MASSIMILIANO GODANI

ECOGRAFIA TRANSCRANICA PARENCHIMALE

NON SOLO PARKINSON…

SINSEC
Società Italiana
Neurosonologia ed
Emodinamica Cerebrale

PLANES AND ACOUSTIC WINDOW

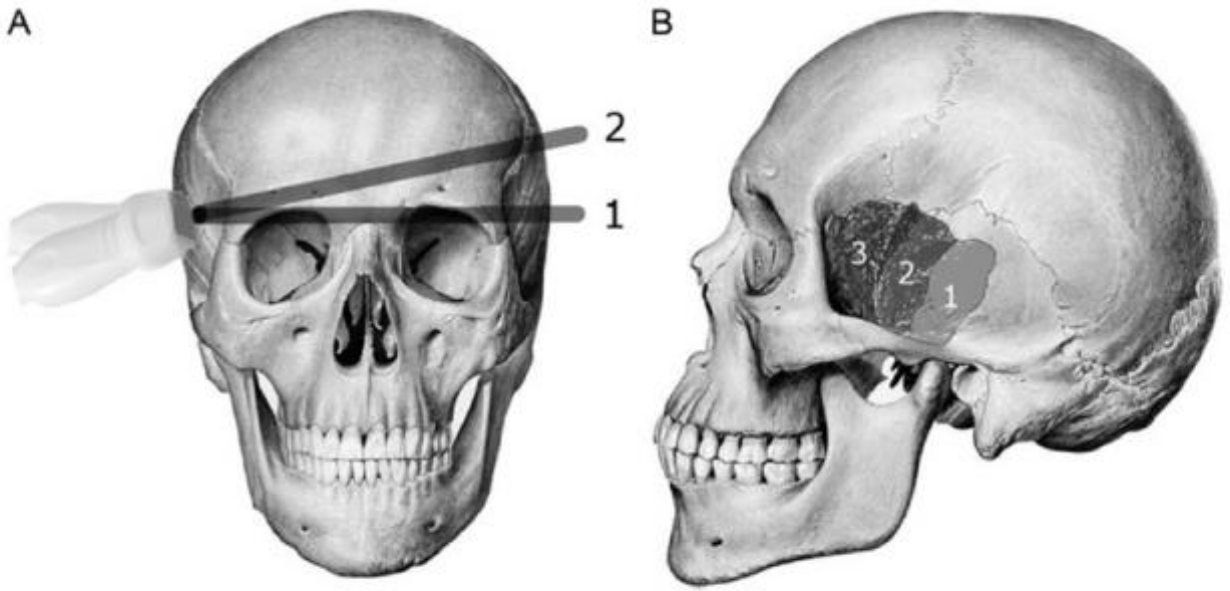
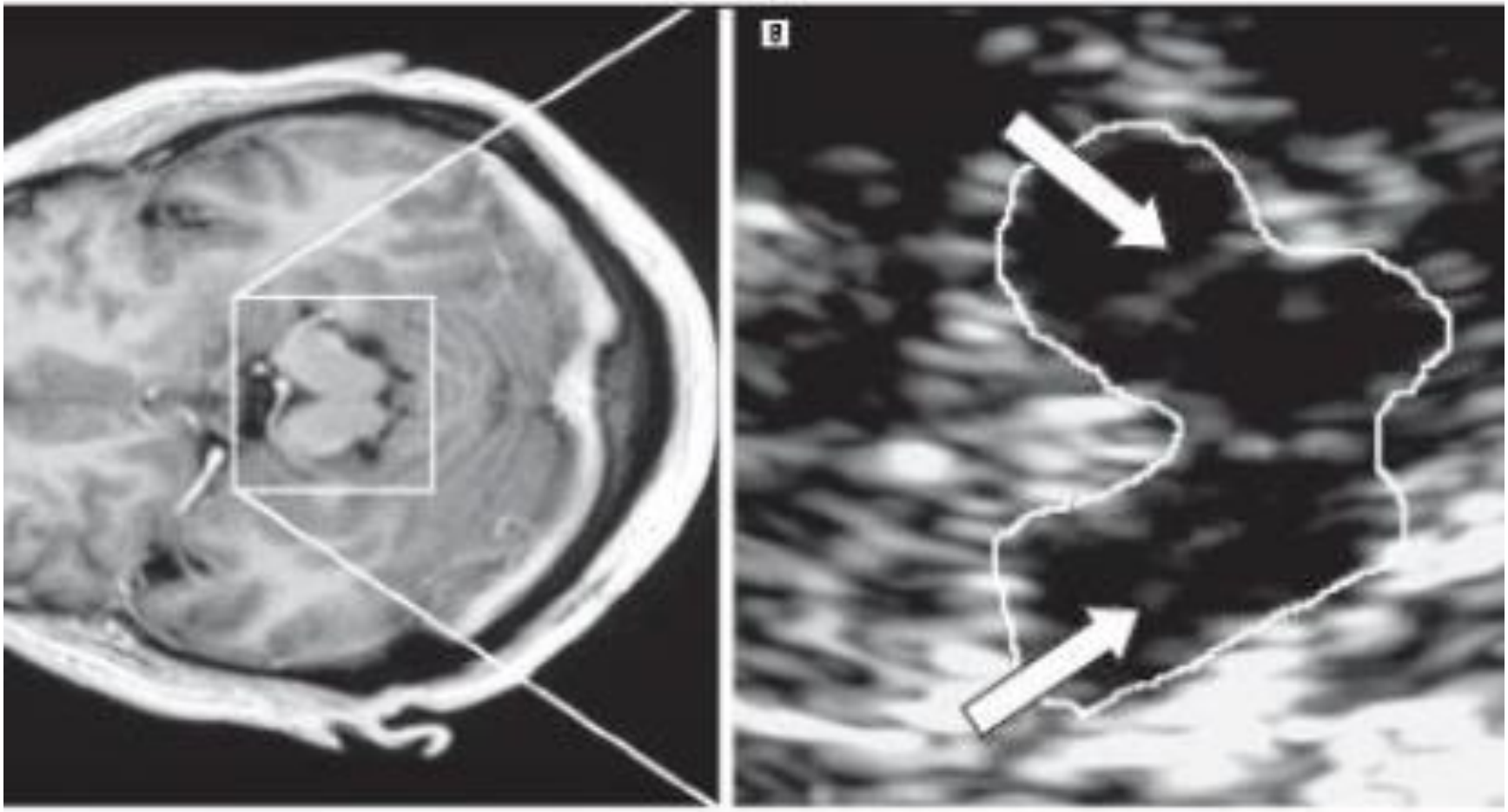
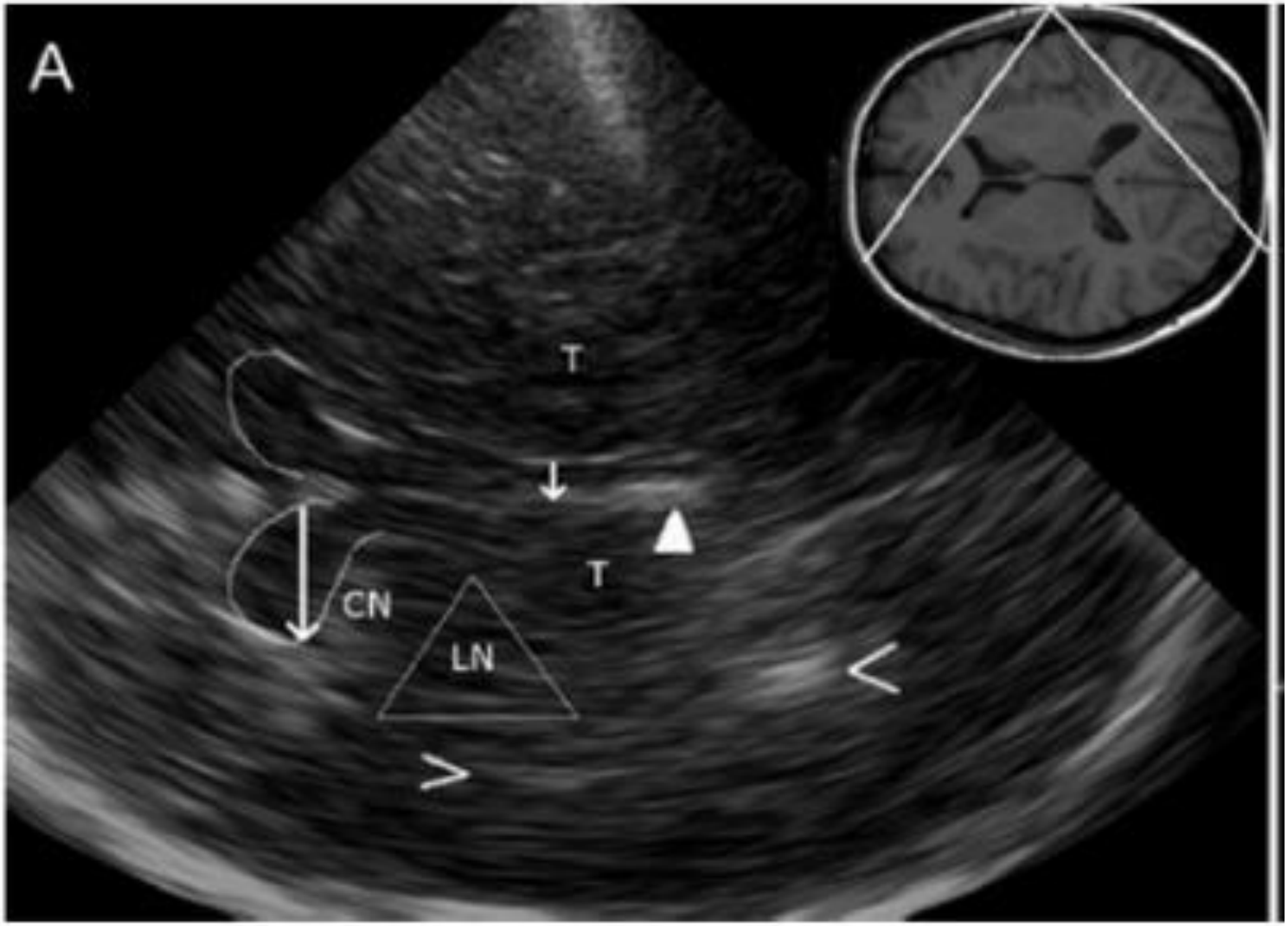


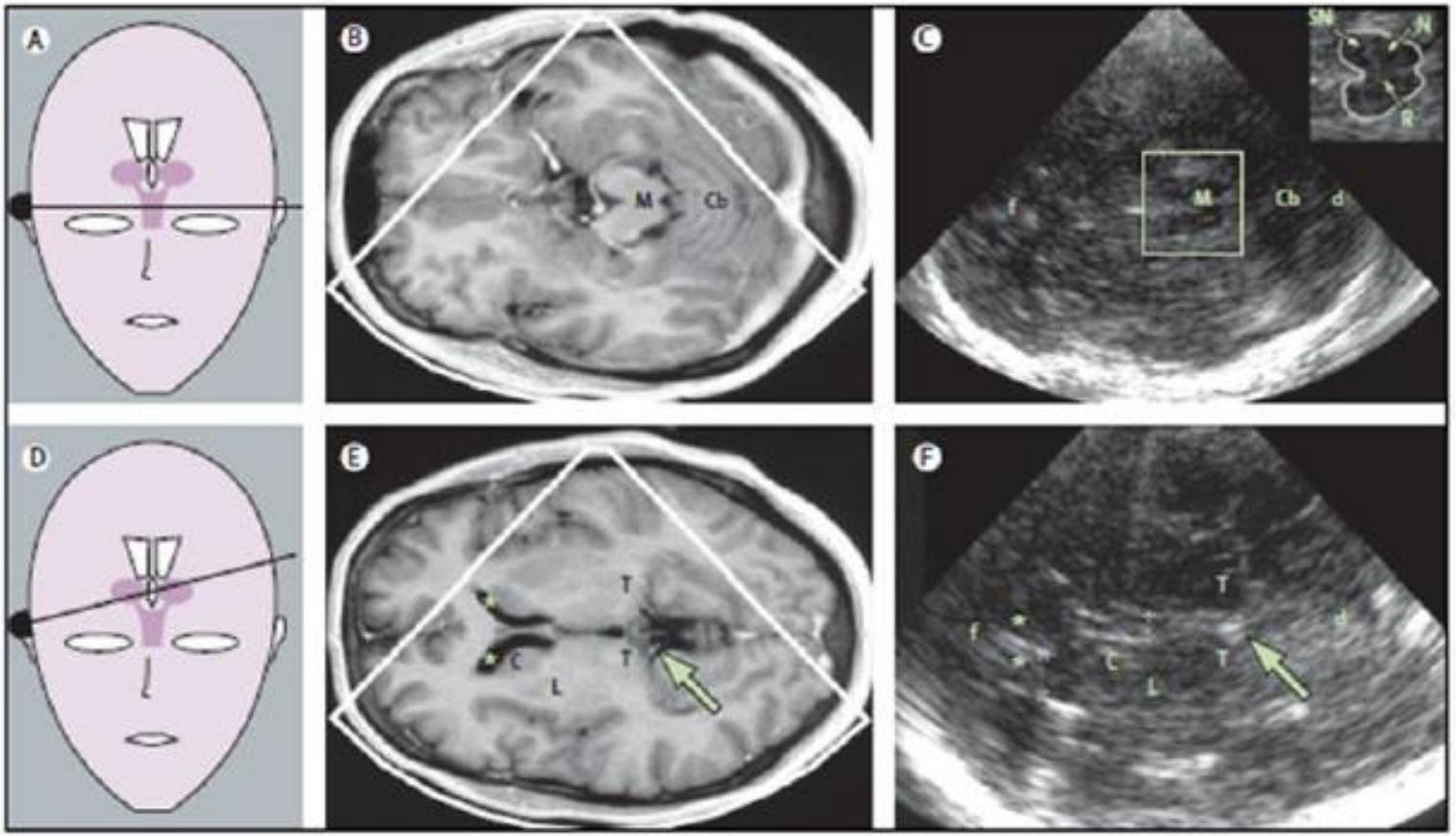
Fig. 1 The most frequently used sonographic planes and acoustic windows. (A) Depiction of the axial imaging planes. The mesencephalic plane (1) can be visualized by holding the transducer parallel to the orbitomeatal line. The third ventricle plane (2) can be seen by tilting the transducer 10–20 degree upward. (B) Depiction of the temporal bone window. The transducer should be moved carefully back and forth in order to find the best window for an optimal TCS examination.

MESENCEPHALIC PLANE



DIENCEPHALIC PLANE




A
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European Journal of Neurology 2013, **20:** 16–34 doi:10.1111/ene.12022

EFNS/MDS-ES GUIDELINES/CME ARTICLE

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

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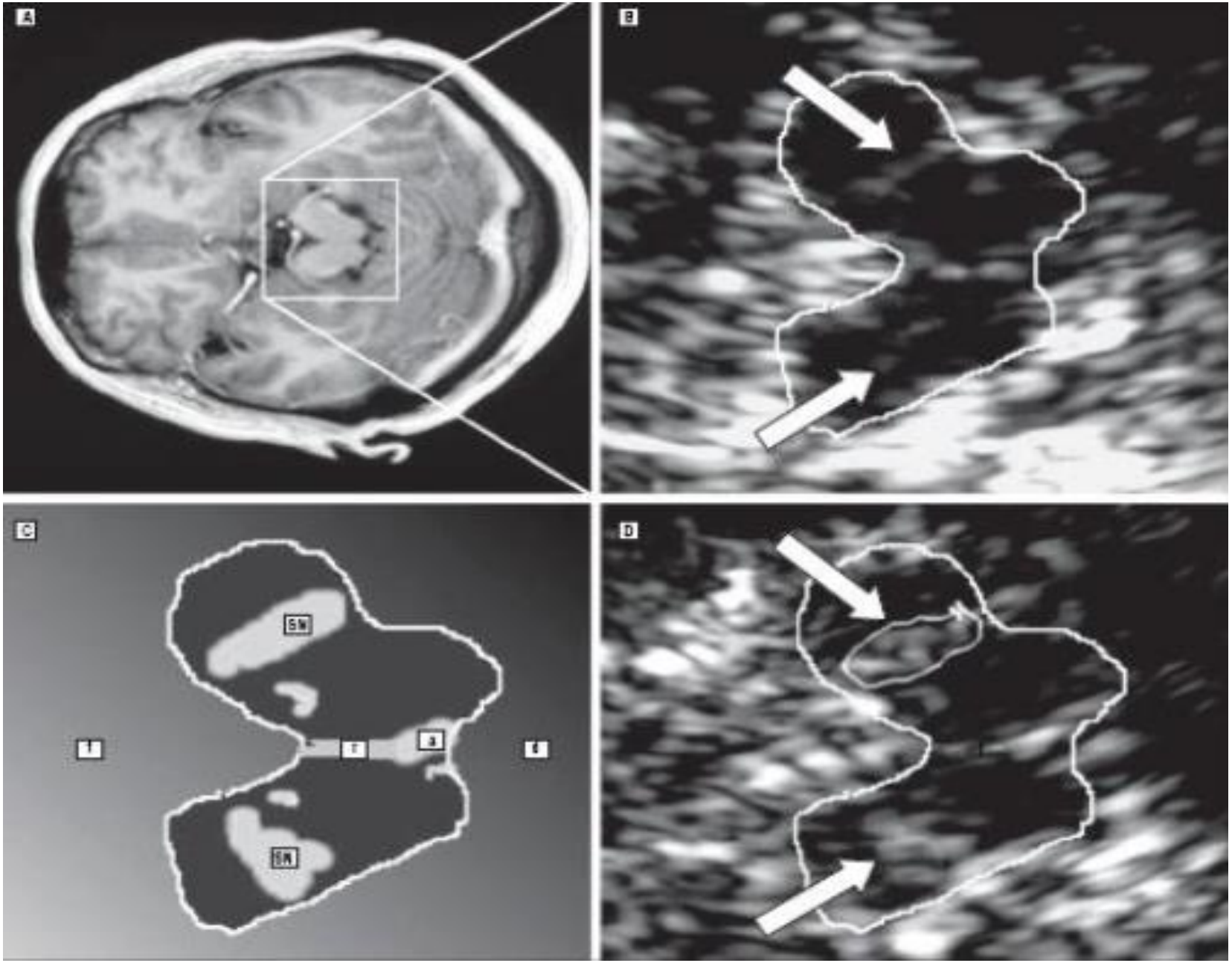
RECOMMENDATIONS
Level A

1) **The early diagnosis of PD.**
2) **Differential diagnosis of PD from atypical Parkinsonian syndromes and secondary Parkinsonian syndromes.**
3) **The detection of subjects at risk for PD.**


A
B
C
SN
SN
D

HYPERECHOGENICITY IN PD

- **SN hyperecogenicity is found in more than 90% of Parkinson's disease patients.**
- **Hyperecogenicity of SN is usually asymmetric.**
- **It could be ipsilateral or contralateral of clinically affected side.**
- **Does not remarkably change in the disease course.**
- **It is unrelated to PD severity.**

VALUES FOR EVERY US SYSTEM

manufacturer/ ultrasound system	probe/ frequency [MHz]	cut-off value [cm²]		references
		SN-h¹	Marked SN-h¹	
Aloka/Prosound Alpha 10	UST-52105/2.5	≥0.19	≥0.25	Mijajlović et al. [20]
Esaote/MyLab25 Gold	PA240/2.5	≥0.20	≥0.25	Go et al. [3]
Esaote/MyLab Twice	PA240/2.5	≥0.24	≥0.30	(own data)
General Electric/Logiq 7	3S/2.5		≥0.24	Stockner et al. [21]
General Electric/Logiq 9	3S/2.5	≥0.20		Fedotova et al. [22]
Philips/HDI 5000 SonoCT	P2 – 4/2.5	≥0.20		Kim et al. [23]
Philips/HP Sonos 5500	S4/2.0 – 2.5	≥0.20	≥0.27	Mehnert et al. [17] Hagenah et al. [18]
Siemens/Acuson Antares	PX4 – 1/2.5	≥0.24	≥0.30	Van de Loo et al. [10] Glaser et al. [24]
Siemens/Sonoline Elegra	2.5PL20/2.6	≥0.20	≥0.25	Berg et al. [16]
Toshiba Aplio XG	PST-20CT/2.5	≥0.16	≥0.22	Vivo-Orti et al. [25]

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Iron accumulation and microglia activation contribute to substantia nigra hyperechogenicity in the 6-OHDA-induced rat model of Parkinson's disease

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Keywords:
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Substantia nigra hyperechogenicity
6-Hydroxydopamine
Deferiprone

ABSTRACT

Introduction: This study aims to explain the mechanisms for the formation of sonographic features of Parkinson's disease (PD) using a 6-hydroxydopamine (6-OHDA) rat model of PD. The iron chelator deferiprone (DFP) was used in the PD model rat to examine the relationship between iron and the echo signal.

