Ecografia cerebrale: l'accuratezza diagnostica

Lo studio NOBIS

Dr Patrizio Prati

Neurologia

CIDIMU Torino
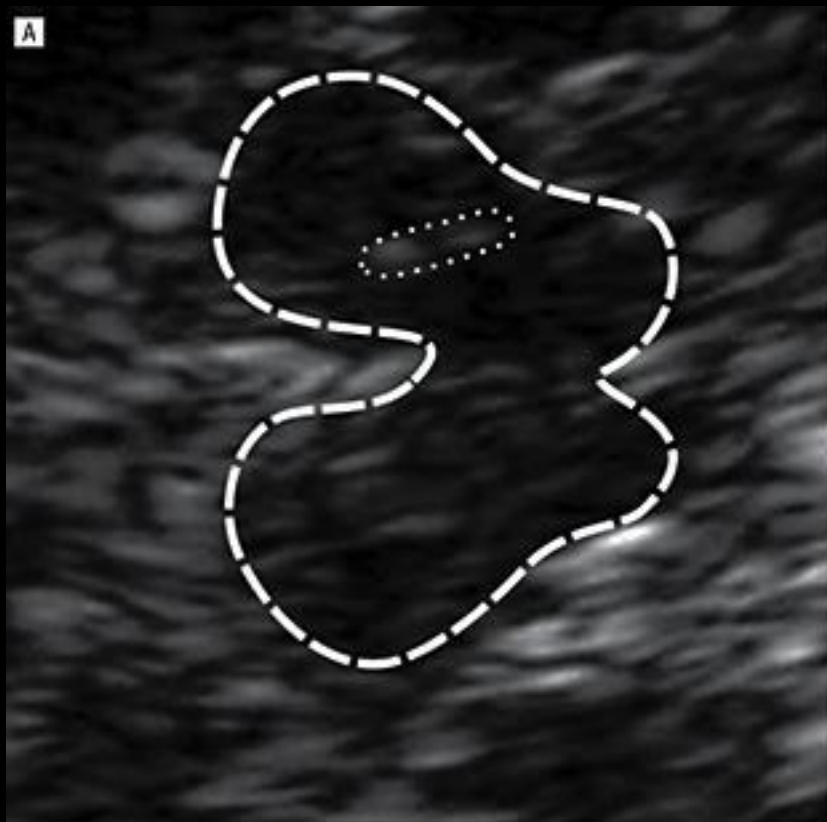
Normal

Parkinson D.

....
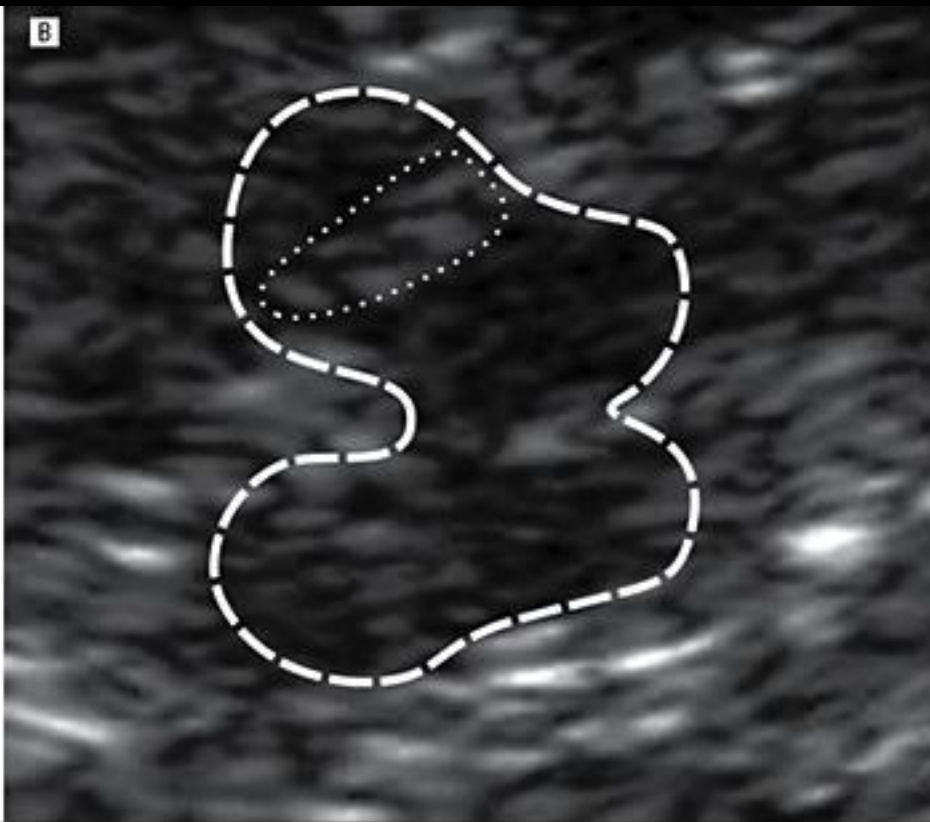
Transcranial Insonation

Ralf W. Baumgartner

Department of Neurology, University Hospital of Zürich, Zürich, Switzerland

How to Measure Substantia Nigra Hyperechogenicity in Parkinson Disease

Detailed Guide With Video

Uwe Walter, MD

EFNS/MDS-ES recommendations for the diagnosis of Parkinson's disease

A. Berardelli[a]*, G. K. Wenning[b], A. Antonini[c], D. Berg[d], B. R. Bloem[e], V. Bonifati[f], D. Brooks[g], D. J. Burn[h], C. Colosimo[i], A. Fanciulli[b], J. Ferreira[j], T. Gasser[d], F. Grandas[k], P. Kanovsky[l], V. Kostic[m], J. Kulisevsky[n], W. Oertel[o], W. Poewe[b], J.-P. Reese[p], M. Relja[q], E. Ruzicka[r], A. Schrag[s], K. Seppi[b], P. Taba[t] and M. Vidailhet[u]

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Transcranial sonography Usefulness

- Routine diagnosis in movement disorders:

  I Differential diagnosis of PD from APS and secondary parkinsonian syndromes

  II Early diagnosis of PD

  III Detection of subjects at risk for PD

- TCS should be used in conjunction with other screening tests.

