was begun	1
$\rightarrow$	67	M 83	11	left stroke, CTA with important movement artifacts, possible left terminal M1 stenosis	normal TCD	planned diagnostic DSA was not performed	1
$\rightarrow$	75	F 66	10	right MCA stroke no occlusion on circle of Willis	post-stenotic right MCA flow signal and inverted ophthalmic artery suggest proximal right carotid artery disease	DSA was performed and ICA stenosis was found; intensive secondary prevention was begun	0

Brunser. Cerebrovasc Dis 2010;30:260–266

#### Rescue of patients in whom rt-PA failed





## What about the hot spot: time < 4.5 hours



- 86 patients
- Evaluated in the first 4.5 hours
  - Brain TC
  - CTA brain and cervical
  - DWI
  - TCD not blinde

## Additional information 56.9.4% (95 CI 46.4 -66.9)



Change in medical management 17.4%(95 CI. 9.4-25.5)

Brunser AM, Submitted J. Neuroimaging



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Change in management depends on vessel oclusion on CTA p =0.000

#### NIHSS 19

Brunser. Submitted J. Neuroimaging





#### TCD increase rt-PA recanalization





Change in the structure of fibrin

Fissures in the clot through which plasma seeps

Increased contact between the clot and t-PA



#### Científico

Penetration of t-PA into a thrombus during thrombolysis



With out Ultrasound Hichcock Stroke. 2010;41[suppl 1]:S50-S53 Departamento Científico Docente Combined Lysis Of Thrombus in Brain ischemia using 2 MHz transcranial Ultrasound and Systemic TPA



## CLOTBUST

ORIGINAL ARTICLE

#### Ultrasound-Enhanced Systemic Thrombolysis for Acute Ischemic Stroke

Andrei V. Alexandrov, M.D., Carlos A. Molina, M.D., James C. Grotta, M.D., Zsolt Garami, M.D., Shiela R. Ford, R.N., Jose Alvarez-Sabin, M.D., Joan Montaner, M.D., Maher Saqqur, M.D., Andrew M. Demchuk, M.D., Lemuel A. Moyé, M.D., Ph.D., Michael D. Hill, M.D., and Anne W. Wojner, Ph.D., for the CLOTBUST Investigators\*

### Primary End-Point: Complete Recanalization SR total NIHSS < 3 OR Recovery By Strates Activities



**Combined End-point during 2 hrs** 

### Sustained Complete Recanalization: TCD TIBI 5 Flow at 30 min Intervals





Fisher's exact test

## **CLOTBUST: Any Early Recanalization on TCD**



**p < 0.001** 

3x2 Chi-Square



## TCD increases the thrombolytic power of rt-PA



Alexandrov. N Engl J Med. 2004

#### Sonothrombolysis CAS compared to CLOTBUST



	CLOTBUST control (rt-PA)	CLOTBUST treatment (ST+rt-PA)	Clínica Alemana Santiago (ST+rt-PA)
Patients	63 (49)	63 (53)	61
Age	70 ±13	67 ±12	66±17,6
NIHSS	17	16	14
Time to bolus	130	150	127
MCA occlusion	100%	100%	88,5%
Complete Recanalización TIBI 4-5	17,6%	46%	44,3%
mRS 0-2 at 3 months	36,7 % (IC: 95%; 0,25- 0,51)	50,9% (IC: 95%; 0,38 - 0,64)	60,6% (IC:95%; 48,1-72)
sHIC	4,8% (IC:95%; 1,1-13,6)	4,8% (IC:95%; 1,1-13,6)	9,8% (IC:95%; 4,3-20,2)

#### $\mathbf{D}$ $\mathbf{D}$ $1 \mathbf{O} \mathbf{I} \cdot \mathbf{I}$ $\mathbf{O} \mathbf{O} \mathbf{I} \mathbf{A} \mathbf{I} \mathbf{A} \mathbf{O} \mathbf{I} \mathbf{O} \mathbf{A} \mathbf{A}$

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## Sono-thrombolysis meta-analysis

#### Recanalization

#### OR 2.99 CI 95 (1.70-5.25)

	Sonothrombolysis 4	F ⊓tPA	rtPA ak	one		Od ds Ratio	Odds	Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixe	od, 95% Cl
1.4.1 Sonothrombolys	IS TOD							
Alexandrov AV 2004	24	63	8	63	33.7%	4.23 [1.72, 10.40]		
Molina 2006 Subtotal (95% CI)	36	75 138	8	36 99	38.2% 71.9%	3.23 [1.30, 8.00] 3.70 [1.95, 7.00]		-
Total events	60		16					1000000
Heterogeneity: Chi <sup>2</sup> = 0	17, df = 1 (P = 0.68); I	<sup>2</sup> =0%						
Test for overall effect: 2	z = 4.02 (P < 0.0001)							
1.4.2 Sonothrombolys	nis TCCD 3	11	3	14	13.0%	1 38 10 22 8 67		•
Engers 2008	ő	7	0	5	13.070	Not estimable		
Larrue 2007 Subtotal (95% CI)	4	8 26	5	10 29	15.1% 28.1%	1.00 [0.16, 6.42]		
Total events	7		8					
Heterogeneity: Chi <sup>2</sup> = 0 Test for overall effect 2	1.06, df = 1 (P = 0.81); l Z = 0.24 (P = 0.81)	²=0%						
Total (95% CI)		164		128	100.0%	2.99 [1.70, 5.25]		$\diamond$
Total events	67		24					
Heterogeneity: Chi <sup>2</sup> = 2 Test for overall effect 2	2.62, df = 3 (P = 0.45); I Z = 3.81 (P = 0.0001)	²=0%					0.01 0.1 Favours rtPA alone	1 10 100 Favours Sonothrombolysis