Methods: Rat models were created using stereotactic injections of 6-OHDA. DFP was administered intragastrically. Transcranial sonography (TCS) was performed to observe the substantia nigra (SN) echo signal of the brain. Immunofluorescence and iron staining were performed to observe the histological characteristics of the hyperechogenic area. The imaging findings were compared with the histopathological findings.

Results: The PD model rat presented a large area of hyperechogenicity in the SN. Ferric ion accumulation and microglia proliferation occurred in the hyperechogenic area. DFP inhibited dopaminergic (DA) neuron necrosis, ferric ion accumulation and microglia proliferation and reduced the hyperechogenic area of the SN.

Conclusions: Both iron aggregation and gliosis contribute to the formation of substantia nigra hyperechogenicity (SNH) in PD. DFP exhibits a neuroprotective effect by inhibiting SNH. Iron deposit and the SNH are correlated with DA neuron necrosis.

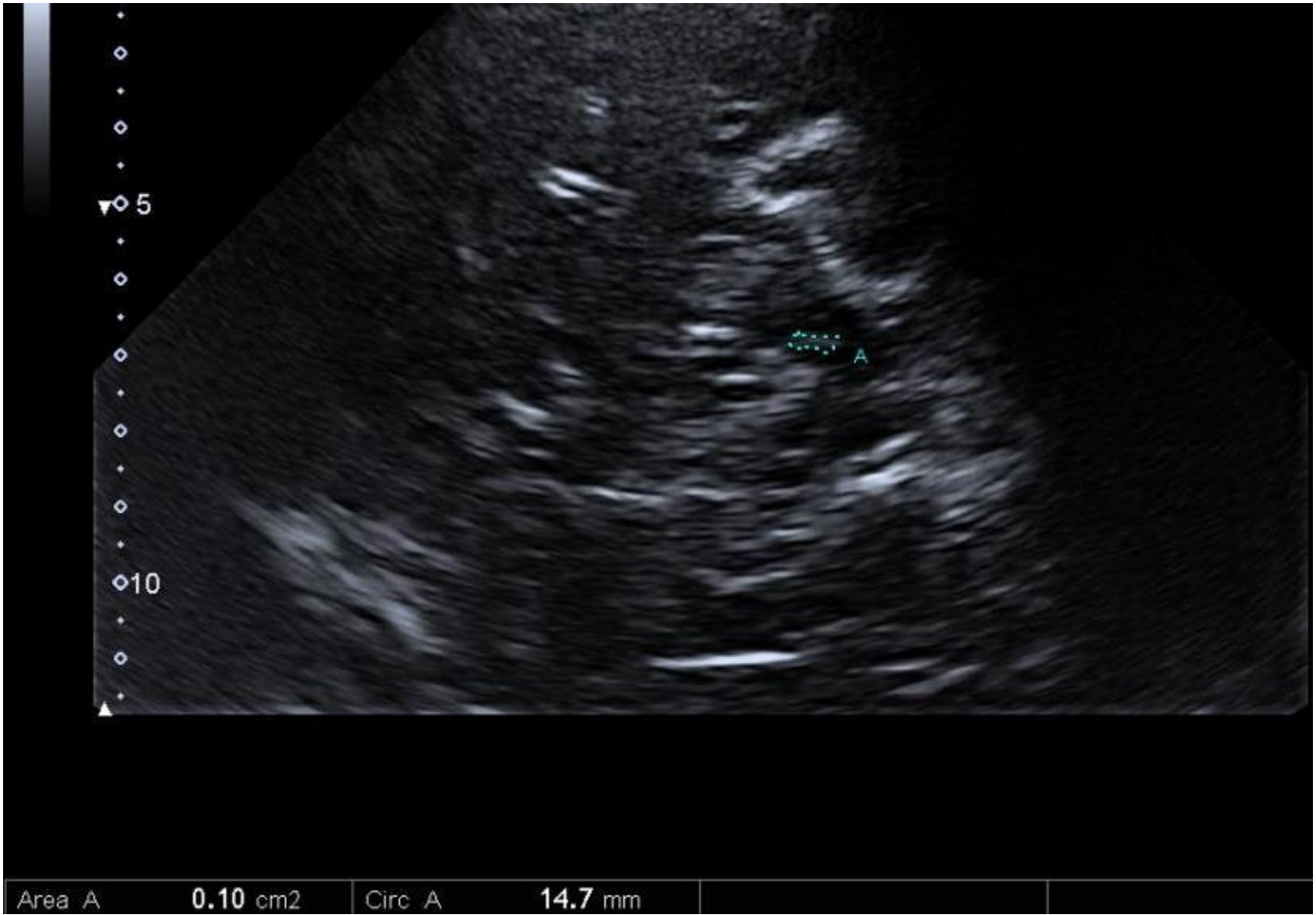
RECOMMENDATIONS
Level A

1) The early diagnosis of PD.
2) Differential diagnosis of PD from atypical Parkinsonian syndromes and secondary Parkinsonian syndromes.
3) The detection of subjects at risk for PD.

TCS FINDINGS IN aPS

- Normal echogenicity of substantia nigra
- Bilateral hyperechogenicity of substantia nigra
- Hyperechogenicity of lenticular nucleus
- Enlargement of third ventricle

PSP-RS



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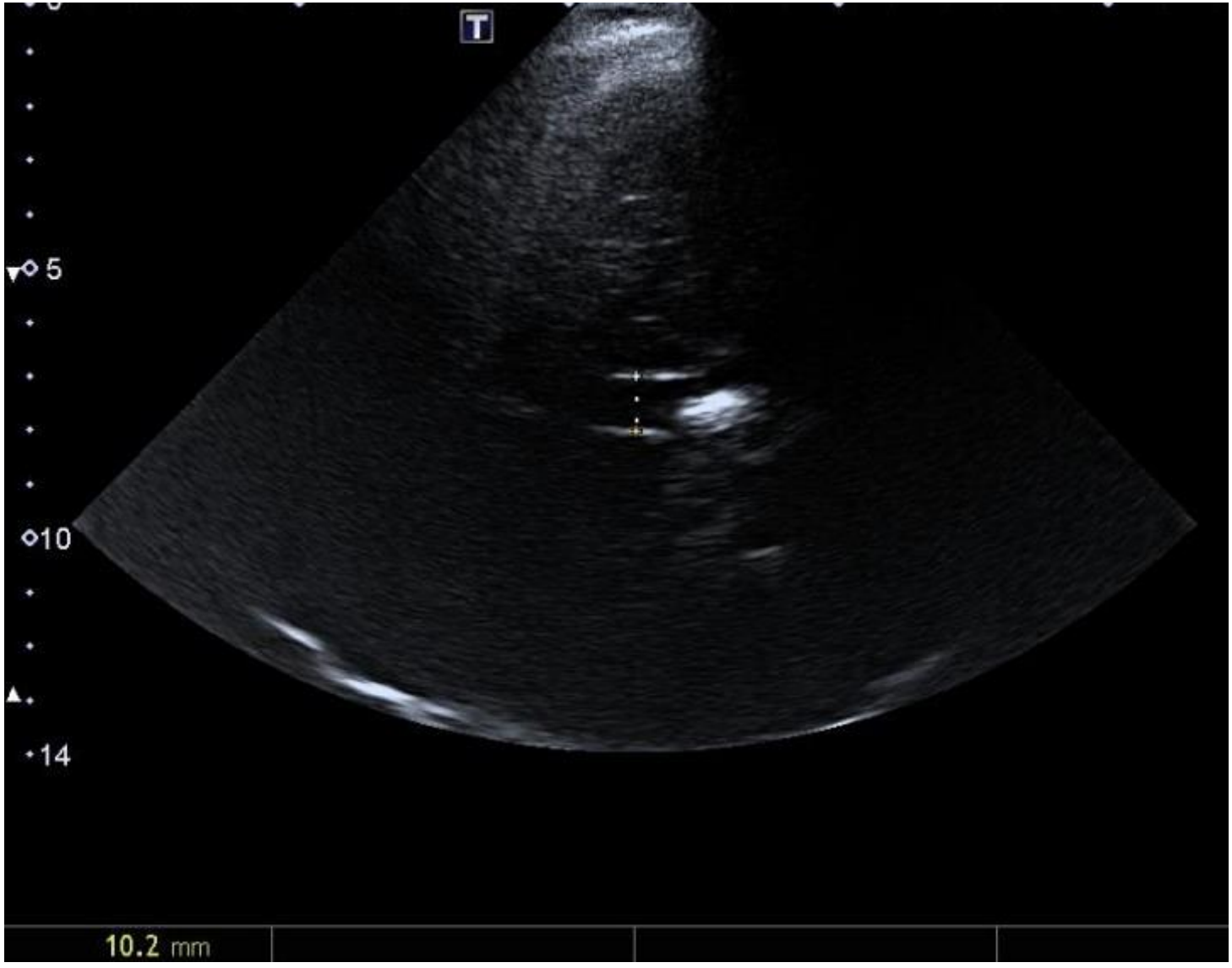

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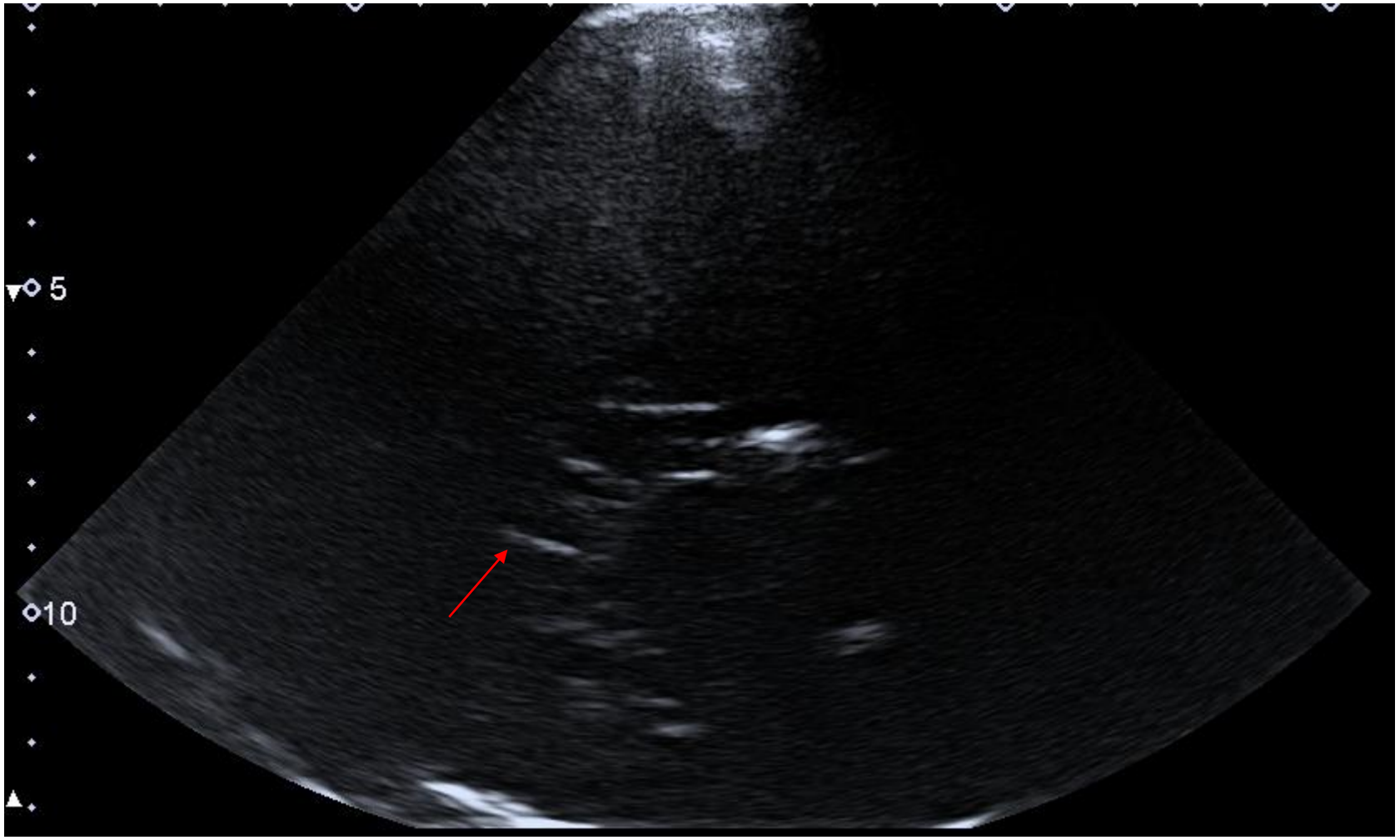