(EFNS Guidelines, Eur J Neurol 2013)

SCIENTIFIC REP⚙RTS

Diagnostic Accuracy of Transcranial Sonography of the Substantia Nigra in Parkinson's disease: A Systematic Review and Meta-analysis

Dun-Hui Li*, Ya-Chao He*, Jun Liu & Sheng-Di Chen

A large number of articles have reported substantia nigra hyperechogenicity in Parkinson's disease (PD) and have assessed the diagnostic accuracy of transcranial sonography (TCS); however, the conclusions are discrepant. Consequently, this systematic review and meta-analysis aims to consolidate the available observational studies and provide a comprehensive evaluation of the clinical utility of TCS in PD. Totally, 31 studies containing 4,386 participants from 13 countries were included. A random effects model was utilized to pool the effect sizes. Meta-regression and sensitivity analysis were performed to explore potential heterogeneity. Overall diagnostic accuracy of TCS in differentiating PD from normal controls was quite high, with a pooled sensitivity of 0.83 (95% CI: 0.81–0.85) and a pooled specificity of 0.87 (95% CI: 0.85–0.88). The positive likelihood ratio, the negative likelihood ratio and diagnostic odds ratio were calculated 6.94 (95% CI: 5.09–9.48), 0.19 (95% CI: 0.16–0.23), and 42.89 (95% CI: 30.03–61.25) respectively. Our systematic review of the literature and meta-analysis suggest that TCS has high diagnostic accuracy in the diagnosis of PD when compared to healthy control.

Reproducibility and diagnostic accuracy of substantia nigra sonography for the diagnosis of Parkinson's disease

Simone van de Loo,[1] Uwe Walter,[2] Stefanie Behnke,[3] Johann Hagenah,[4] Matthias Lorenz,[1] Matthias Sitzer,[1] Rüdiger Hilker,[1] Daniela Berg[5]

SN (mean ±SD) by patient condition

variable		cases (N=22)	controls (N=10)	P (t-test)
SN+ ipsilateral	mean±SD	0.26±0.05	0.19±0.08	= 0.01
SN+ contralateral	mean±SD	0.27±0.05	0.19±0.06	= 0.002

Intra-inter observer reliability of SN[+]

	SN[+] planimetry ICC	
	Ipsilateral	Controlateral
Intra-observer ICC	0.97 (0.99)	0.93 (0.93)
Inter-obsever ICC	0.84 (0.86)	0.89 (087)

ROC curves (AUC)

ROC curves (AUC)

AUC: 0.83
Cut-off: 0.24 cm^2
Sensitivity: 0.88
Specificity: 0.62

CrossMark
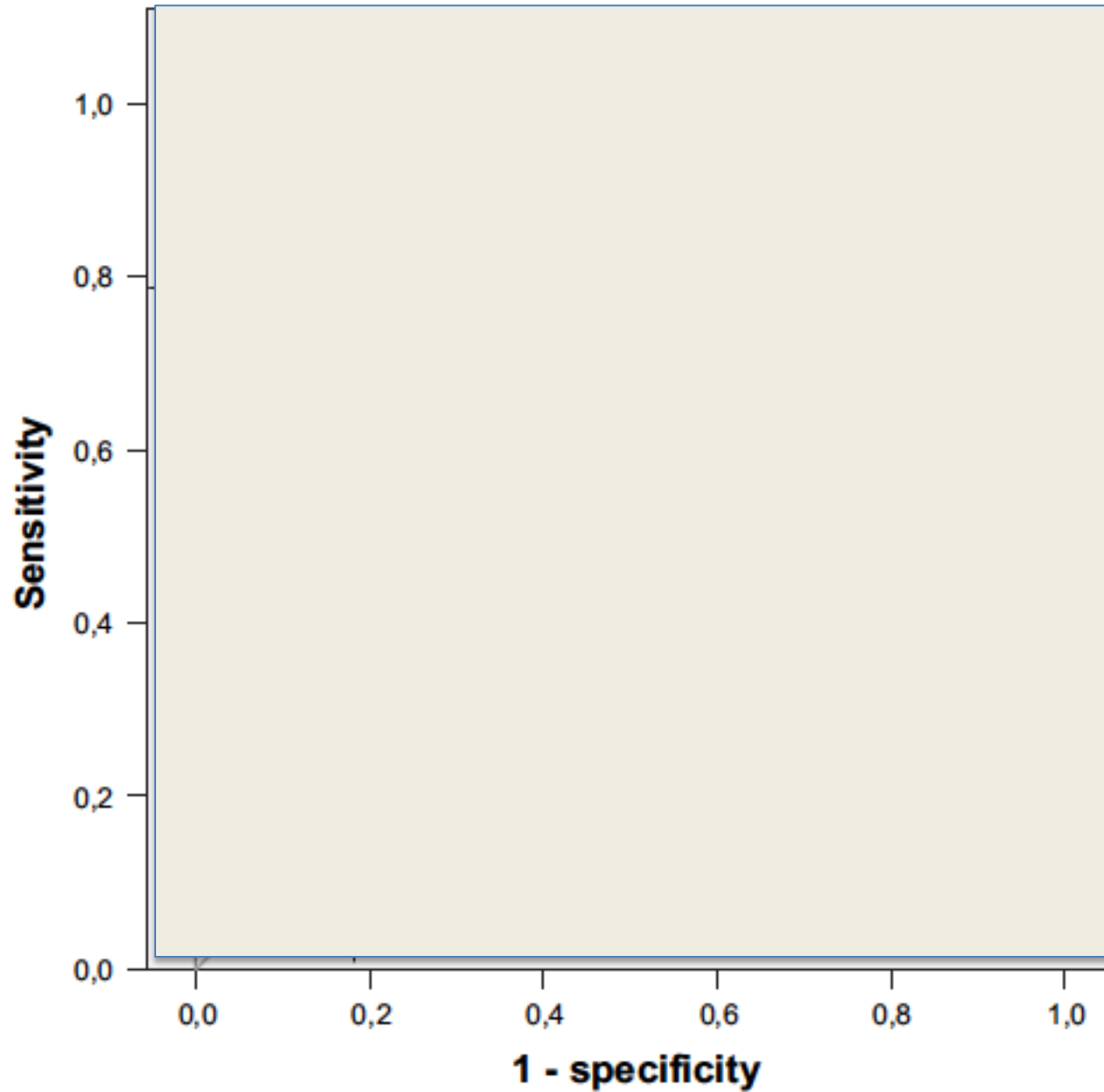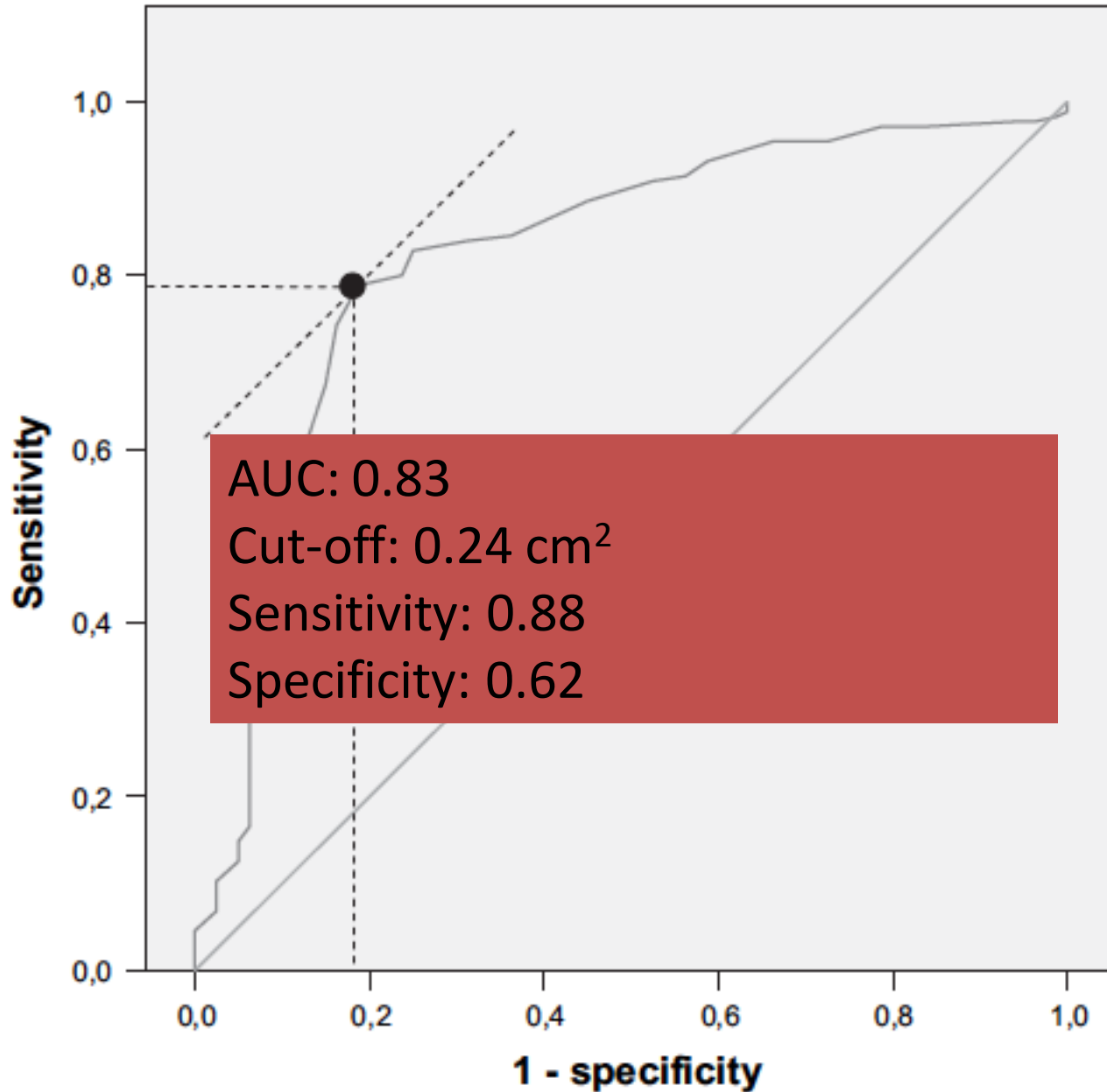
The measuring of substantia nigra hyperechogenicity in an Italian cohort of Parkinson disease patients: a case/control study (NOBIS Study)