Tsivgoulis. Stroke.2010;41:280=4



## Sono-thrombolysis meta-analysis

#### RISK of ICH : OR 1.26, 95 CI (0.44-3.6

	Sonothrombolysis + rtPA		rtPA ale	one		Odds Ratio	Odds Ratio
Study or Subgroup	Events	Tota	Events	Tota	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.2.1 Sonothromboly	sis TCD						
Alexandrov AV 2004	3	63	3	63	45.3%	1.00 [0.19, 5.15]	<b>+</b>
Molina 2006	2	75	2	36	41.7%	0.47 [0.06, 3.45]	
Subtotal (95% CI)		138		99	87.1%	0.74 [0.21, 2.64]	
Total events	5		5				
Heterogeneity: Chi2 =	0.34, df = 1 (P = 0.56); l	<sup>2</sup> =0%					
Test for overall effect:	Z = 0.46 (P = 0.65)						
1.2.2 Sonothromboly	sis TCCD						
Eggers 2003	2	11	0	14	5.6%	7.63 [0.33, 177.14]	
Eggers 2008	1	7	0	5	7.4%	2.54 [0.09, 75.76]	
Larrue 2007	0	9	0	11		Not estimable	
Subtotal (95% CI)		27		30	12.9%	4.73 [0.49, 45.89]	
Total events	3		0				
Heterogeneity: Chi <sup>2</sup> =	0.22, df = 1 (P = 0.64); l	²=0%					
Test for overall effect:	Z = 1.34 (P = 0.18)						
Total (95% CI)		165		129	100.0%	1.26 [0.44, 3.60]	
Total events	8		5				
Heterogeneity: Chi <sup>2</sup> = 1	2.45, df = 3 (P = 0.48); l	²=0%					
Test for overall effect:	Z = 0.43 (P = 0.67)						Favours tPA alone Favours Sonothromholysis

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## Sonothrombolysis-Metaanalysis mRS 0-1 at day 90

	Sonothrombolysis	+ rtPA	rtPA ale	one		Odds Ratio	Odids Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Fixed, 95% Cl	M-H, Fixed, 95% Cl
1.6.1 Sonothromboly	sis TCD						
Alexandrov AV 2004	22	53	14	49	51.3%	1.77 [0.78, 4.05]	+
Molina 2006	30	75	9	36	44.0%	2.00 [0.83, 4.84]	+
Subtotal (95% CI)		128		85	95,3%	1.88 [1.03, 3.43]	•
Total events	52		23				
Heterogeneity: Chi <sup>2</sup> = 1	0.04, df = 1 (P = 0.85);	1ª = 0%					
Test for overall effect.	Z = 2.05 (P = 0.04)						
1.6.2 Sonothromboly	sis TCCD						
Eggers 2003	3	11	0	14	1.9%	11.94 [0.55, 260.28]	
Eggers 2008	1	7	0	5	2.8%	2 54 [0.09, 75.76]	
Subtotal (95% CI)		18		19	4.7%	6.34 [0.69, 58.01]	
Total events	4		0				
Heterogeneity: Chiz = I	0.44, df = 1 (P = 0.51);	1#= 0%					
Test for overall effect:	Z = 1.63 (P = 0.10)						
Total (95% CI)		146		104	100.0%	2.09 [1.17, 3.71]	
Total events	56		23				
Heterogeneity: Chi2 = 1	1.40, df = 3 (P = 0.71);	= 0%					
Test for overall effect:	Z = 2.50 (P = 0.01)						Favours ntPA alone Favours Sonothrombolysi

OR 1.88, 95% CI (1.03-3.43)

Tsivgoulis. Stroke.2010;41:280-4

Donartamont



## Rescue of endovenous t-PA failure







Affected MCA <0.6 Contralateral MCA

#### Saqqur.Stroke 2005;36:865-868





Detection in angioocclusion Sensitivity: 94% (63-99) Specificity 100% (lower 54)

#### Departamento Científico Docente Reocclusion during EV t\_PA NIHSS 10 NIHSS 19



Min 41

Min 47

Min 49

TCD and endovascular theraphy Accuracy of ultrasound for recanalization





Brain haemorrage risk increases with contrast injection

Accuracy of TCD for recanalization Sen 88% Spe 89% PPV: 81% Tsivgoulis. Stroke.2019:143:943460





## TCD and other uses in stroke

## Detection of microembolic signs (MES)





• Higher risk of AIS in patients with CAD.