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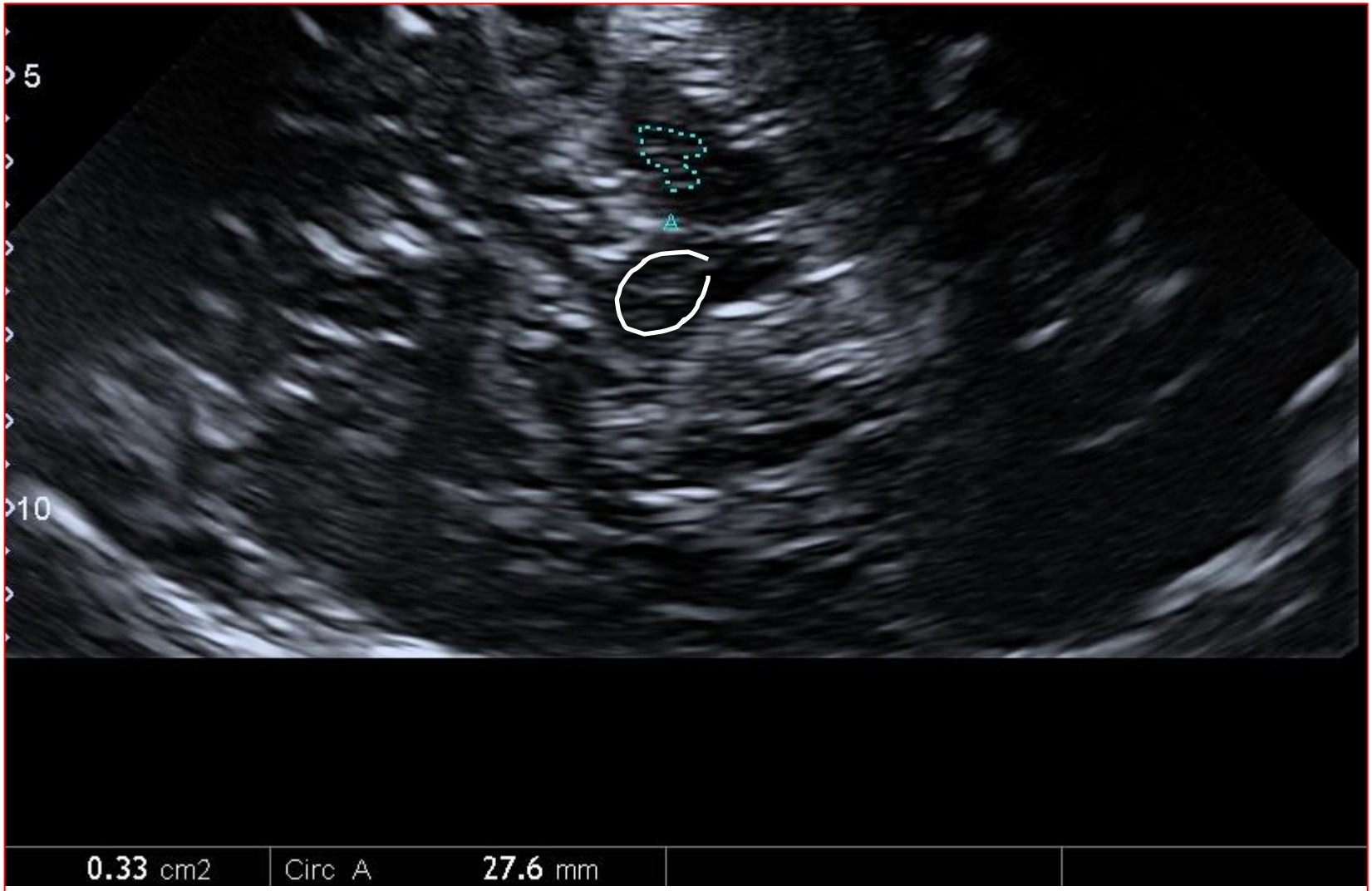
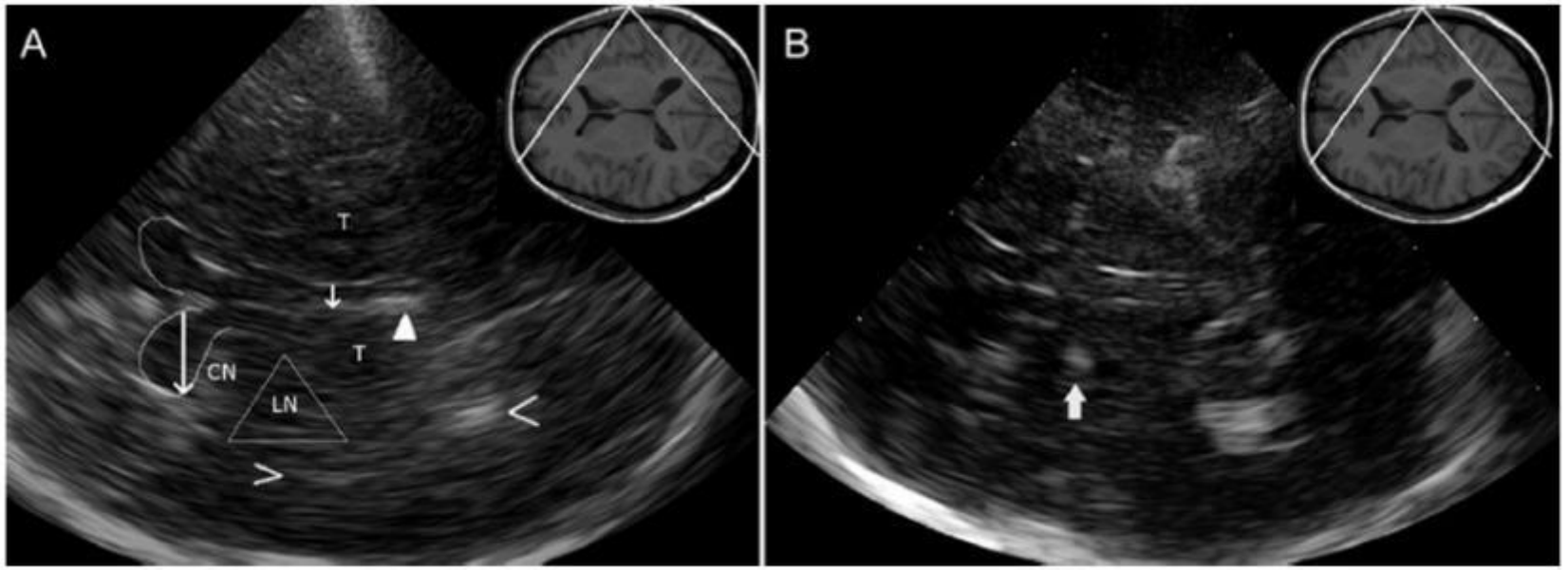
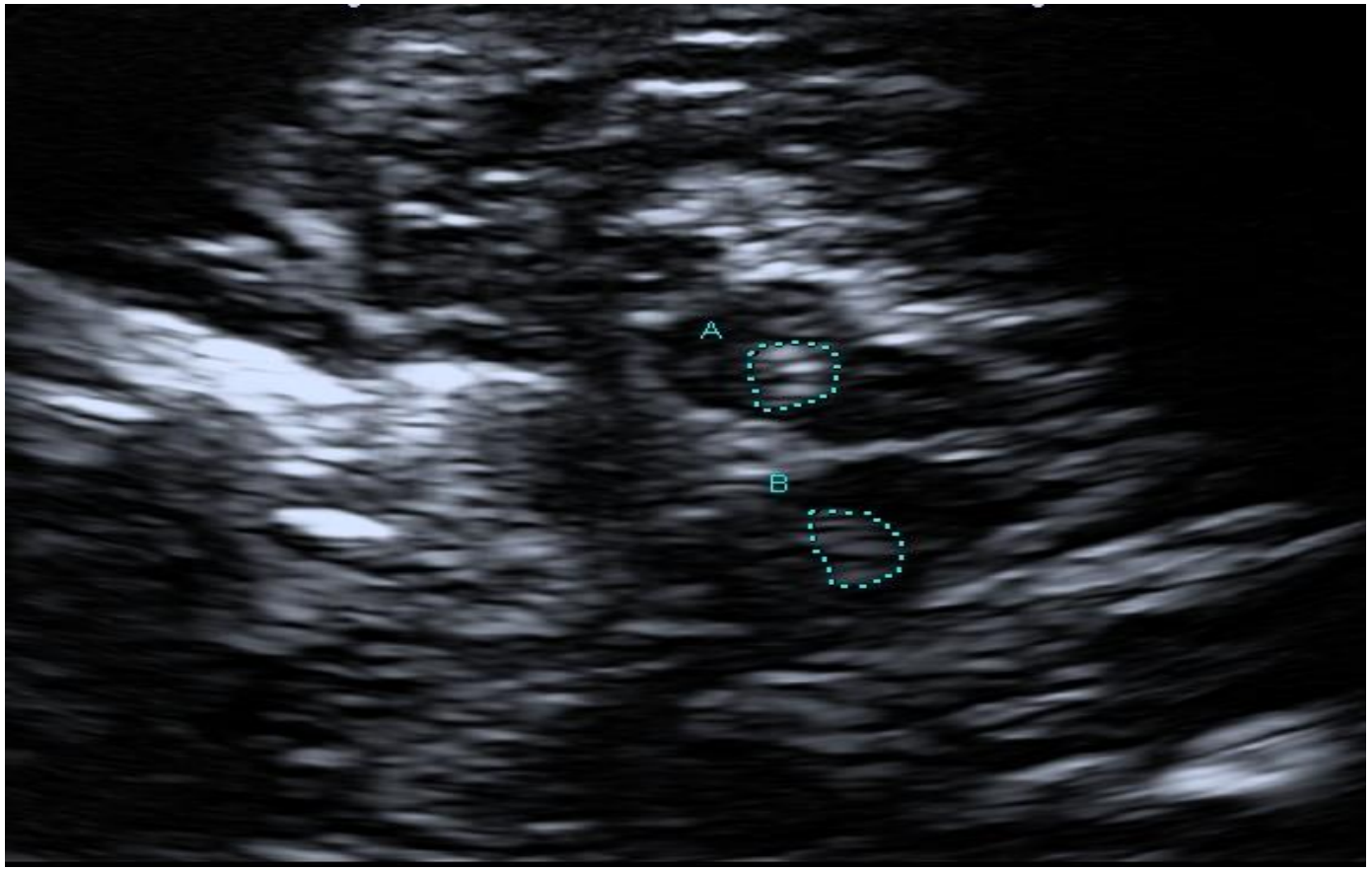


MSA-P



DLB



The specificity and sensitivity of transcranial ultrasound in the differential diagnosis of Parkinson's disease: a prospective blinded study

Alexandra Gaenslen, Barbara Unmuth, Jana Godau, Inga Liepelt, Adriana Di Santo, Katherine Johanna Schweitzer, Thomas Gasser, Hans-Jürgen Machulla, Matthias Reimold, Kenneth Marek, Daniela Berg

Summary

Background Increased echogenicity of the substantia nigra (SN), as determined by transcranial sonography (TCS), is characteristic of idiopathic Parkinson's disease (iPD). The results of initial retrospective studies indicate that this ultrasound sign is specific for iPD and can help to differentiate it from atypical parkinsonian syndromes (aPS); however, these early studies were done in patients with later disease stages and known clinical diagnosis. We aimed to determine the diagnostic value of TCS in the early stages of parkinsonian syndromes, when the clinical symptoms often do not enable a definite diagnosis to be made.

Methods 60 patients who presented with the first, but still unclear, clinical symptoms of parkinsonism had TCS in this prospective blinded study. Investigators were blinded to the results of the clinical investigations, the ultrasound findings, and the diagnosis at time of investigation. The patients were followed-up every 3 months for 1 year to assess and re-evaluate the clinical symptoms. The patients in whom a clinical diagnosis could not be made with certainty were investigated with raclopride PET or dopamine transporter single-photon emission computed tomography (SPECT), or both.

Findings A clinical diagnosis of parkinsonism could not be established at baseline in 38 patients. At 12 months, 39 patients were clinically categorised as having iPD. Compared with endpoint diagnosis, the sensitivity of TCS at baseline was 90·7% and the specificity was 82·4%; the positive predictive value of TCS for iPD was 92·9% and the classification accuracy was 88·3%.

Interpretation TCS is an easy to implement, non-invasive, and inexpensive technique that could help in the early differential diagnosis of parkinsonian syndromes. The routine use of TCS in the clinic could enable disease-specific therapy to be started earlier.

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Published Online
April 3, 2008
DOI:10.1016/S1474-4422(08)70067-X

See **Reflection and Reaction** page 376

Center of Neurology, Department of Neurodegeneration and Hertie Institute of Clinical Brain Research (A Gaenslen MD, B Unmuth, J Godau MD, I Liepelt PhD, A Di Santo MD, K J Schweitzer MD, T Gasser MD, D Berg MD); **Department of Radiopharmacy and PET Center** (H-J Machulla PhD) **and Department of Nuclear Medicine and PET Center** (M Reimold MD), **University of Tübingen, Germany; and Institute for Neurodegenerative Disorders, Yale University Hospital, New Haven, CT, USA** (K Marek MD)

Review Article

Transcranial Sonography of the Substantia Nigra for the Differential Diagnosis of Parkinson's Disease and Other Movement Disorders: A Meta-Analysis

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[2]*Department of Transcranial Sonography, The First Affiliated Hospital of Zhengzhou University, Zhengzhou University, Zhengzhou 450000, China*

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Academic Editor: Carlo Colosimo

This meta-analysis aimed to evaluate the accuracy of hyperechogenicity of the substantia nigra (SN) for the differential diagnosis of Parkinson's disease (PD) and other movement disorders. We systematically searched the PubMed, EMBASE, Cochrane Library, and China National Knowledge Infrastructure databases for relevant studies published between January 2015 and May 2020. Eligible articles comparing the echogenicity of the SN between patients with PD and those with other movement disorders were screened, and two independent reviewers extracted data according to the inclusion and exclusion criteria. Statistical analyses were conducted using STATA (version 15.0) (Stata Corporation, College Station, TX, USA), Review Manager 5.3 (Cochrane Collaboration), and Meta-DiSc1.4 to assess the pooled diagnostic value of transcranial sonography (TCS) for PD. Nine studies with a total of 1046 participants, including 669 patients with PD, were included in the final meta-analysis. Our meta-analysis demonstrated that hyperechogenicity of the SN had a pooled sensitivity and specificity of 0.85 (0.82, 0.87) and 0.71 (0.66, 0.75), respectively, for distinguishing idiopathic Parkinson's disease from other movement disorders. Furthermore, the area under the curve of the summary receiver operating characteristic was 0.94. Transcranial sonography of the SN is a valuable tool for the differential diagnosis of PD and other movement disorders.

RECOMMENDATIONS
Level A

1) The early diagnosis of PD.
2) Differential diagnosis of PD from atypical Parkinsonian syndromes and secondary Parkinsonian syndromes.
3) The detection of subjects at risk for PD.

The PRIPS study: screening battery for subjects at risk for Parkinson's disease

D. Berg[a,b], J. Godau[a,b], K. Seppi[c], S. Behnke[d], I. Liepelt-Scarfone[a,b], S. Lerche[a,b], H. Stockner[c], A. Gaenslen[a,b], P. Mahlknecht[c], H. Huber[a,b], K. Srulijes[a,b], J. Klenk[e], K. Fassbender[d], W. Maetzler[a,b,e], W. Poewe[c] and the PRIPS study group

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Keywords:
hyposmia, Parkinson's disease, screening, substantia nigra, ultrasound

Received 22 March 2012
Accepted 28 May 2012

Background and purpose: Screening batteries to narrow down a target-at-risk population are essential for trials testing neuroprotective compounds aiming to delay or prevent onset of Parkinson's disease (PD).

Methods: The PRIPS study focuses on early detection of incident PD in 1847 at baseline PD-free subjects, and assessed age, male gender, positive family history, hyposmia, subtle motor impairment and enlarged substantia nigra hyperechogenicity (SN+).

Results: After 3 years follow-up 11 subjects had developed PD. In this analysis of the secondary outcome parameters, sensitivity and specificity of baseline markers for incident PD were calculated in 1352 subjects with complete datasets (10 PD patients). The best approach for prediction of incident PD comprised three steps: (i) prescreening for age, (ii) primary screening for positive family history and/or hyposmia, and (iii) secondary screening for SN+.

Conclusion: With this approach, one out of 16 positively screened participants developed PD compared to one out of 135 in the original cohort. This corresponds to a sensitivity of 80.0%, a specificity of 90.6% and a positive predictive value of 6.1%. These values are higher than for any single screening instrument but still too low for a feasible and cost-effective screening strategy which might require longer follow-up intervals and application of additional instruments.

PRIPS STUDY

- In the PRIPS study 1847 subjects were evaluated with TCS at baseline and after three and five years.
- 21 individuals developed PD (1.7%).
- 4 of the 21 incident PD cases had insufficient temporal bone acoustic window.
- Of the 17 patients with incident PD 14 had displayed SN hyperechogenicity at baseline (80 %).
- The overall relative risk of participants with SN hyperechogenicity at baseline to develop PD after 5 years was 20.6 times higher.

Two pilot studies have demonstrated that the intraoperative visualization with TCS and the TCS-assisted insertion of deep brain stimulation electrodes are feasible and safe.

The main advantage of the intraoperative TCS monitoring was that the distance of the DBS electrode tip to an artery at the anatomic target.

Moreover TCS can be recommended for the postoperative monitoring of DBS electrode position.

ELSEVIER
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Bartels E, Bartels S, Poppert H (Editors):
New Trends in Neurosonology and Cerebral Hemodynamics – an Update.
Perspectives in Medicine (2012) 1, 344–348

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Intra- and post-operative monitoring of deep brain implants using transcranial ultrasound

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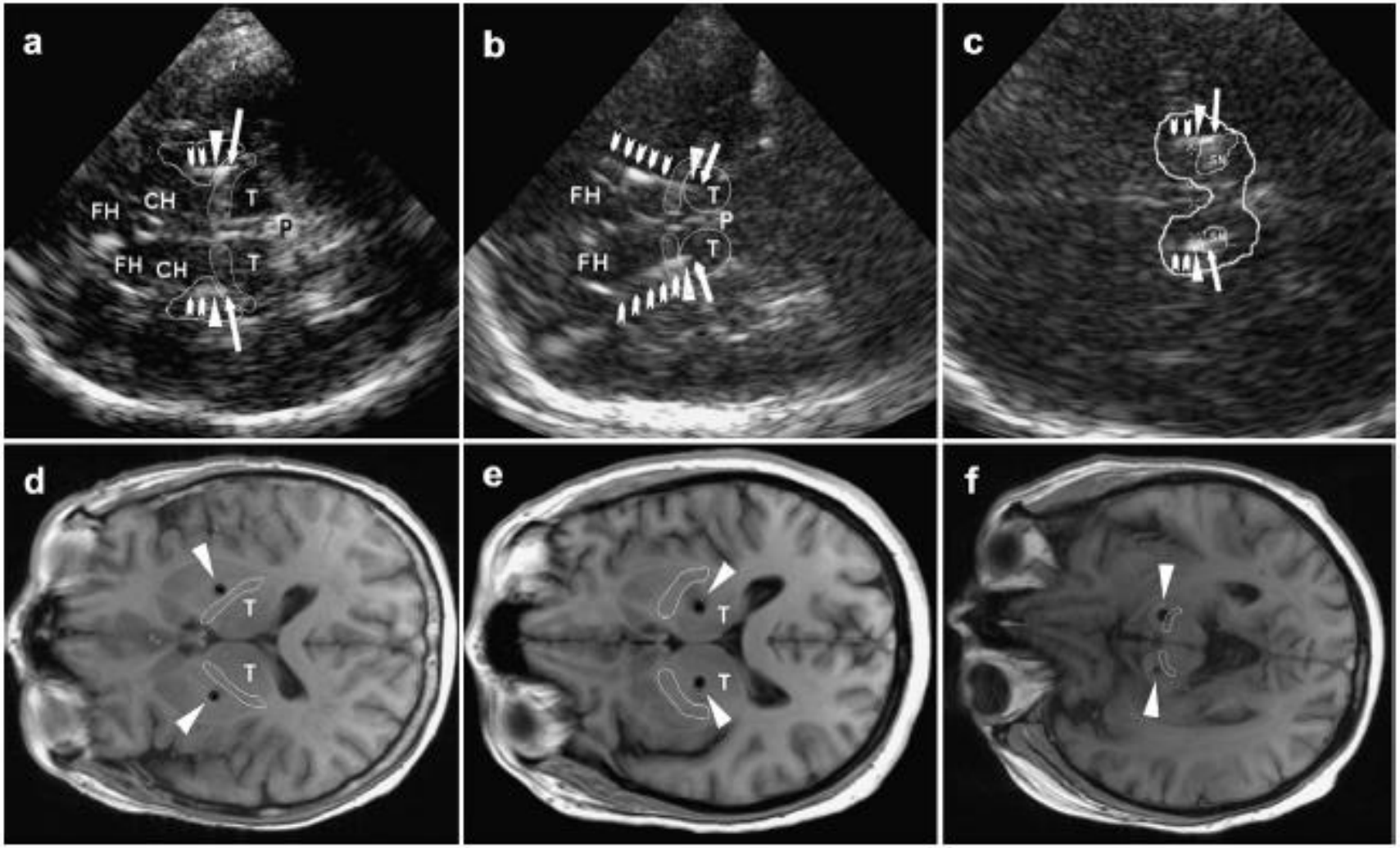
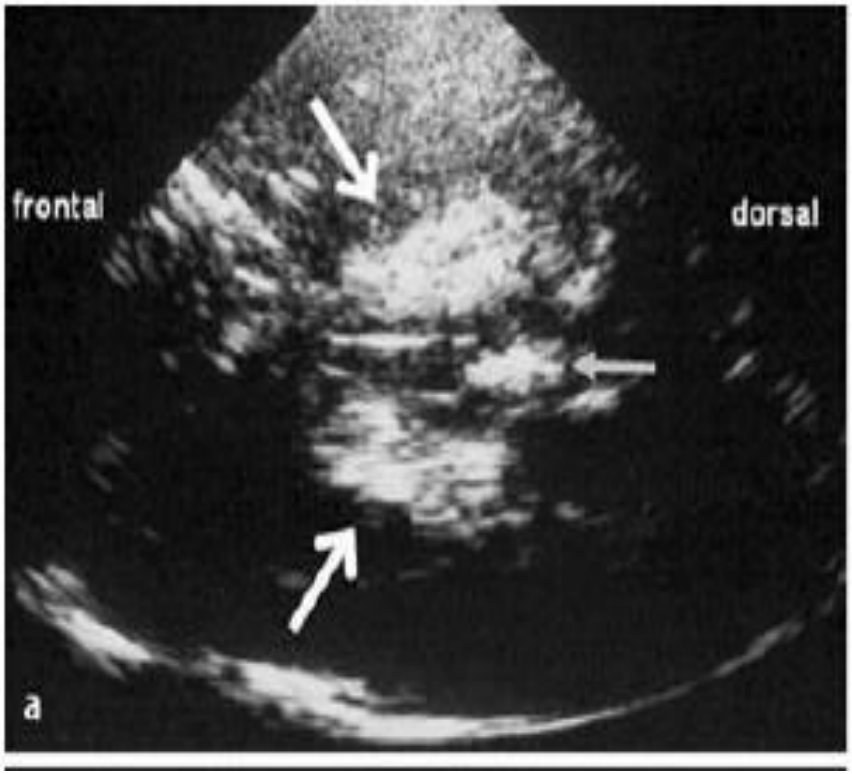
KEYWORDS
Transcranial sonography;
Deep brain stimulation;
Ultrasound-guided procedure;
Post-operative monitoring;
Electrode position control