Patrizio Prati[1] · A. Bignamini[4] · L. Coppo[2] · A. Naldi[2] · C. Comi[2] ·
R. Cantello[2] · G. Gusmaroli[3] · U. Walter[5]

Novara Biella Study (NOBIS Study)

Design:

    Cross sectional examiner blinded

Work-up

    Clinical

    Diagnostic

 Objectives

    Accuracy and reproducibility of TCS SN$^+$ measurements

Patients

Local Ethic Committee

Movement Disorder Outpatient Clinics of the University Department of Novara Hospital

Biella Hospital Neurology Department

Full medical history

Thorough general medical and neurological examination,

Family and personal history,

Motor symptoms (including the period of onset of symptoms and the type of the same),

Treatment,

Assessment scales of clinical severity and the illness duration.

Subjects

54 Subjects (25 cases and 29 controls)

Patients (6 F 19 M). Mean age (64.9 ± 9.6 y)

Controls (6 F 23 M). Mean age (62.5 ± 10.2 y)

Two expert neurosonologist (PP LC) blinded to the clinical condition

(Prati et al. J Neural Transm 2017)

Patients (Diagnosis)

- The CT or cerebral RMI
- DAT Scan
- Clinical diagnostic criteria UK PARKINSON'S DISEASE SOCIETY BRAIN BANK
- Severity (UPDRS)
- Stages (Hoehn & Yahr)
- The clinically dominant side in case of clinical asymmetry, or otherwise the body side of the motor symptoms onset were also reported.

Patients (Diagnosis)
Exclusion criteria

- Multistemic atrophy (MSA),

- Progressive supranuclear palsy (PSP),

- Dementia with Levy bodies (DLB),

- Corticobasal degeneration (CBD),

- Concomitant vascular encephalopathy,

- Previous head trauma,

- Poor prognosis in the short term for comorbid conditions.

(Prati et al. J Neural Transm 2017)

Statistical analysis

- Differences cases/controls
  - T-test or chi square test
- Multifactor analysis
  - Repeated-measures analysis of variance
- Correlation measures and potential predictors
  - Pearson's, Kendall's and Spearman's tecnique
- Agreement between readers
  - CCC, Precision, accuracy, Total deviation Index
- Agreement intra-readers
  - Test-retest reliability, Bland and Altman
- ROC curves and concordance between readers
  - Unweighted Cohens's kappa
- Reliability of inter-raters estimated
  - Krippendorff's alpha, ICC according to Cronbach
- Sensitivity, specificity, PPV, NPV

Transcranial Sonograpy

● *Review*

TRANSCRANIAL BRAIN PARENCHYMA SONOGRAPHY IN MOVEMENT DISORDERS: STATE OF THE ART

Uwe Walter,* Stefanie Behnke,[†] Jens Eyding,[‡] Ludwig Niehaus,[§] Thomas Postert,[‡¶] Günter Seidel,[∥] and Daniela Berg[#**]

*Department of Neurology, University of Rostock, Rostock, Germany; [†]Department of Neurology, University of the Saarland, Homburg, Germany; [‡]Department of Neurology, St. Josef Hospital, Ruhr-University Bochum, Bochum, Germany; [§]Department of Neurology II, Otto-von-Guericke-University Magdeburg, Magdeburg, Germany; [¶]Department of Neurology, St. Vincenz Hospital Paderborn, Paderborn, Germany; [∥]Department of Neurology, University Hospital Schleswig-Holstein, Campus Lübeck, Lübeck, Germany; [#]Institute for Medical Genetics, University of Tübingen, Tübingen, Germany; [**]Hertie Institute for Brain Research, University of Tübingen, Tübingen, Germany