Srinivasan J. Stroke 1996

• Increase risk of AIS.

Iguchi Y.JNNP 2008

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Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology\*

#### TCD

E.

Diagnosis of PFO Sensitivity 70-100%, Specificity >95% Superior to Trastoraxic Ecocardiogram



# Patient with a cryptogenic AIS and a PFO

nâ.



## TCD allows follow up of changes in flow



#### 43 years, male patient R carotid dissection



#### 36 hours of aggressive treatment





# TCD and brain death / intracranial pressure

#### Consensus for the diagnosis of intracranea Provincente Lemana. and circulatory arrest using TCD



#### Journal of the Neurological Sciences 159 (1998) 145–150

## TCD and intracranial pressure



#### MCA velocity=35cm/seg

nâ.



#### Low velocities

PI > 1.2



### Monitoring head trauma with TCD

Low velocities:
 (<35 cm/seg), High PI (>1.2) first
 Early ICH
 OR 3.2 for bad prognosis
 72 hrs

Acta Neurochir (Wien). 2002;144(11):1141.

• Vasospasm:

ACM (>120 cm/seg, Lind > 3)

J Neurosurg 1992;77:575-3

• Hyperhemia:

•Associated with traumatic SAH, 27-40% severe head trauma, risk of stroke and bad prognosis.

ACM (>120 cm/seg ACM, Lin < 3) •Risk of brain edema.

J Neurosurg. 2003;98(4):793-9.

Lost of autoregulation: (static o dynamic)

• PPC dependence, Mortality of 47% vs 11%

Acta Neurochir Suppl. 2002;81:117-9.





PICO 176 MEDIA 132 DIAST 94 P.I. 0,62 A% 0

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# Accuracy of TCD in the diagnosis of brain dead



- Sensitivity: 100%
- Specificity: 98%
- PPV: 96.1
- NPV: 100



## In comparison with EEG







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#### Its not afected by drugs

## Patient 33 years, Glasgow 3, intubated and sedated





¿What to do?



FREEZE Export of screen image is allowed.





## TCD and brain death

#### 75 patients in coma

Pretest posibility: 40%

- P LHR: 45
- N LHR: 0



Brunser. JMC 2015:23; 29-33.



## Were are the false negatives?

Patients with:•Ventricular drains

#### •Skull defects

Infratentorial lesions



#### Brunser. JMC 2015;23: 29-33. Thompson. Crit Care 2014;3:534-8





## TCD and subarachnoidal hemorrhage





# Acurracy of ICD and angiography for symptomatic vasospasm in anterior circulation .

<u>TCD</u>

Sensitivity: 73%

<u>Angiography</u>

Sensitivity: 80%

Suarez.Critical Care Medicine.2002;30:1348-1355.

Acurracy of TCD and angiography for symptomatic VSP in anterior circulation





Sensitivity: 73%

<u>Angiography</u>

Sensitivity: 80%

Suarez.Critical Care Medicine.2002;30:1348-1355.

## Diagnosis of vasospasm by TCD

Vasoespasm	ACM/ICA	Velocity
Mild	3-6	100-140 cm/seg
<u>Moderate</u>	3-6	140-200 cm/seg
<u>Severe</u>	> 6	> 200 cm/seg

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# TCD velocities increase 24-48 horas before clinical deterioration.



GATIFERA

Wardlaw. J Neurosurg.1998;88:272-276

#### Departamento Científico Docente Asymptomatic patient on his day 7 of SAH





Lindengard: 7.8



#### TCD allows to control therapies in SAH partamento



















### TCD allows to control therapies in SAH

#### Day 7 , patient with decrease of level of concious





#### **Treatment:** external drain











### TCD in SUC of Clínica Alemana



#### Experience 2005-2008

Evaluated:

97 pacients /241 examinations

#### Diagnosis:

- 26 ischemic strokes
- 21 SHA
- 11 head injury
- 9 ICH
- 5 circulatory arrest
- 24 other







Questions to the intensivist:

1- Did TCD provide you with usefull information?

2-Are you going to change your treatmen?

3-How?







### TCD gives useful information

## 93/97 patients (96%)





#### **Technical limitations**



#### 10% Patients with suboptimal windows

Table 4. Regression analysis for a non-ideal temporal window.\*

Variable	OR† I.C. 95.0%
Mechanical ventilation	1.4 (0.73-2.822)
Sex	2.3 (1.51-3.45)
Age ≥ 80	N.A. ‡
Age 60-79	1.62 (1.04-2.54)
Age <60	13.87 (7.80-24.64)

\*The dependent variable was a non-ideal window. †Odds ratio; ‡Not applicable

Brunser. San Diego.2002 (Texas University) Brunser. Cape Town South Africa 2004 Brunser A. *Brain and Behavier*