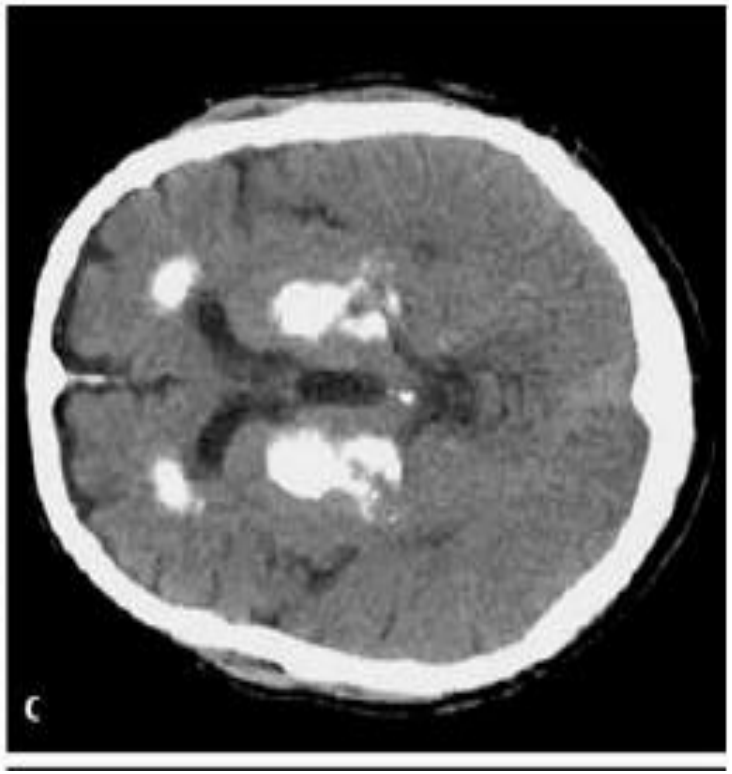
Summary Transcranial sonography (TCS) of the brain parenchyma meanwhile allows a high-resolution imaging of deep brain structures in the majority of adults. A new application of TCS is the intra- and post-operative visualization with TCS and the TCS-assisted insertion of deep brain stimulation (DBS) electrodes. In pilot studies it has been shown that the TCS-assisted insertion of DBS electrodes into the subthalamic nucleus and the globus pallidus interna is feasible and safe provided the exact knowledge on the extent of electrode TCS imaging artifacts. Even more, TCS can be recommended for the post-operative monitoring of DBS electrode position. Dislocation of a DBS electrode can be easily detected. In a recent longitudinal study we could demonstrate that TCS measures of lead coordinates agreed with MRI measures in anterior–posterior and medial–lateral axis, and that the TCS-based grading of optimal vs suboptimal lead location predicts the clinical 12 months outcome of patients with movement disorders. Currently, an international multi-center study is being planned to further prove the value of TCS in the post-operative monitoring of DBS electrode position. This trial is intended to start in 2012, and is still open for joining. The obvious advantages of TCS will promote its increasing use for the intra- and post-operative monitoring of deep brain implants.

TCS APPLICATIONS IN DBS



FAMILIAL IDIOPATIC BASAL GANGLIA CALCIFICATIONS





RESTLESS LEGS SYNDROME

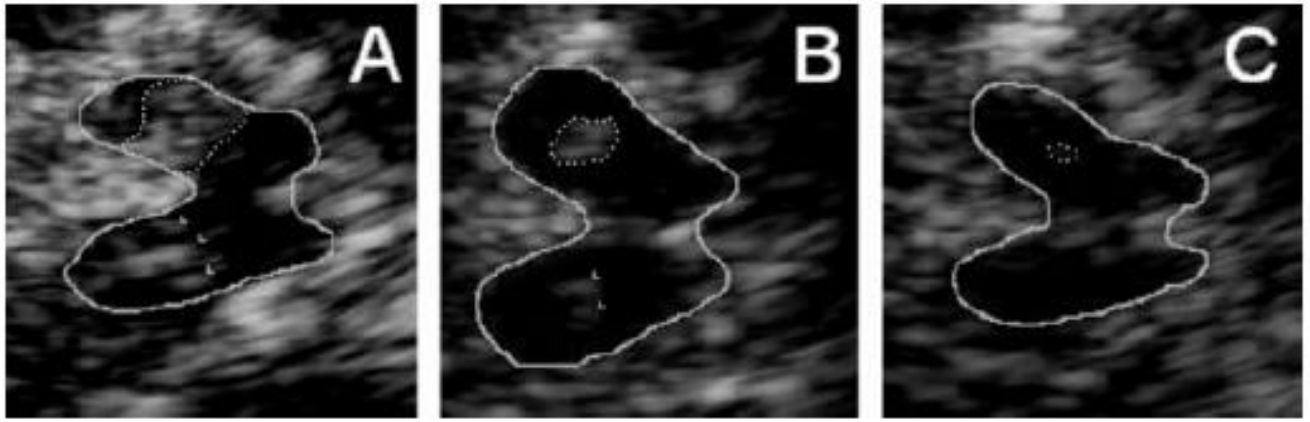
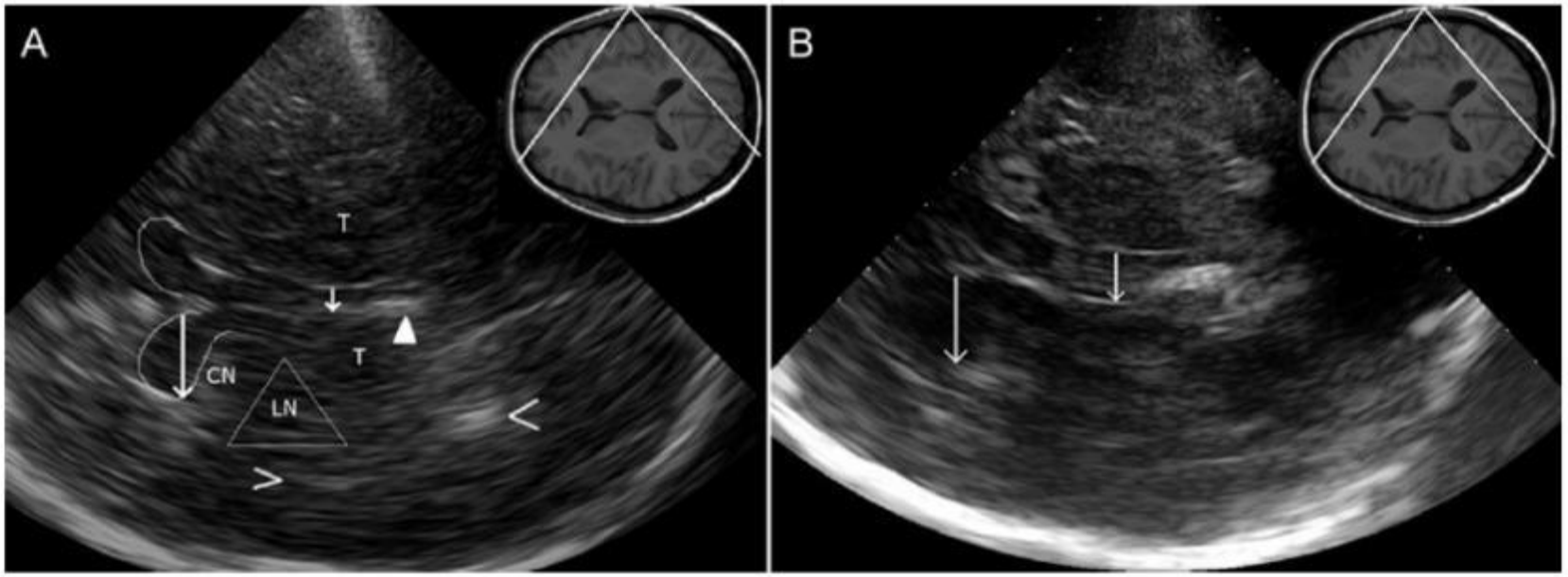


FIG. 1. Representative ultrasound images of the human mesencephalic brainstem. **A:** Patient with Parkinson's disease (PD, image for comparison). **B:** Healthy control. **C:** Restless legs syndrome (RLS) patient. Substantia nigra (SN, marked contralaterally with arrows) appears hyperechogenic in the hypoechogenic brainstem area (full line). The area of hyperechogenic SN signals is planimetrically measured from the ipsilateral side (dotted line). B shows a regularly sized SN area of echogenicity. A: SN hyperechogenicity (SN area ≥ 0.19 cm^2 on one or both sides) is typical for idiopathic PD. C: In the majority of RLS patients, the SN is hypoechogenic (SN sum area of both sides ≤ 0.2 cm^2) and is often not delineable contralaterally.

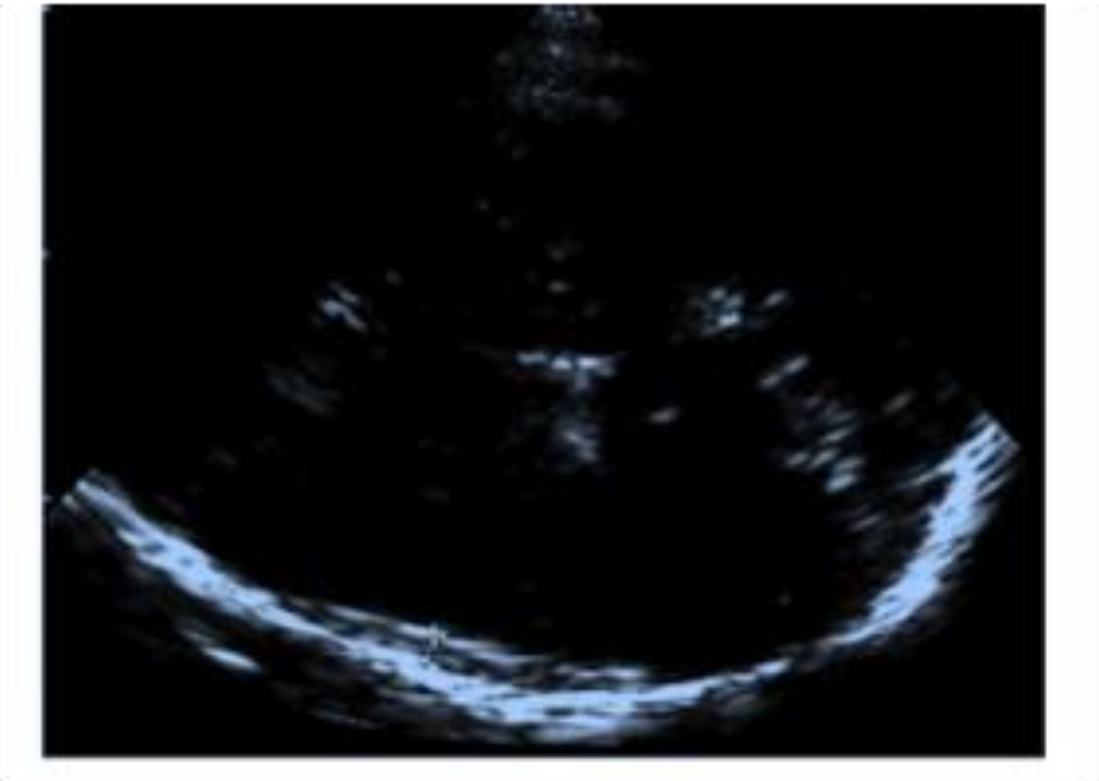
HYDROCEPHALUS



THIRD VENTRICLE AND FRONTAL HORN

AGE	FRONTAL HORN	THIRD VENTRICLE
< 60 YEARS	< 17 MM	< 7MM
> 60 YEARS	< 20 MM	< 10 MM

SUBDURAL HEMATOMA



frontiers in Neurology

ORIGINAL RESEARCH
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doi: 10.3389/fneur.2018.00374

Bedsided Transcranial Sonographic Monitoring for Expansion and Progression of Subdural Hematoma Compared to Computed Tomography

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[1]Department of Neurology, University Medical Center, University of Freiburg, Freiburg, Germany, [2]Department of Neurology, Albertinen Hospital Hamburg, Teaching Hospital of the University of Hamburg, Hamburg, Germany

Introduction: Transcranial high-resolution ultrasonography reliably allows diagnosis and monitoring of intracerebral hemorrhage in adults. Sonographic monitoring of subdural hematoma (SDH) has not been evaluated in adults so far. This study investigates the reliability of transcranial gray-scale sonography (TGS) in monitoring acute and chronic SDH in adults.

Methods: TGS was performed in 47 consecutive patients with either acute or chronic SDH confirmed by cerebral CT. Four patients were excluded due to insufficient bone window. After identification of SDH in TGS extent was measured and correlated with extent of SDH on cerebral computer tomography (CCT). If possible measurement was performed at least on 2 days to evaluate the possibility to monitor SDH with TGS.

Results: In 43 patients with SDH, 76 examinations were performed with 2 examinations in 23 patients and 3 examinations in 10 patients. Overall extent of SDH correlated significantly between TGS and CCT ($r = 0.962$). Accordingly correlation was high during each single examination time point. In patients in need for surgical evacuation sonographic measurement yielded a sensitivity of 90.9% and specificity of 93.8% in predicting surgical evacuation ($p < 0.001$).

Discussion: Imaging of SDH with TGS is possible in patients with SDH and extent of SDH correlates significantly between TGS and CCT during initial as well as during follow-up examination. Thus monitoring of SDH with TGS at patients' bedside is possible.

Keywords: subdural hematoma, neurotrauma, neurocritical care, transcranial sonography, monitoring

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Transcranial Duplex Sonography Predicts Outcome following an Intracerebral Hemorrhage

P. Camps-Renom, J. Méndez, E. Granell, F. Casoni, L. Prats-Sánchez, A. Martínez-Domeño, D. Guisado-Alonso, J. Martí-Fàbregas, and R. Delgado-Mederos

ABSTRACT

BACKGROUND AND PURPOSE: Several radiologic features such as hematoma volume are related to poor outcome following an intracerebral hemorrhage and can be measured with transcranial duplex sonography. We sought to determine the prognostic value of transcranial duplex sonography in patients with intracerebral hemorrhage.

MATERIALS AND METHODS: We conducted a prospective study of patients diagnosed with spontaneous intracerebral hemorrhage. Transcranial duplex sonography examinations were performed within 2 hours of baseline CT, and we recorded the following variables: hematoma volume, midline shift, third ventricle and lateral ventricle diameters, and the pulsatility index in both MCAs. We correlated these data with the CT scans and assessed the prognostic value of the transcranial duplex sonography measurements. We assessed early neurologic deterioration during hospitalization and mortality at 1-month follow-up.

RESULTS: We included 35 patients with a mean age of 72.2 ± 12.8 years. Median baseline hematoma volume was 9.85 mL (interquartile range, 2.74–68.29 mL). We found good agreement and excellent correlation between transcranial duplex sonography and CT when measuring hematoma volume ($r = 0.791$; $P < .001$) and midline shift ($r = 0.827$; $P < .001$). The logistic regression analysis with transcranial duplex sonography measurements showed that hematoma volume was an independent predictor of early neurologic deterioration (OR, 1.078; 95% CI, 1.023–1.135) and mortality (OR, 1.089; 95% CI, 1.020–1.160). A second regression analysis with CT variables also demonstrated that hematoma volume was associated with early neurologic deterioration and mortality. When we compared the rating operation curves of both models, their predictive power was similar.

CONCLUSIONS: Transcranial duplex sonography showed an excellent correlation with CT in assessing hematoma volume and midline shift in patients with intracerebral hemorrhage. Hematoma volume measured with transcranial duplex sonography was an independent predictor of poor outcome.