Measures

- – *original*, performed at subjects' interview by the same sonologist who performed the exam;

- – *re-reading*, performed approximately one month later by each sonologist on own exams;

- – *cross-reading*, performed approximately at the time of re-reading, by each sonologist on the recods supplied by the other sonologist

(Prati et al. J Neural Transm 2017)

Demographic profile

		cases (N=25)	controls (N=29)	P
sex	N females (%)	6 (24.0%)	8 (27.6%)	0.764[a]
age (years)	Mean SD	64.9±9.6	62.5±9.9	0.371[b]
years from diagnosis	mean±SD	5.3±3.8	–	
	median [range]	4 [1-12]		
affected side, N (%)	right	12 (48.0%)		
	left	8 (32.0%)		
	both	5 (20.0%)		
UPDRS score	mean±SD	9.44±6.42	–	
	median [range]	8 [2-28]		
HY score	mean±SD	1.46±0.58	–	
	median [range]	1 [1-3]		
treatment	L-DOPA	7 (28.0%)		
	dopamine agonists	6 (24.0%)		
	dopamine agonists+MAO-I	4 (16.0%)		
	L-DOPA+dopamine agonists+MAO-I	4 (16.0%)		
	L-DOPA+dopamine agonists	2 (8.0%)		
	none	1 (4.0%)		
	L-DOPA+MAO-I	1 (4.0%)		
L-DOPA dose, mg/day (N=14)	mean±SD	339±194	–	
	median [range]	300 [100-700]		

(Prati et al. J Neural Transm 2017)

Correlation between SN⁺ and PD

- No correlation with
  - UPDRS
  - H&Y
  - Years from diagnosis

- No difference between
  - Right and left SN readings
  - Ipsilateral and controlateral side

(Prati et al. J Neural Transm 2017)

SN⁺ (mean ±SD) by patient condition and sonologist

reader	variable		cases (N=25)	controls (N=29)	P (t-test)	[IC 95%]
1	*SN* right	mean±SD	0.24±0.09	0.14±0.04	<0.001	-0.10 [-0.14; -0.06]
	SN, left	mean±SD	0.24±0.05	0.15±0.04	<0.001	-0.09 [-0.11; -0.06]
	SN, mean	mean±SD	0.24±0.06	0.14±0.04	<0.001	-0.10 [-0.12; -0.06]
	III ventricle	mean±SD	4.13±1.98	5.11±2.63	0.122	

SN⁺ (mean ±SD) by patient condition and sonologist

reader	variable		cases (N=25)	controls (N=29)	P (t-test)	[IC 95%]
1	*SN* right	mean±SD	0.24±0.09	0.14±0.04	<0.001	-0.10 [-0.14; -0.06]
	SN, left	mean±SD	0.24±0.05	0.15±0.04	<0.001	-0.09 [-0.11; -0.06]
	SN, mean	mean±SD	0.24±0.06	0.14±0.04	<0.001	-0.10 [-0.12; -0.06]
	III ventricle	mean±SD	4.13±1.98	5.11±2.63	0.122	
2	*SN*, right	mean±SD	0.25±0.10	0.14±0.05	<0.001	-0.11 [-0.15: -0.06]
	SN, left	mean±SD	0.23±0.07	0.15±0.05	<0.001	-0.08 [-0.11; -0.05]
	SN , mean	mean±SD	0.24±0.07	0.15±0.05	<0.001	-0.09 [-0.13; -0.06]
	III ventricle	mean±SD	4.81±2.30	6.04±2.44	0.061	

(Prati et al. J Neural Transm 2017)

Estimates of agreement inter-raters
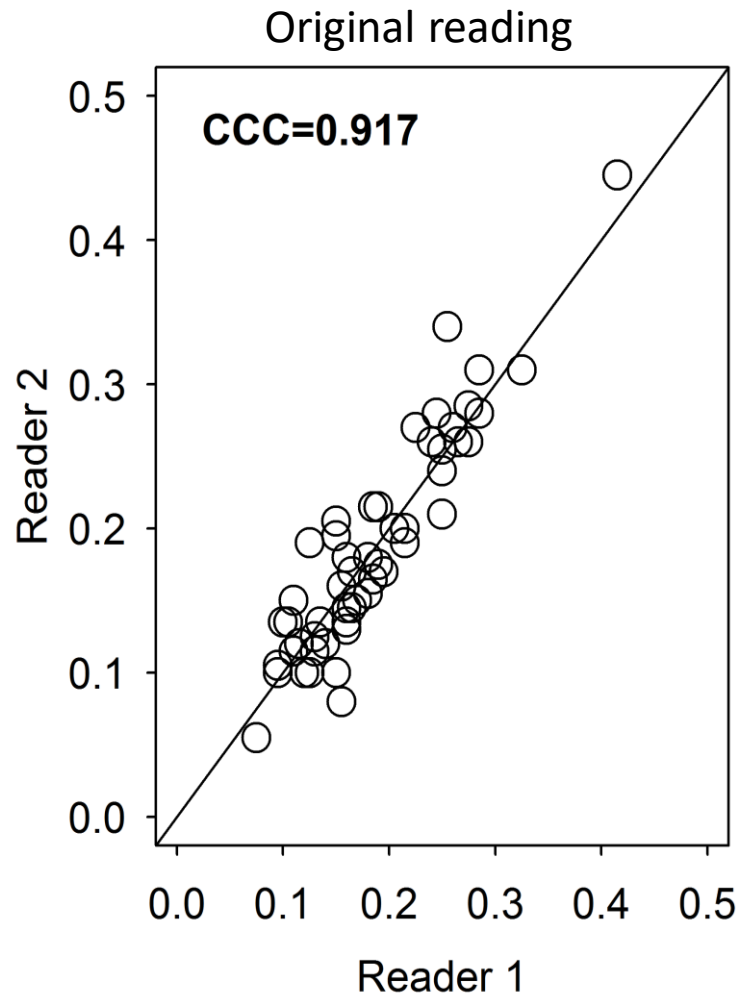
Estimates of agreement inter-raters

Reading	Measure	Estimator	Estimate	One-sided 97.5% confidence limit	95% confidence interval
Original	Mean of left and right	CCC	0.917	0.863	
		Precision	0.922	0.869	
		Accuracy	0.994	0.960	
		TDI	0.048	0.059	
		CP	0.999	0.991	
		ICC	0.918		0.863–0.952

CCC: Concordance correlation coefficient;
ICC: Intraclass correlation coefficient, two-way random effect model
TDI Total deviation index
CP   Coverage probability

(Prati et al. J Neural Transm 2017)
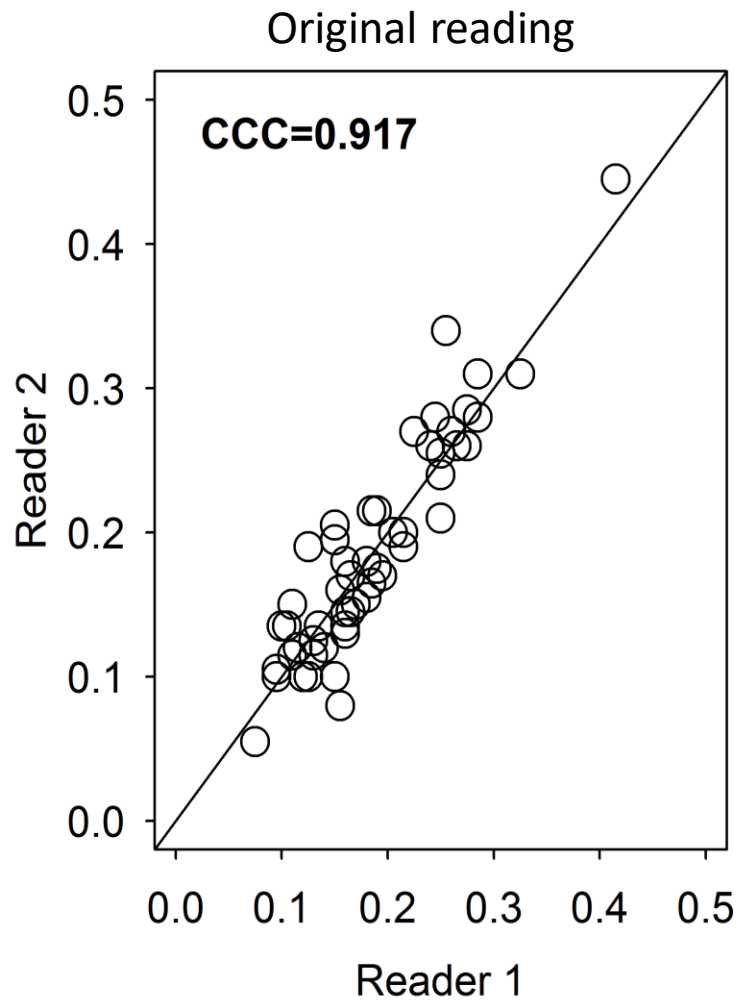
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		TDI	0.048	0.059	
		CP	0.999	0.991	
		ICC	0.918		0.863–0.952
Cross-reading	Mean of left and right	CCC	0.919	0.865	
		Precision	0.924	0.872	
		Accuracy	0.995	0.959	
		TDI	0.048	0.058	
		CP	0.999	0.993	
		ICC	0.921		0.865–0.953

CCC concordance correlation coefficient, *TDI* total deviation index, *CP* coverage probability, *ICC* intra-class correlation coefficient, two-way random effect model

(Prati et al. J Neural Transm 2017)
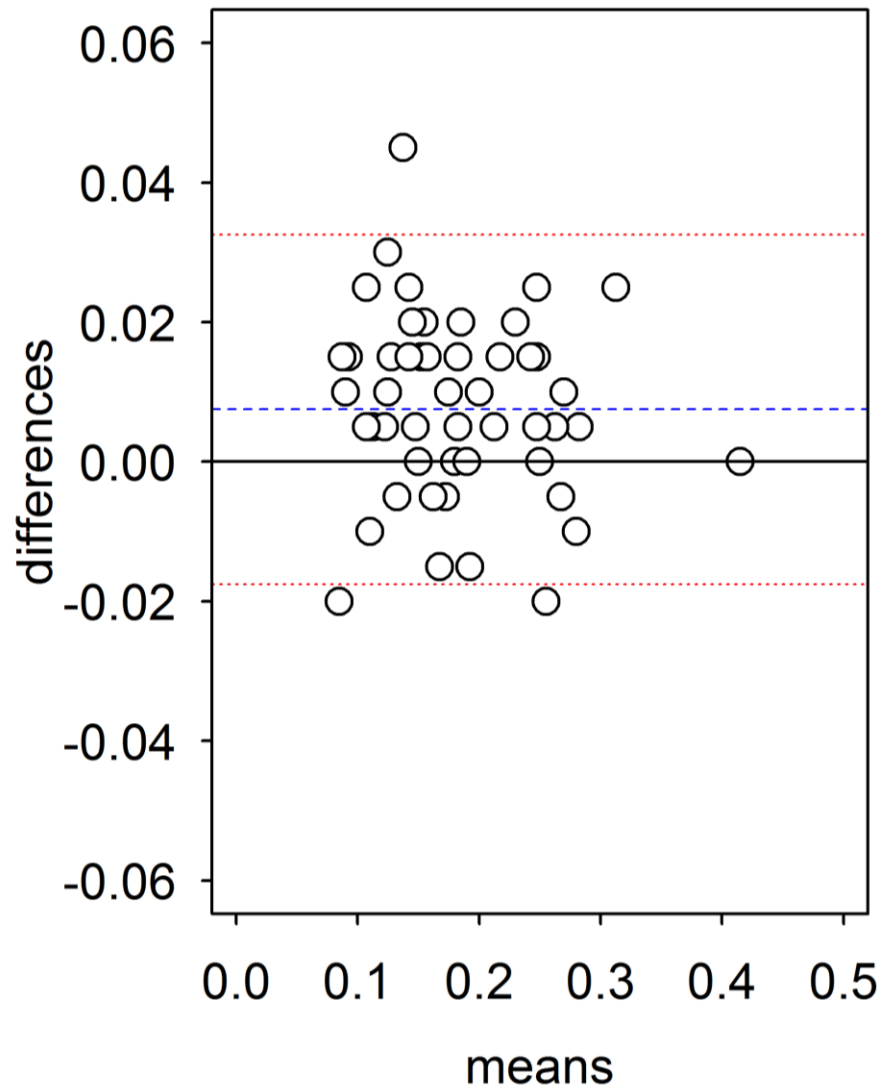
Agreement inter-raters

Original reading

CCC=0.917

Reader 2 (y-axis) vs Reader 1 (x-axis)

(Prati et al. J Neural Transm 2017)