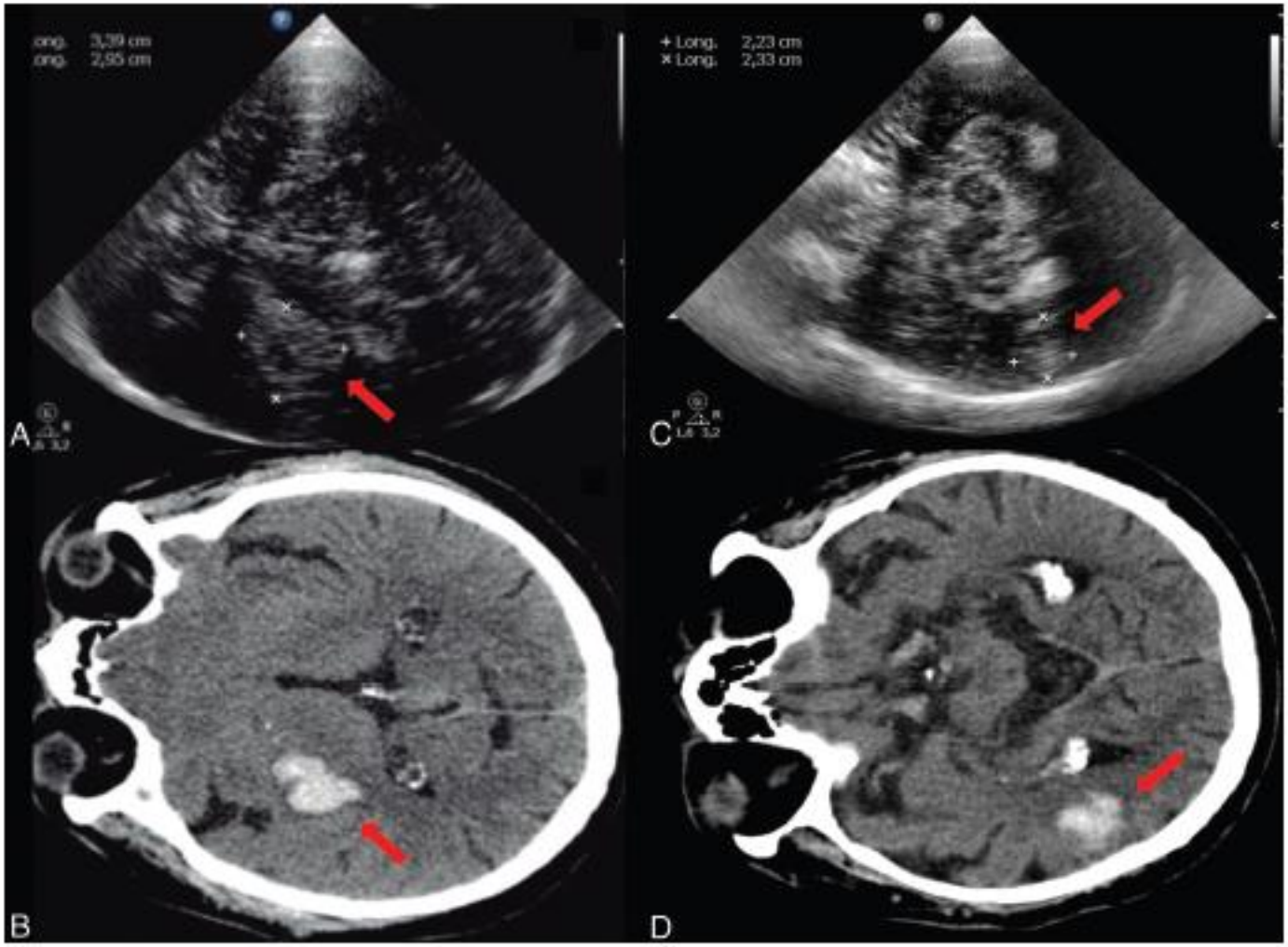


FIG 1. *A* and *B*, A right basal ganglia hemorrhage, assessed by TDS and CT, respectively. The *red arrows* correspond to the axial and longitudinal diameters. *C* and *D*, A right temporal lobar ICH in another patient, assessed by TDS and CT, respectively.

PLOS ONE

RESEARCH ARTICLE

The use of transcranial ultrasound and clinical assessment to diagnose ischaemic stroke due to large vessel occlusion in remote and rural areas

Daria Antipova[1]*, Leila Eadie[1], Stephen Makin[1], Helen Shannon[2], Philip Wilson[1], Ashish Macaden[3]

1 Centre for Rural Health, University of Aberdeen, Inverness, United Kingdom, **2** Department of Radiology, Raigmore Hospital, NHS Highland, Inverness, United Kingdom, **3** Department of Stroke and Rehabilitation Medicine, Raigmore Hospital, NHS Highland, Inverness, United Kingdom

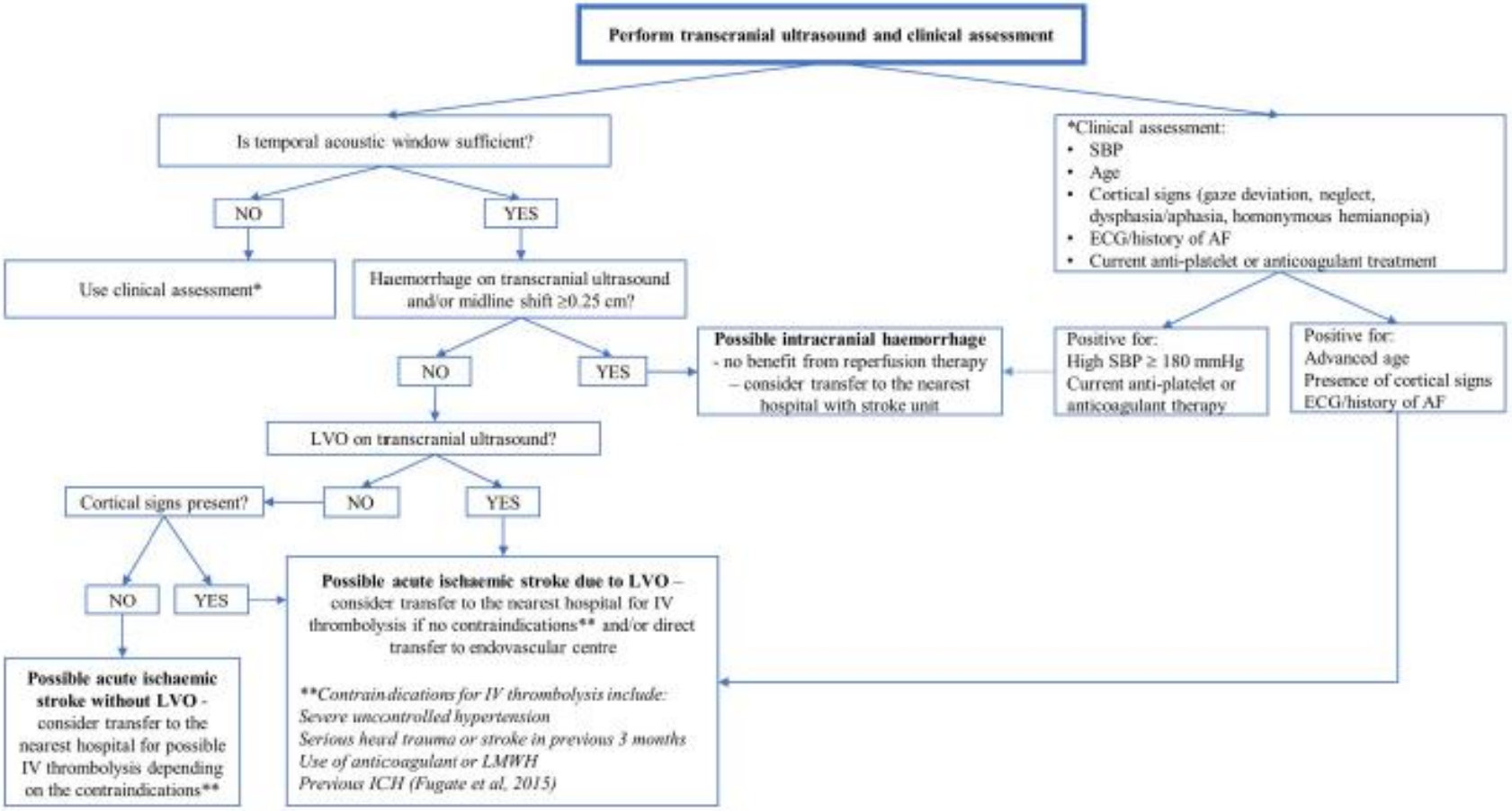
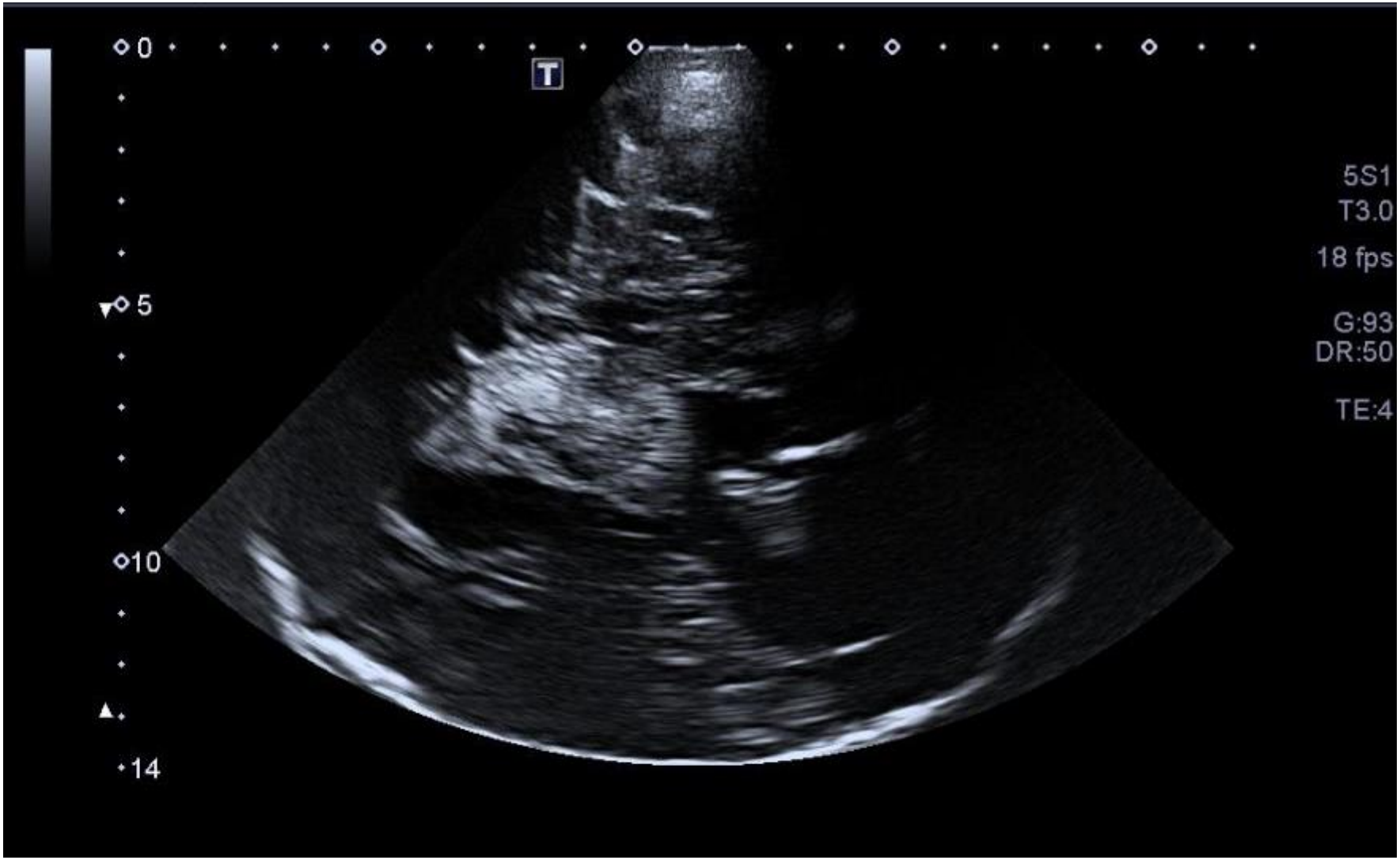


Fig 7. Tentative "TUCA" model for pre-hospital triage of suspected stroke patients based on transcranial ultrasound and clinical assessment for remote and rural communities. According to the current guidelines in the UK IV tPA can be given within 4.5 hours of stroke symptom onset. Mechanical thrombectomy can be performed within 6 hours of the onset of stroke symptoms; an extended time window of 6 to 24 hours from the time the patient was last known to be well can be offered in selected cases. Abbreviations: AF—atrial fibrillation; ECG—electrocardiography; ICH—intracranial haemorrhage; IV tPA—intravenous thrombolysis with tissue plasminogen activator; LMWH—low molecular weight heparin; LVO—large vessel occlusion; SBP—systolic blood pressure (mmHg).

TREMOR

- A 24 years-old man presented to our laboratory with a three months history of tremor sensation in his left arm.
- The neurological examination showed slight postural and telekinetic tremor in his left arm.
- No history of familial tremor was present.
- He didn’t take any drugs.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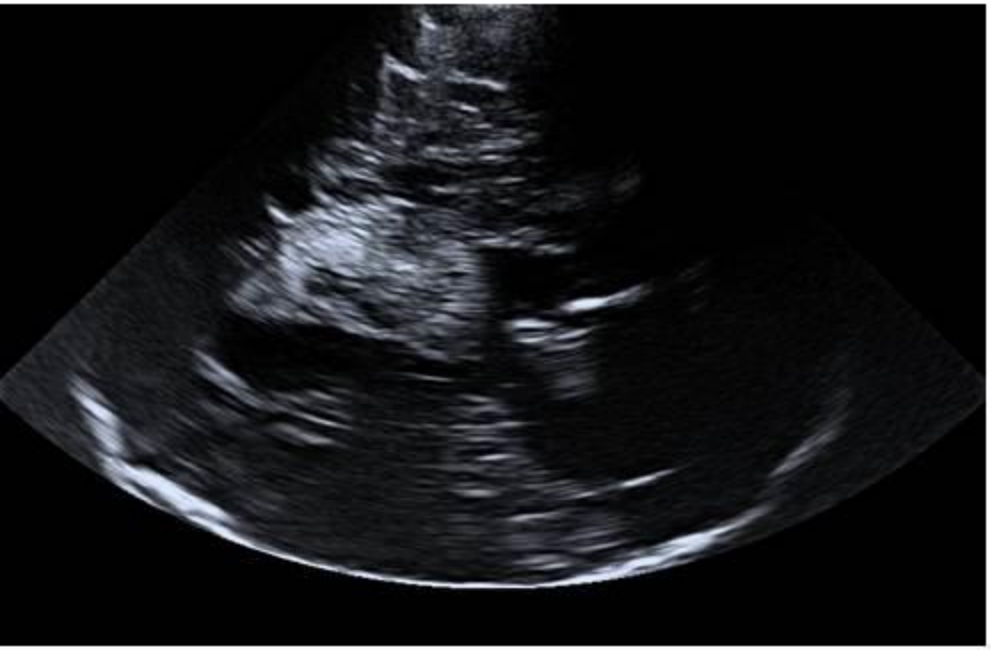