Agreement inter-raters

Original reading | Cross-reading

CCC=0.917 | CCC=0.919

(Prati et al. J Neural Transm 2017)
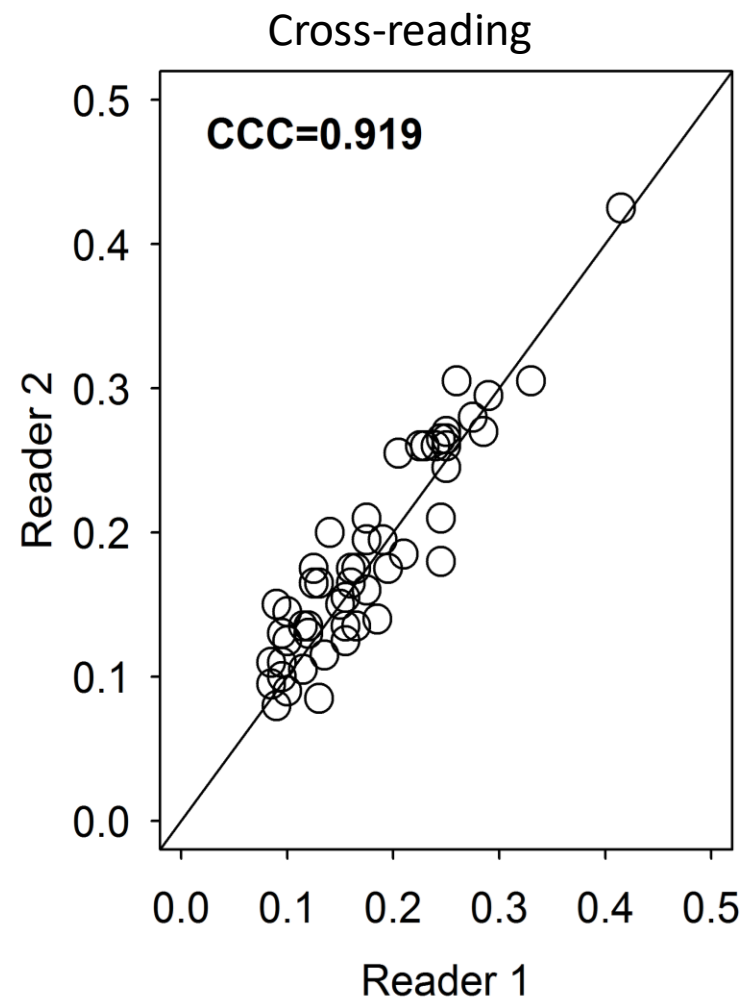
Agreement intra-raters

Bland and Altman difference plots: original and re-reading mean values of the SN$^+$measurements.

Reader 1

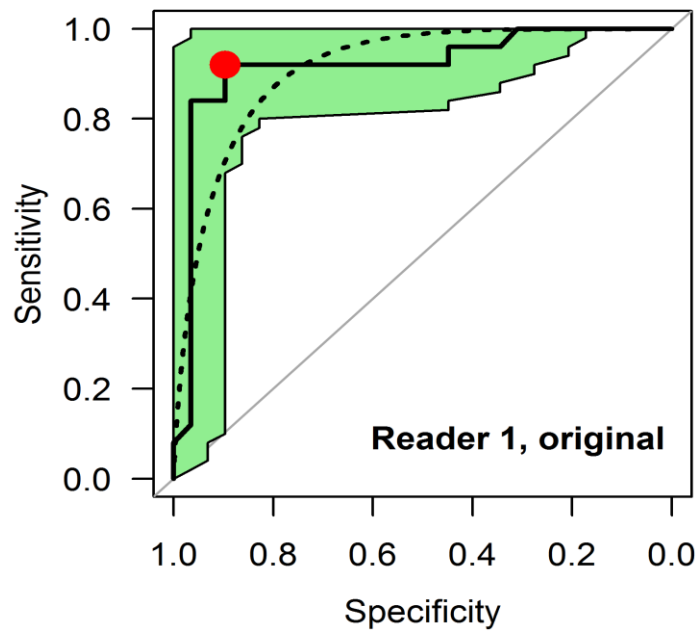# Bland and Altman difference plots: original and re-reading mean values of the SN⁺measurements.
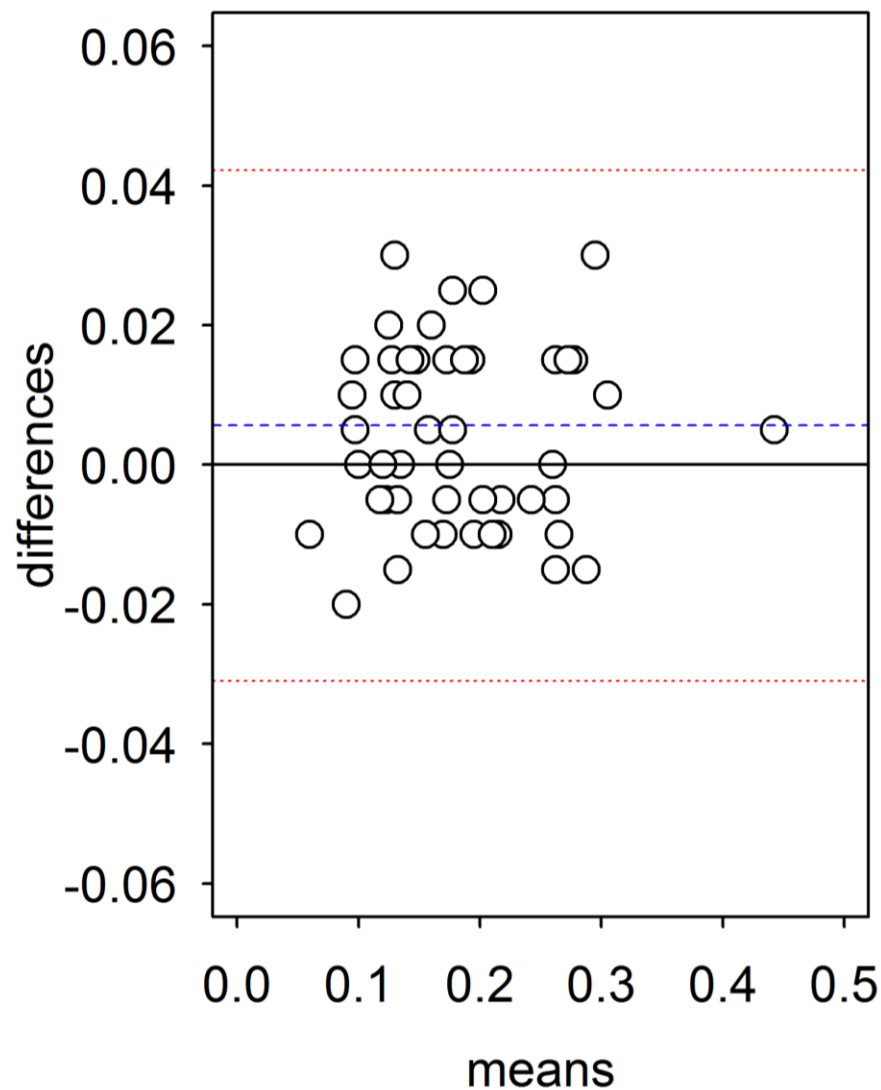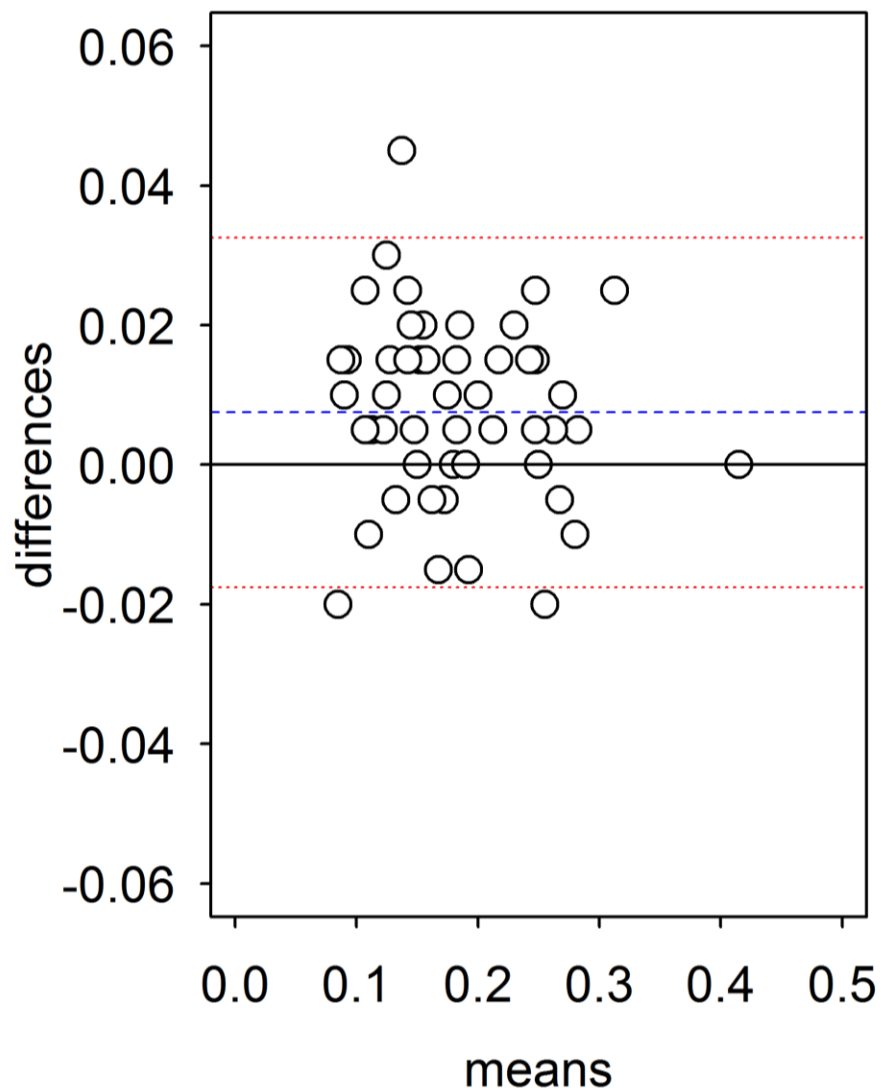
Left panel: reader 1; right panel: reader 2.
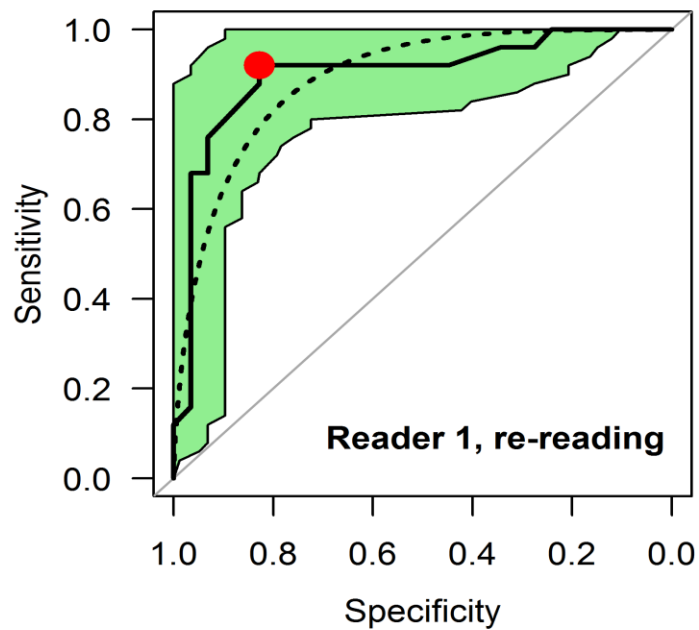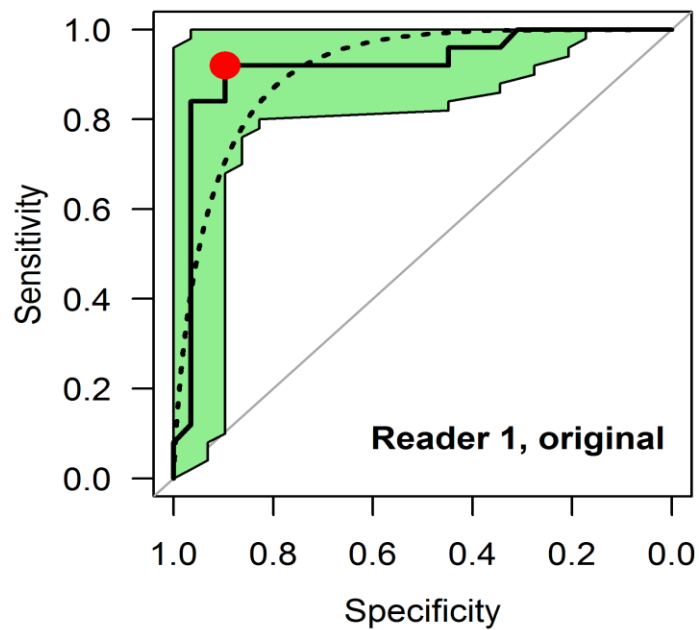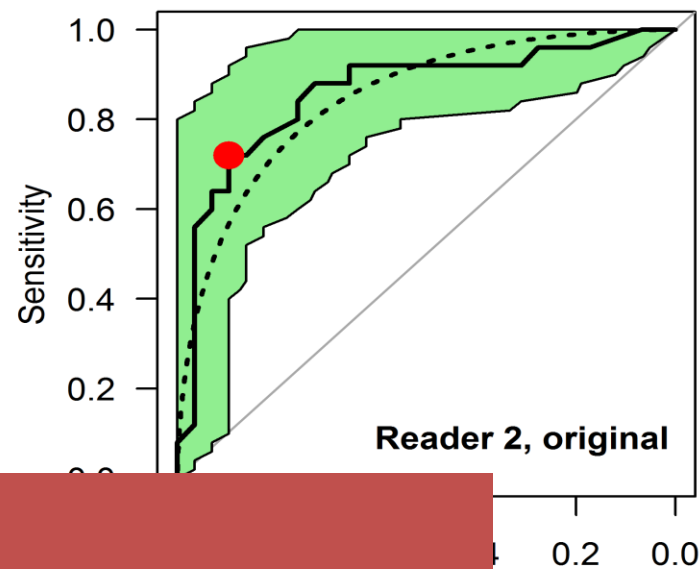
ROC curves and AUC
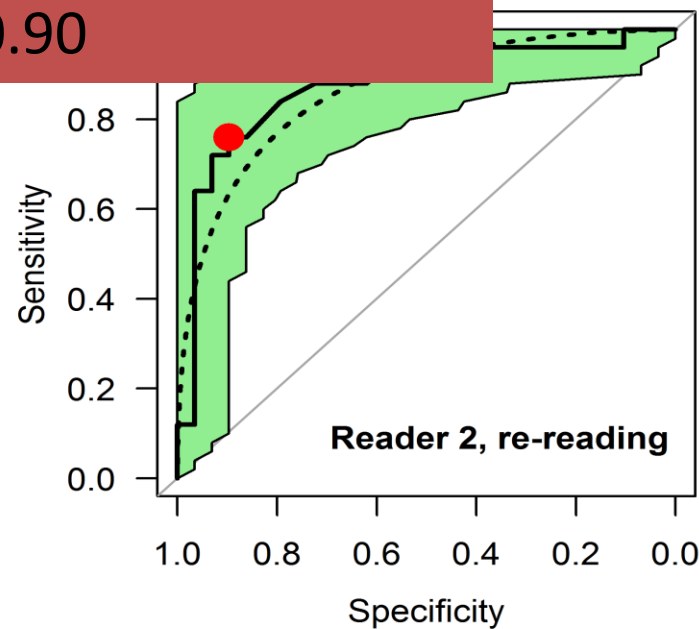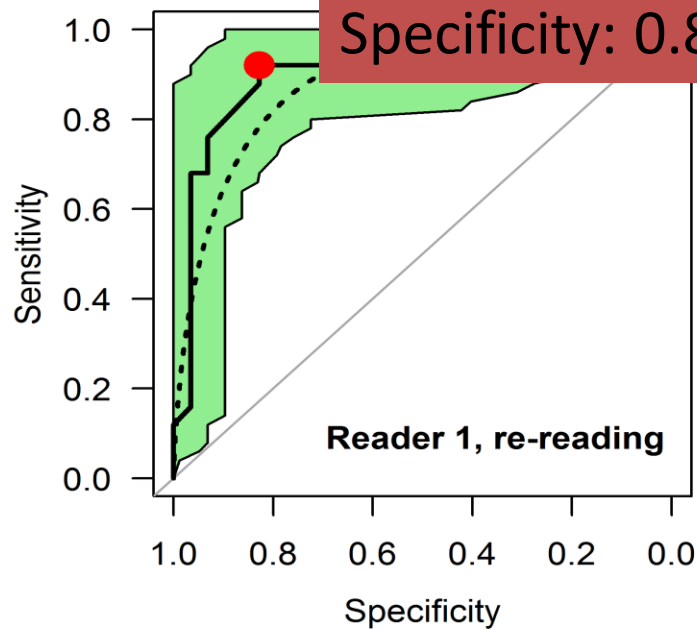## (Measurements at original and re-reading)