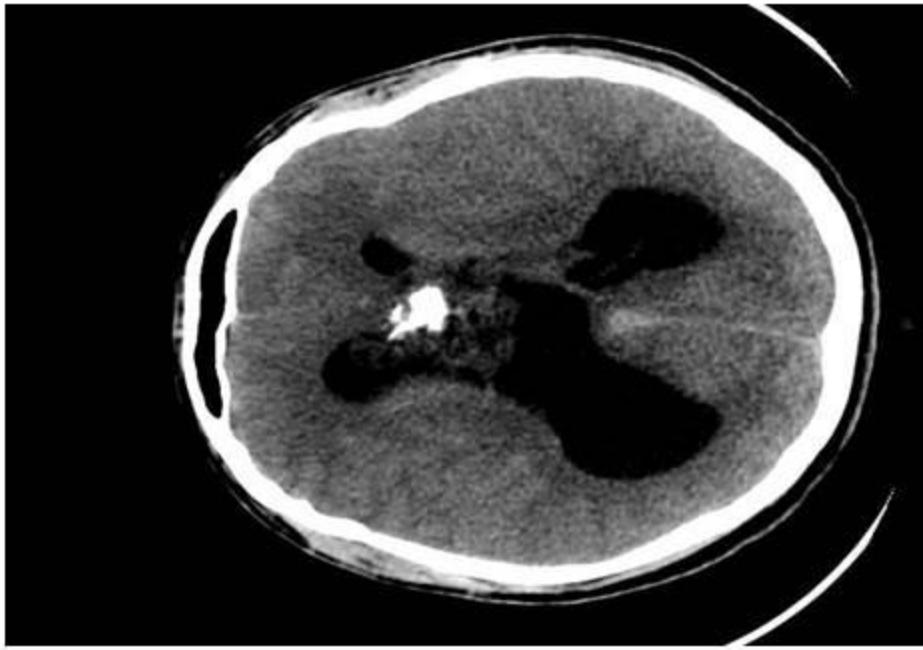

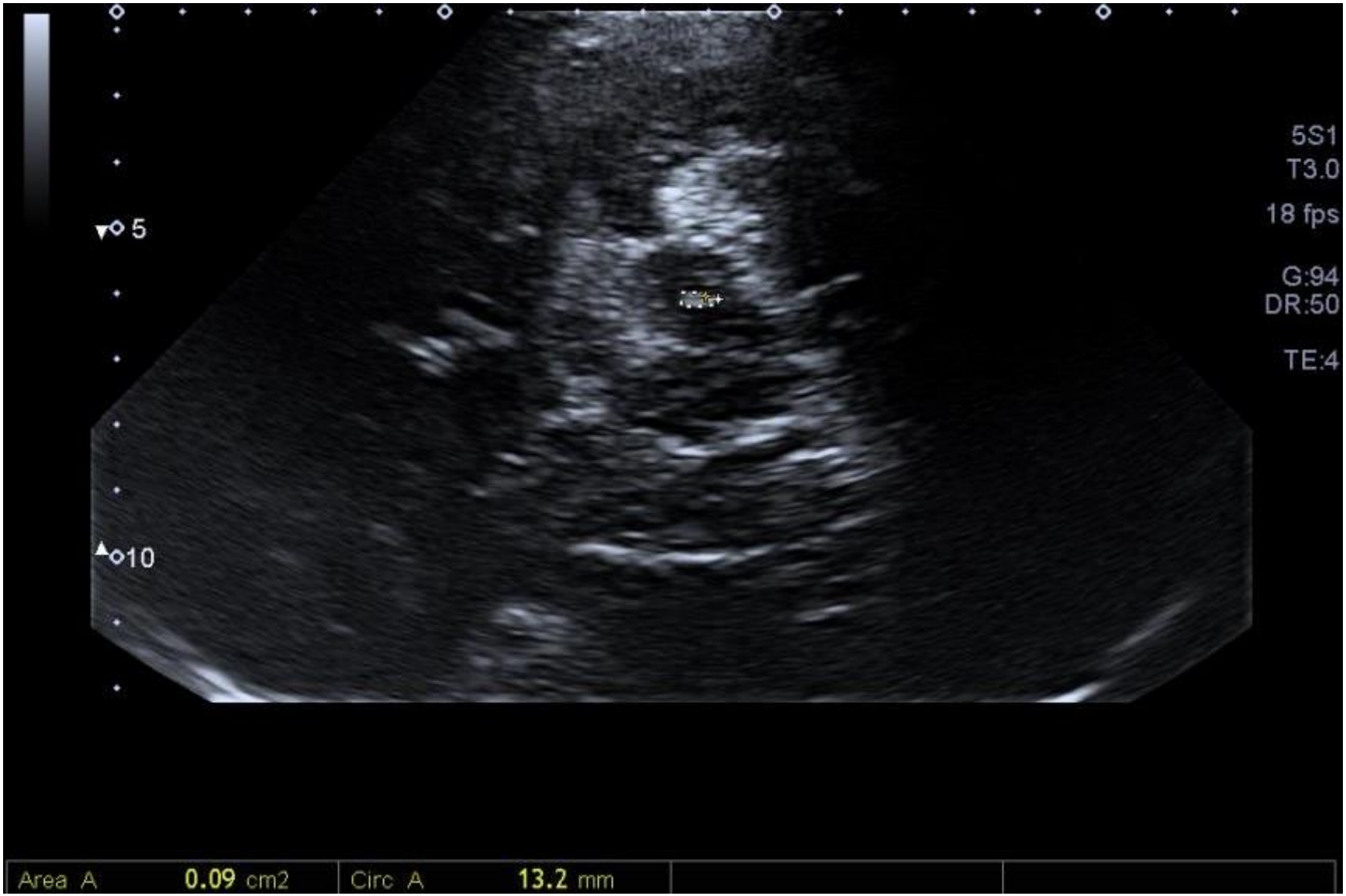
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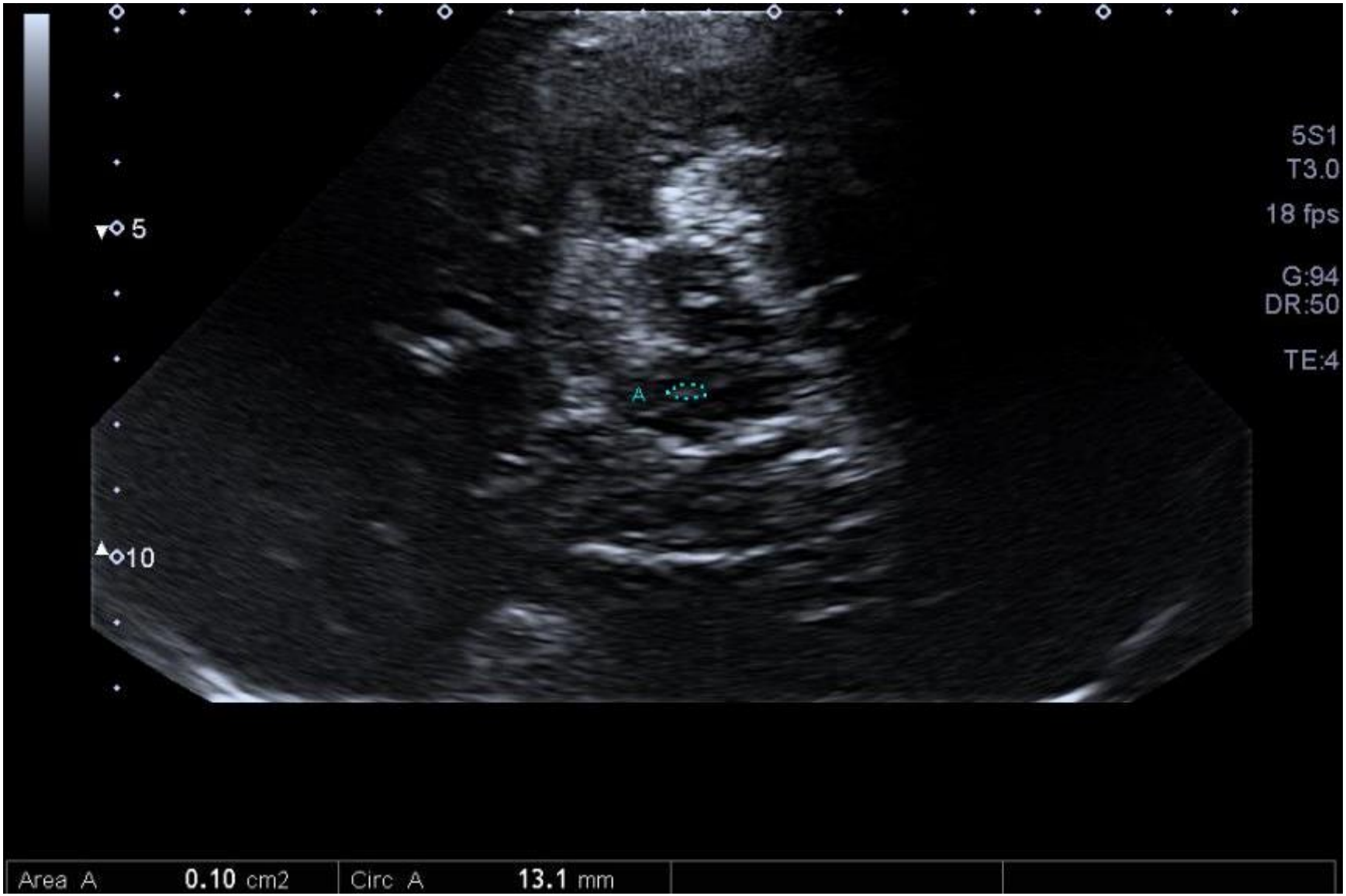
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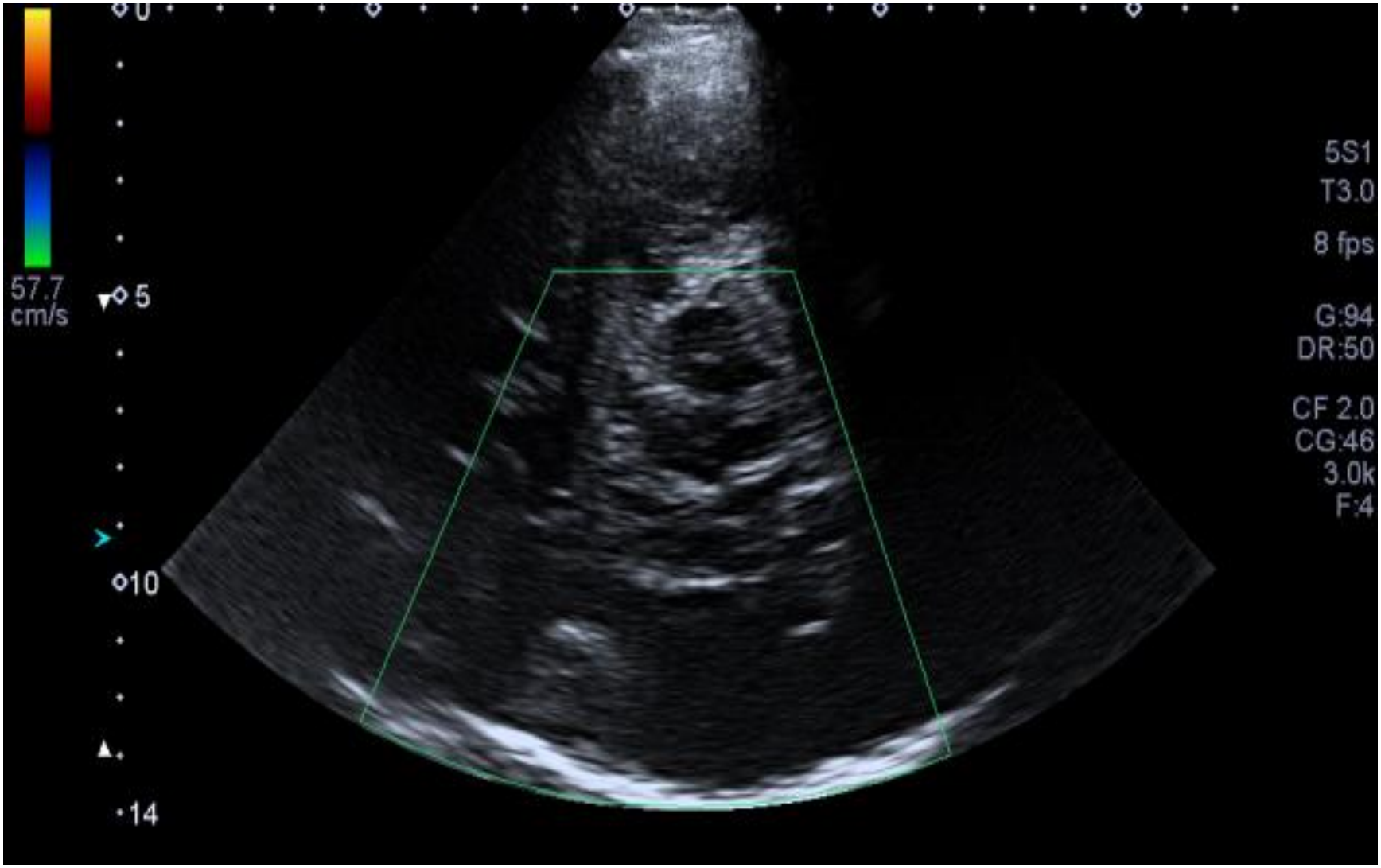
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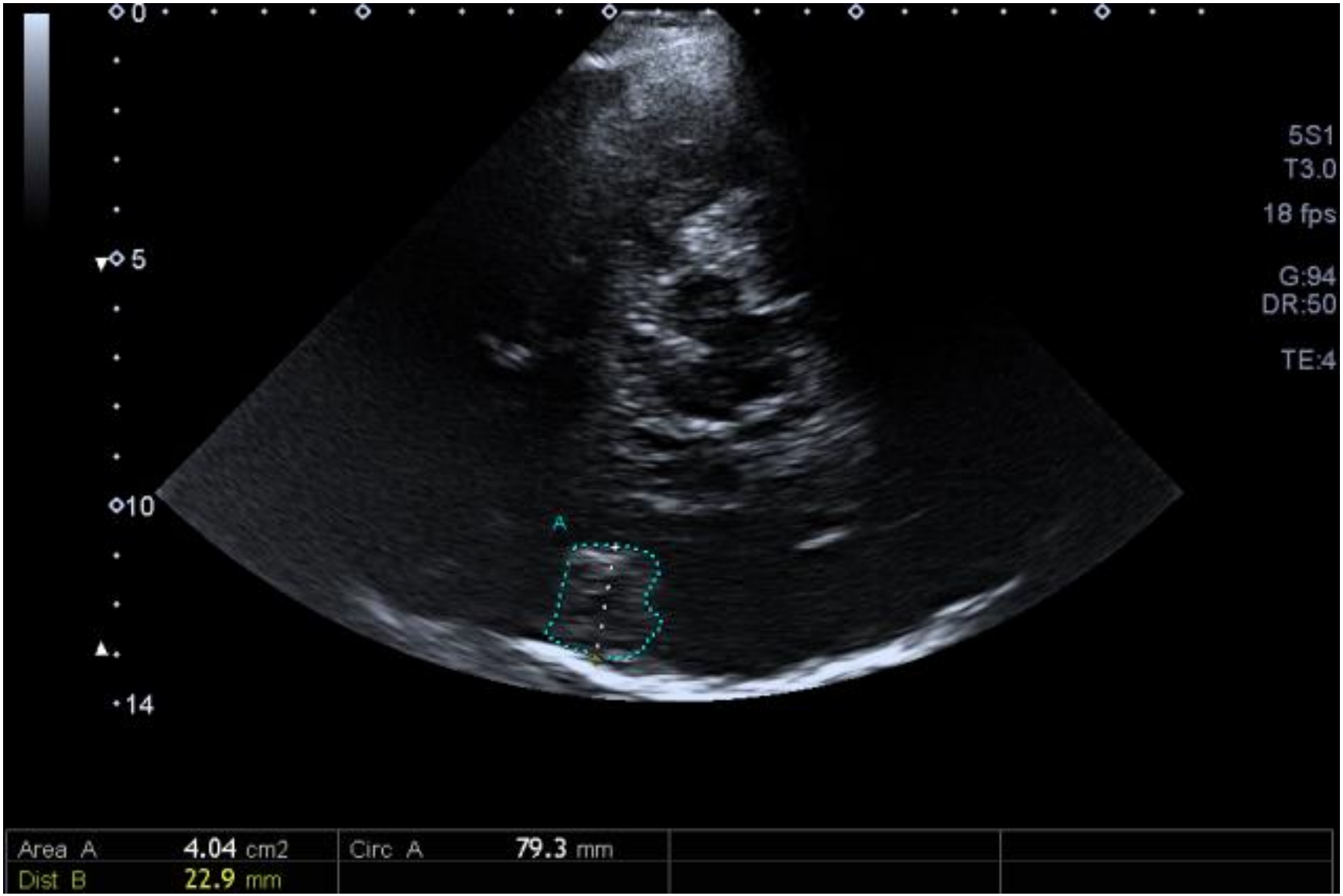
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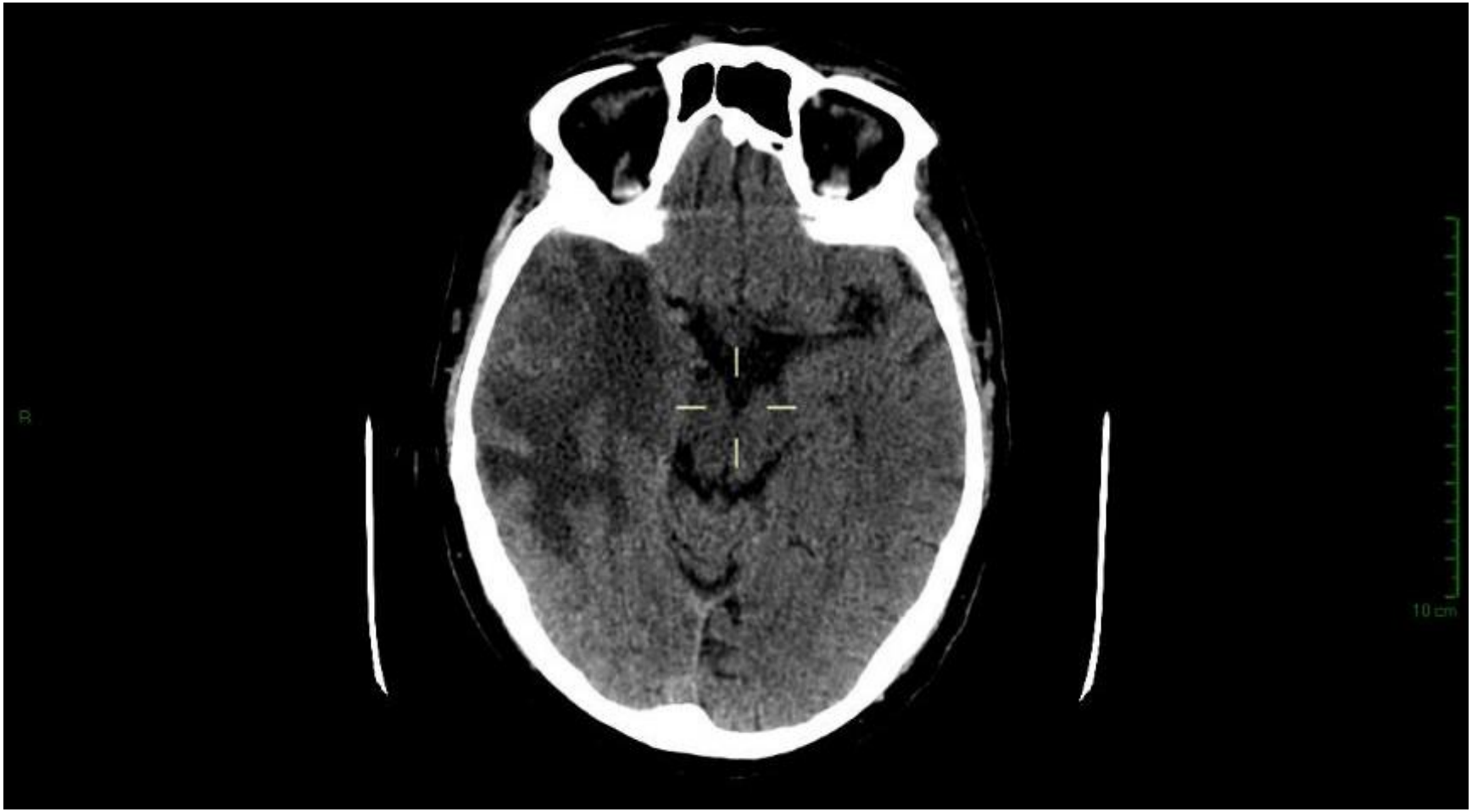
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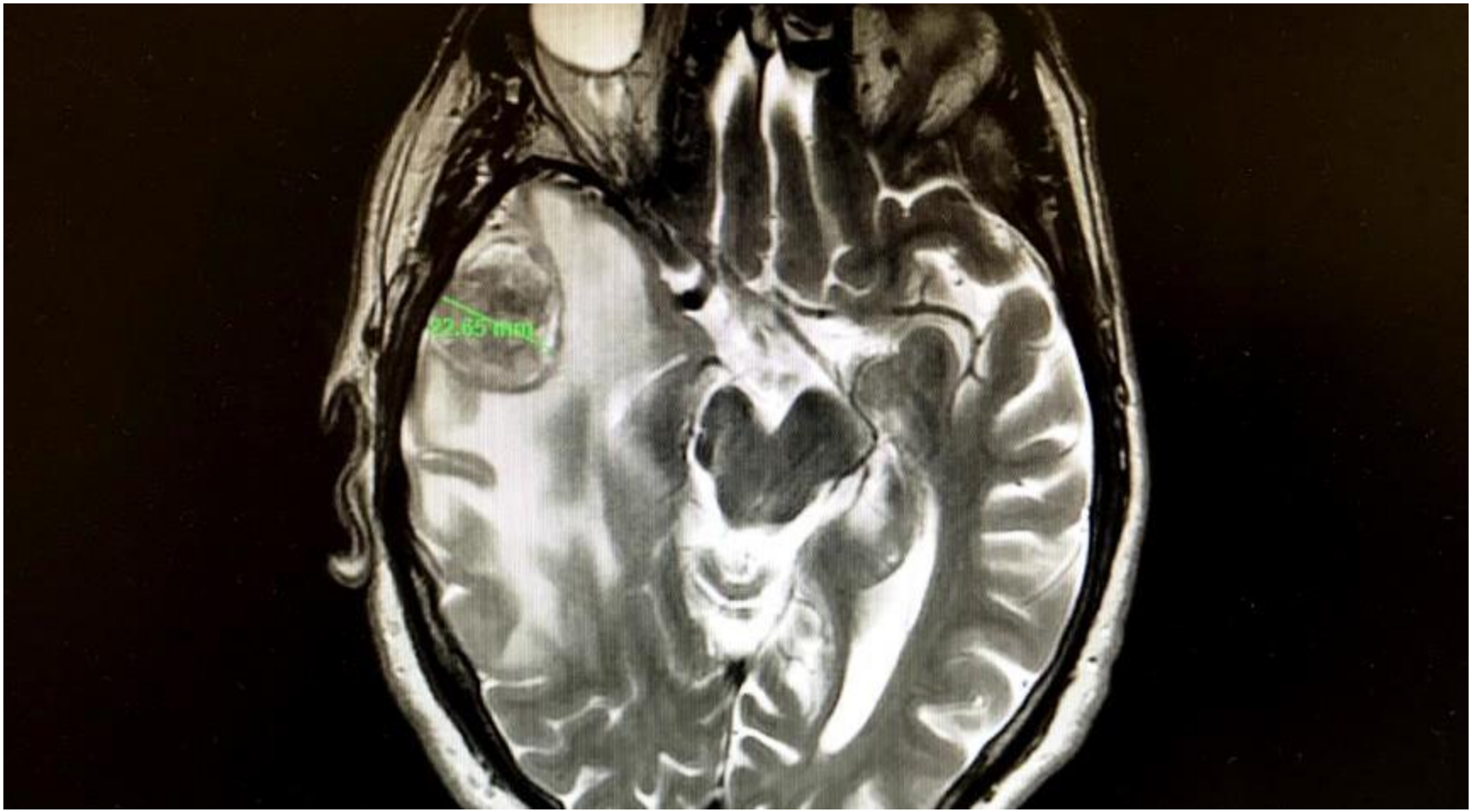
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An unusual gait disorder at the Emergency Department: role of the quantitative assessment of parenchymal transcranial Doppler sonography

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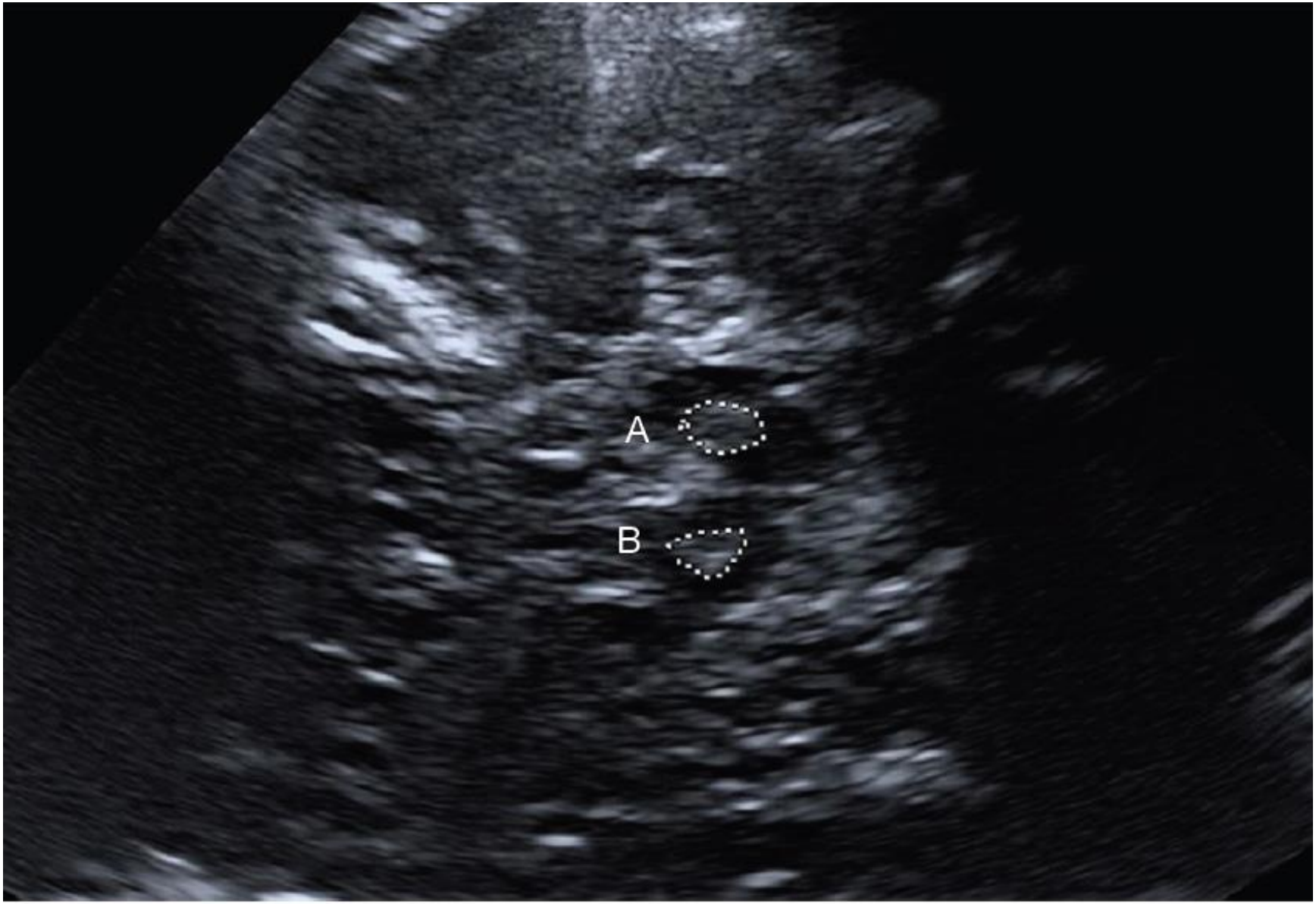
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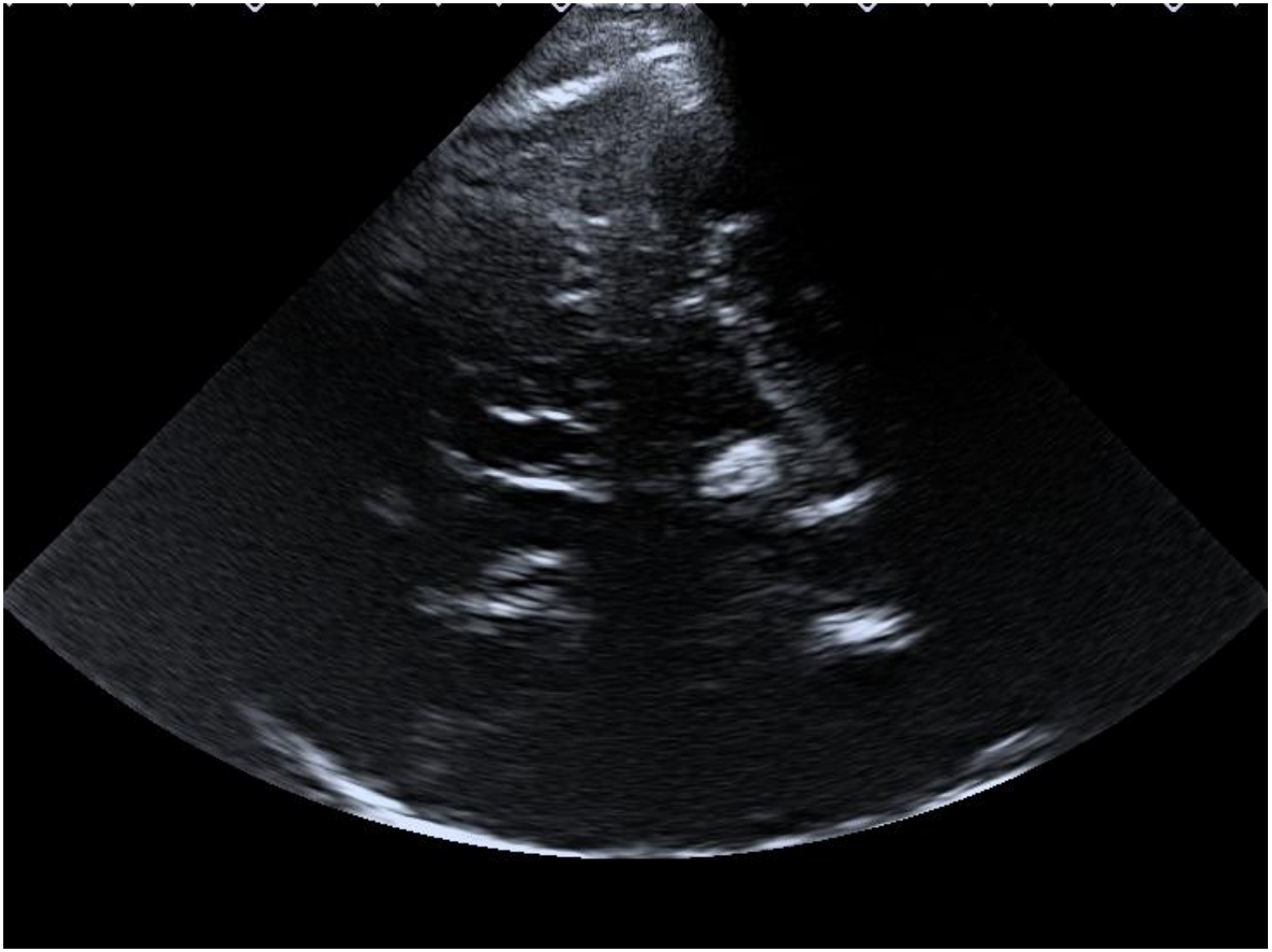

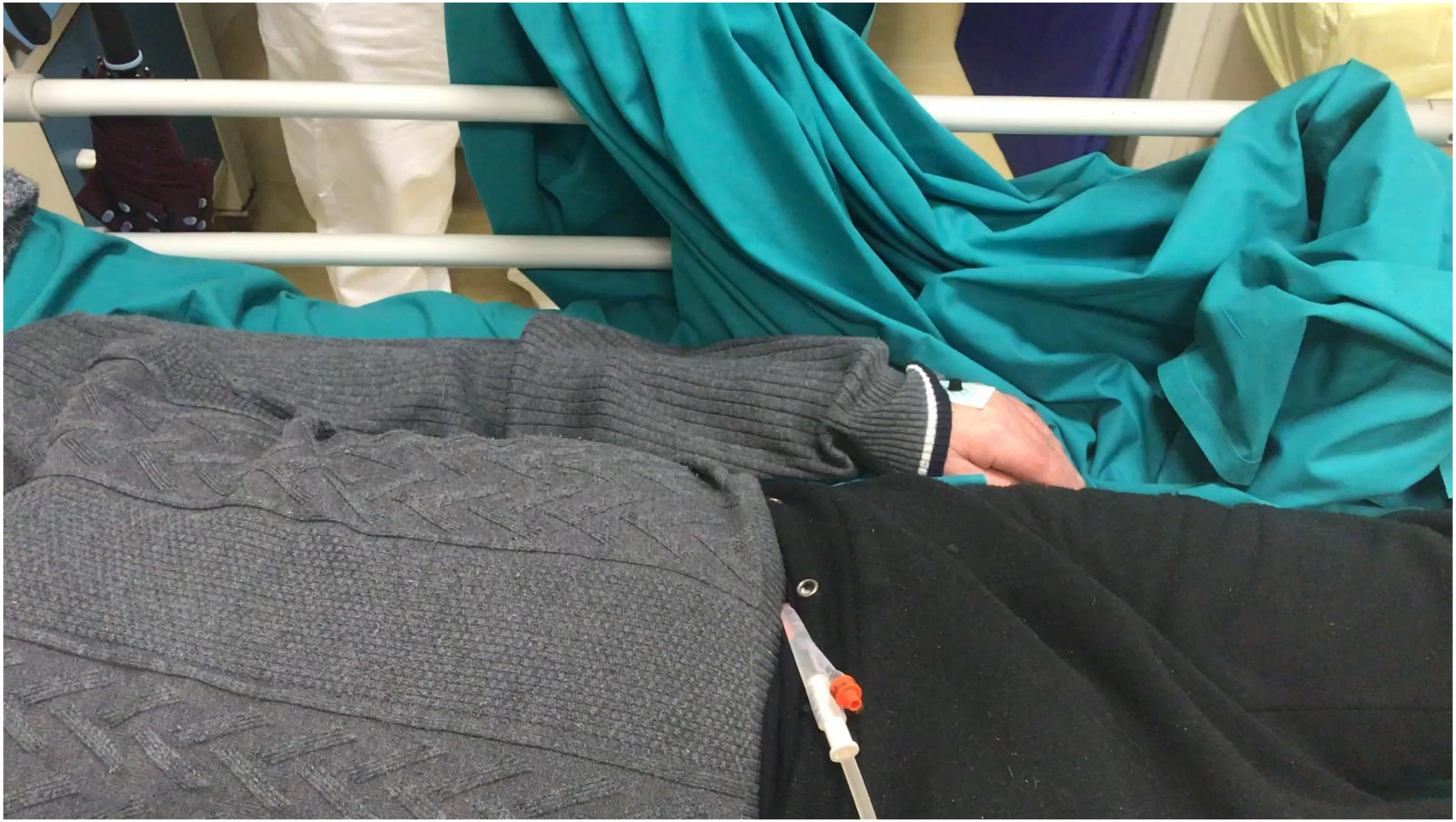

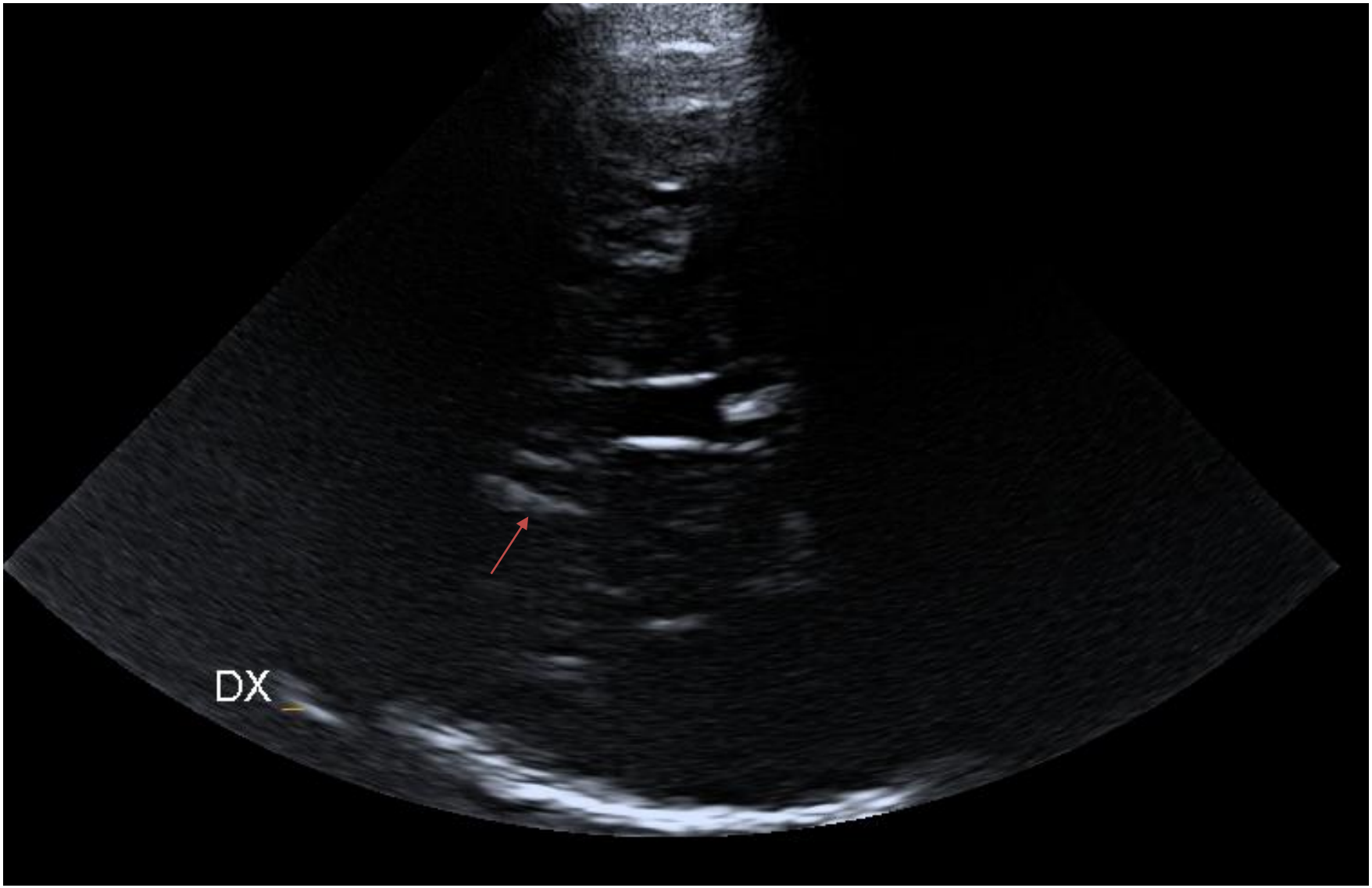
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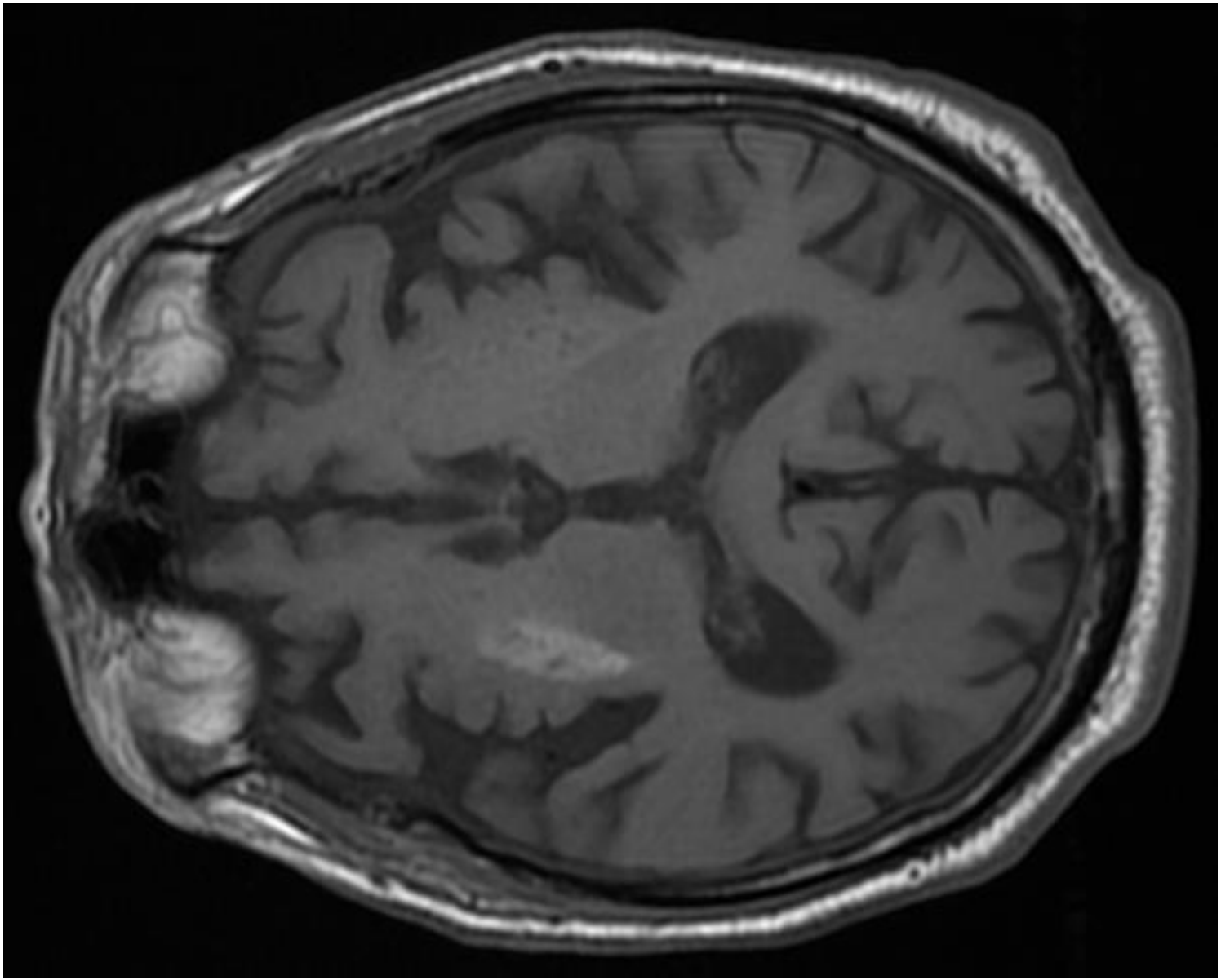