Reader 1, original

Reader 1, original
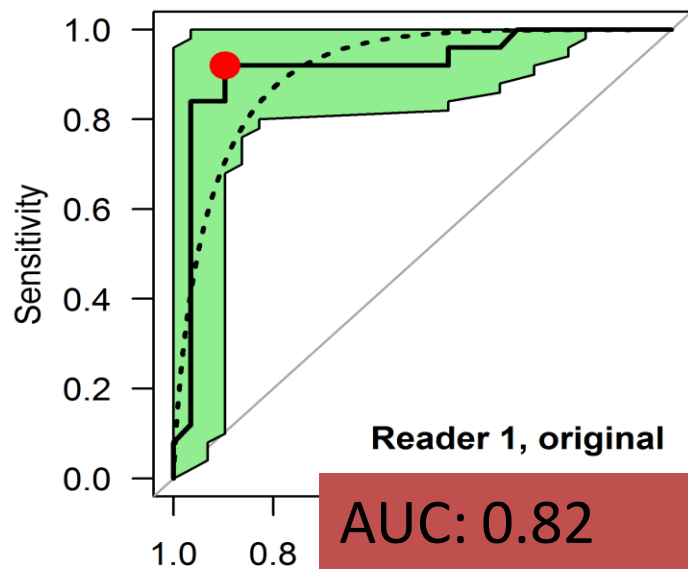
Reader 1, re-reading

AUC: 0.82
Cut-off: 0.18 cm^2
Sensitivity: 0.72-0.92
Specificity: 0.83-0.90

Validation of the diagnostic test
(original reading with cut-off of 0.18 cm^2)

(Prati et al. J Neural Transm 2017)

Validation of the diagnostic test
(original reading with cut-off of 0.18 cm^2)

	READER 1
Sensitivity	0.92 [0.740; 0.990]
Specificity	0.89 [0.726; 0.978]

Validation of the diagnostic test
(original reading with cut-off of 0.18 cm^2)

Sensitiv	0]
Specifici	8]
PPV	0.88 [0.698; 0.976]
NPV	0.92 [0.765; 0.991]
Diagnostic accuracy	0.90 [0.797; 0.969]

Prevalence: 1.5 % > 60
PPV: 0.12
NPV: 0.90
Prevalence: 4 % > 85
PPV: 0.27
NPV: 0.90

(Prati et al. J Neural Transm 2017)

Sensitivity and Specificity of SN⁺measuring

	NOBIS	Prestel	Gaenslen	Van de Loo	Dun-Hui
Sensitivity	0.90	0.85	0.90	0.88	0.83
Specificity	0.89	0.82	0.92	0.62	0.87

(Prati et al. J Neural Transm 2017)

NOBIS Conclusions

- PD patients showed a significant bilateral enlargement of the hyperechogenic SN area in comparison with controls

- No relationship between the SN area and the duration or severity of the disease

- The most reliable measure for practical purposes was the mean between right-side and left-side measurements

- The agreement between readers was good to very good, with a unified intra, inter-observer and total CCC of 0.81, 0.90 and 0.79

- The best cut-off point estimated from the ROC curves was 0.18 cm^2, corresponding to a sensitivity of 0.92 (CI: 0.74-0.99), and a specificity of 0.89 (CI: 0.72- 0.97)

- The our diagnostic accuracy's estimates are comparable to those of the literature

Transcranial Sonography: conclusions

- TCS is a non invasive, safe, convenient, available, repeatible neuroimage technique

- TCS has an high accuracy in the diagnosis of PD

- The limits of TCS are the quality of temporal bone and the experience of the examinator