diagnostics

MDPI

Case Report

Diabetic Striatopathy: Parenchymal Transcranial Sonography as a Supplement to Diagnosis at the Emergency Department

Massimiliano Godani [1] and Giuseppe Lanza [2,3,*]

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Abstract: *Background*: Diabetic striatopathy (DS) is a rare condition with a debated pathophysiology; a local metabolic dysfunction is the most likely hypothesis. We present a case of DS mimicking an acute stroke, outline a few uncommon/atypical features, and report for the first time the parenchymal transcranial sonography (pTCS) findings. *Case Report*: An 86-year-old man, treated for insulin-dependent diabetes, presented at an emergency department because of the occurrence of isolated choreo-athetotic movements in his left limbs with fluctuations in the location, frequency, and duration. The blood glucose level was 569 mg/dL. Both urgent and follow-up brain computed tomography (CT) were negative for recent lesions whereas pTCS revealed hyperechogenicity in the right lenticular nucleus. Subsequent magnetic resonance imaging (MRI) showed T1-weighted hyperintensity in the right putamen with negative diffusion-weighted imaging. The symptoms were responsive to glucose control and haloperidol administration, although they persisted during sleep. *Conclusions*: Unlike previously described cases characterized by hemichorea and/or hemiballism, our patient presented with a stroke-like onset of unilateral irregular choreo-athetotic movements. Notably, based on CT alone, it would not have been possible to distinguish DS from a stroke. In this scenario, the pTCS hyperechogenicity of the right lenticular nucleus helped to hypothesize a metabolic disorder, which was subsequently confirmed by MRI.

Keywords: diabetic striatopathy; differential diagnosis; neuroimaging; metabolic dysfunction; emergency

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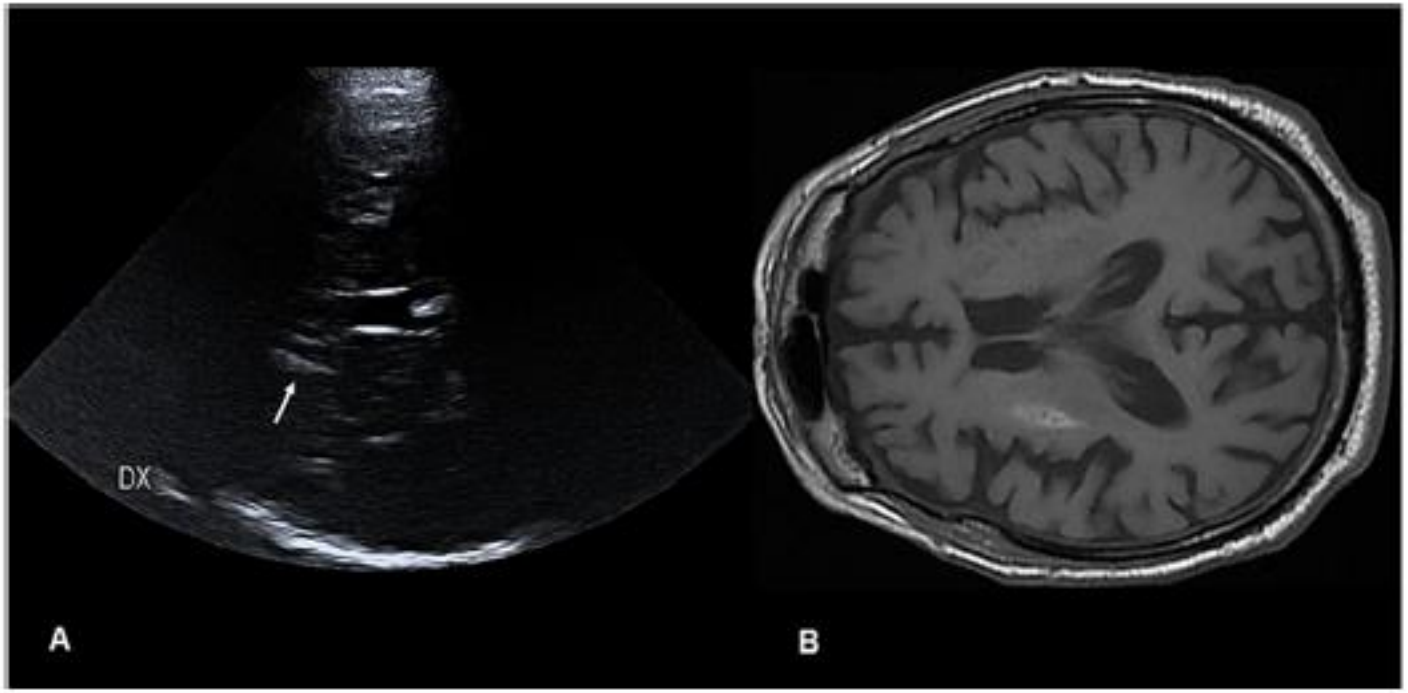

Figure 1. (**A**) (*left panel*) Parenchymal transcranial sonography showing hyperechogenicity in the right (DX) lenticular nucleus (*white arrow*); (**B**) (*right panel*) axial brain magnetic resonance imaging showing a T1-weighted hyperintensity in the right putamen.

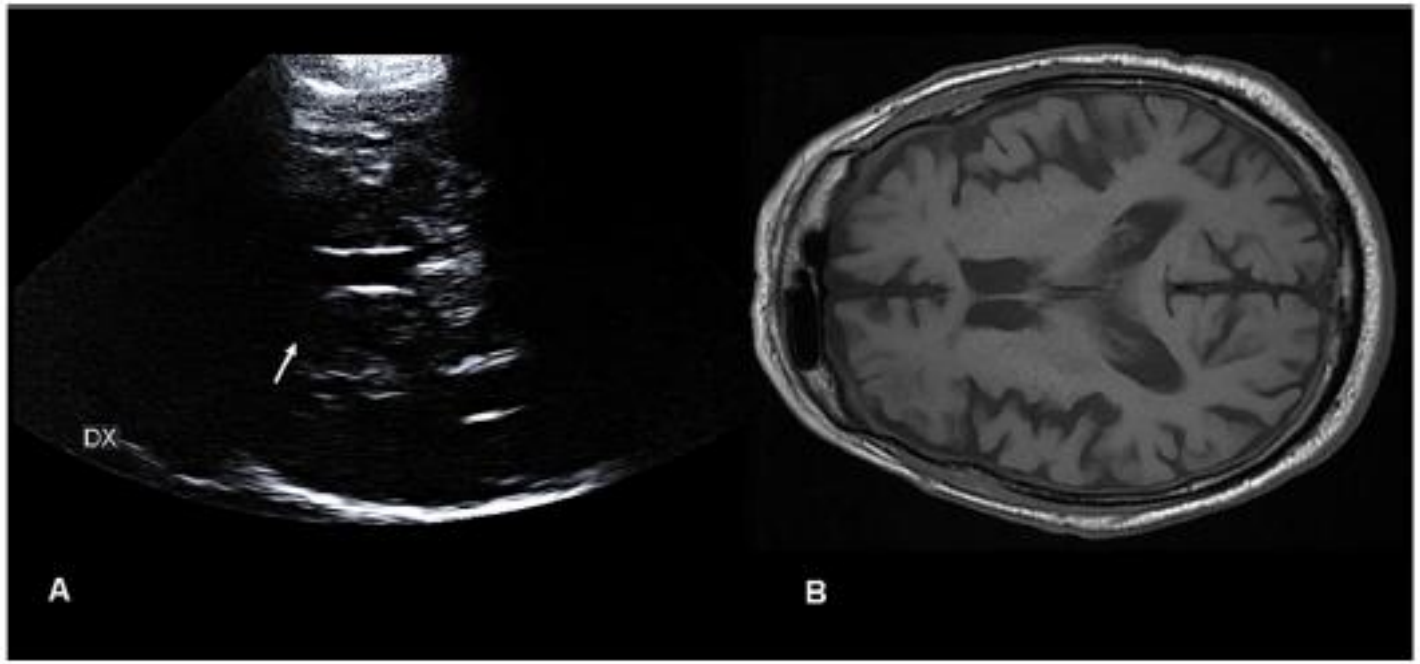

Figure 2. (**A**) (*left panel*) Parenchymal transcranial sonography showing the complete resolution of the hyperechogenicity in the right (DX) lenticular nucleus previously observed (*white arrow*); (**B**) (*right panel*) axial brain magnetic resonance imaging showing normal T1-weighted intensity in the right putamen.

LIMITATIONS AND ADVANTAGES

- **The main limitation is the dependence of image quality from temporal acoustic bone and/or the sonographer's experience.**

- **The midbrain structures are not or only partial assessable in 5-10% of white individuals while the basal ganglia in 10-20%.**

- **The advantages are wide availability, the same sensitivity of functional neuroimaging without invasiveness, low costs and short investigation times**

CONCLUSIONS

pTCS is an essential investigation for a movement disorders specialist but in our experience it could be very helpful also as diagnostic screening tool especially in patients coming from Emergency.

We suggest using pTCS as an extension of the clinical neurological examination

XXI CORSO NAZIONALE DI

ULTRASONOLOGIA VASCOLARE DIAGNOSI E TERAPIA

20-22 APRILE 2023

E IN ITALIA?

Nelle raccomandazioni per la diagnosi di malattia di Parkinson promosse da una *task force* della European Federation of Neurological Societies (EFNS) e della Movement Disorder Society-European Section, l'utilizzo della ecografia transcranica è indicata con un livello di evidenza A[9]. Si rimanda al paragrafo corrispondente del quesito 6 per maggiori dettagli sullo schema di classificazione delle prove per i test diagnostici promosso dalla EFNS[10]. La *task force* sottolinea che questa tecnica non è universalmente utilizzata e richiede una particolare esperienza. Inoltre a causa della bassa specificità dell'ecografia transcranica nella diagnosi di malattia di Parkinson, questa tecnica dovrebbe essere utilizzata insieme ad altri test.

Considerando le finalità delle raccomandazioni redatte in questa linea guida, orientate verso la pratica clinica corrente e la sanità pubblica, e le difficoltà nell'esecuzione del test (con la necessità di un operatore esperto e la limitazione imposta all'esecuzione dell'esame subordinata alla qualità della finestra trans temporale) si ritiene di non dover raccomandare l'uso dell'ecografia transcranica nella malattia di Parkinson.

TCS IN secondary PARKINSONISM

- Secondary parkinsonism syndromes are induced by causes other than degeneration of the nigrostriatal system.
- CT and MRI usually can reveal the etiology of these movement disorders.
- TCS findings is equally important or even more so than the findings from CT or MRI because calcifications can be seen earlier with ultrasound.
- TCS is very useful as screening or monitoring tool

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Analyzing the co-localization of substantia nigra hyper-echogenicities and iron accumulation in Parkinson's disease: A multi-modal atlas study with transcranial ultrasound and MRI

Seyed-Ahmad Ahmadi[a,b,d], Kai Bötzel[a], Johannes Levin[a], Juliana Maiostre[a], Tassilo Klein[e], Wolfgang Wein[f], Verena Rozanski[g], Olaf Dietrich[c], Birgit Ertl-Wagner[c,h], Nassir Navab[d], Annika Plate[a,*]

In this work, we acquired and analyzed a multi-modal atlas of the adult human brain incorporating TCS and QSM-MRI. Both modalities are capable of detecting iron accumulation, which accompanies the neurodegenerative process in Parkinson's disease. Our study concludes that PD-related increases in TCS and QSM signals demonstrate a high overlap along the entire axial extent of the midbrain. We confirm the established finding of iron accumulation in the substantia nigra pars compacta, and produce evidence that the ventral tegmental area and its sub-nuclei feature comparable alterations as well. Our results imply an earlier functional involvement of the mesolimbic system, rather than an isolated nigrostriatal loss of dopamine neurons.

ORIGINAL CONTRIBUTION

Transcranial Brain Sonography Findings in Discriminating Between Parkinsonism and Idiopathic Parkinson Disease

Uwe Walter, MD; Dirk Dressler, MD; Thomas Probst, MD; Alexander Wolters, MD; Mazen Abu-Mugheisib, MD; Matthias Wittstock, MD; Reiner Benecke, MD

Background: In several pilot studies, transcranial brain sonography findings of substantia nigra and lenticular nucleus discriminated between idiopathic Parkinson disease (PD) and atypical parkinsonian disorders.

Objective: To study the use of transcranial brain sonography in excluding the diagnosis of idiopathic PD in patients with sporadic parkinsonism.

Design and Setting: All patients with parkinsonism admitted to our movement disorder clinic from January 1, 2003, through December 31, 2005, who fulfilled clinical diagnostic criteria for definite PD, probable parkinsonian variant of multiple-system atrophy (MSA-P), or probable progressive supranuclear palsy (PSP) were prospectively studied with transcranial brain sonography by an investigator blinded to clinical diagnoses.

Patients: Eligible patients included 138 with sporadic idiopathic PD (82 men and 56 women; mean±SD age, 67.1±9.8 years; mean±SD disease duration, 7.5±6.3 years; mean±SD motor score on the Unified Parkinson Disease Rating Scale, 32.6±18.1), 21 with MSA-P (10 men and 11 women; mean±SD age, 65.4±9.5 years; mean±SD duration of disease, 3.1±2.0 years; mean±SD motor score, 33.5±16.1), and 22 with PSP (13 men and 9 women; mean±SD age, 71.2±5.5 years; mean±SD duration of disease, 3.4±2.4 years; mean±SD motor score, 46.2±18.9). In 7 patients, transcranial brain sonography was not possible owing to insufficient temporal acoustic bone windows.

Main Outcome Measures: Sensitivity, specificity, and predictive value of transcranial brain sonography in indicating an atypical parkinsonian syndrome rather than idiopathic PD in patients with sporadic parkinsonism.

Results: Normal echogenic substantia nigra indicated MSA-P rather than PD (sensitivity, 90%; specificity, 98%; positive predictive value, 86%), whereas third-ventricle dilatation of more than 10 mm in combination with lenticular nucleus hyperechogenicity indicated PSP rather than PD (sensitivity, 84%; specificity, 98%; positive predictive value, 89%). Normal echogenic substantia nigra combined with lenticular nucleus hyperechogenicity indicated MSA-P or PSP (sensitivity, 59%; specificity, 100%; positive predictive value, 100%). In parkinsonism with age at onset younger than 60 years, normal echogenic substantia nigra alone indicated MSA-P or PSP (sensitivity, 75%; specificity, 100%; positive predictive value, 100%).

Conclusions: Distinct transcranial brain sonography findings can exclude the diagnosis of PD in patients with sporadic parkinsonism. Sonographic discrimination of atypical parkinsonian syndromes from PD is clearer in patients with onset of parkinsonism at younger than 60 years.

Arch Neurol. 2007;64(11):1635-1640

REVIEW

CME

MDS Research Criteria for Prodromal Parkinson's Disease

Daniela Berg, MD,[1*] Ronald B. Postuma, MD, MSc,[2*] Charles H. Adler, MD, PhD,[3] Bastiaan R. Bloem, MD, PhD,[4] Piu Chan, MD, PhD,[5] Bruno Dubois, MD, PhD,[6] Thomas Gasser, MD,[1] Christopher G. Goetz, MD,[7] Glenda Halliday, PhD,[8] Lawrence Joseph, PhD,[9] Anthony E. Lang, OC, MD, FRCPC,[10] Inga Liepelt-Scarfone, PhD,[1] Irene Litvan, MD,[11] Kenneth Marek, MD,[12] José Obeso, MD, PhD,[13] Wolfgang Oertel, MD,[14] C. Warren Olanow, MD, FRCPC,[15] Werner Poewe, MD,[16] Matthew Stern, MD,[17] and Günther Deuschl, MD[18]

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[5]*Xuanwu Hospital of Capitol of Medical University, Beijing, China*
[6]*Hopital De La Salpetriere, Paris, France*
[7]*Rush University Medical Center, Chicago, Illinois, USA*
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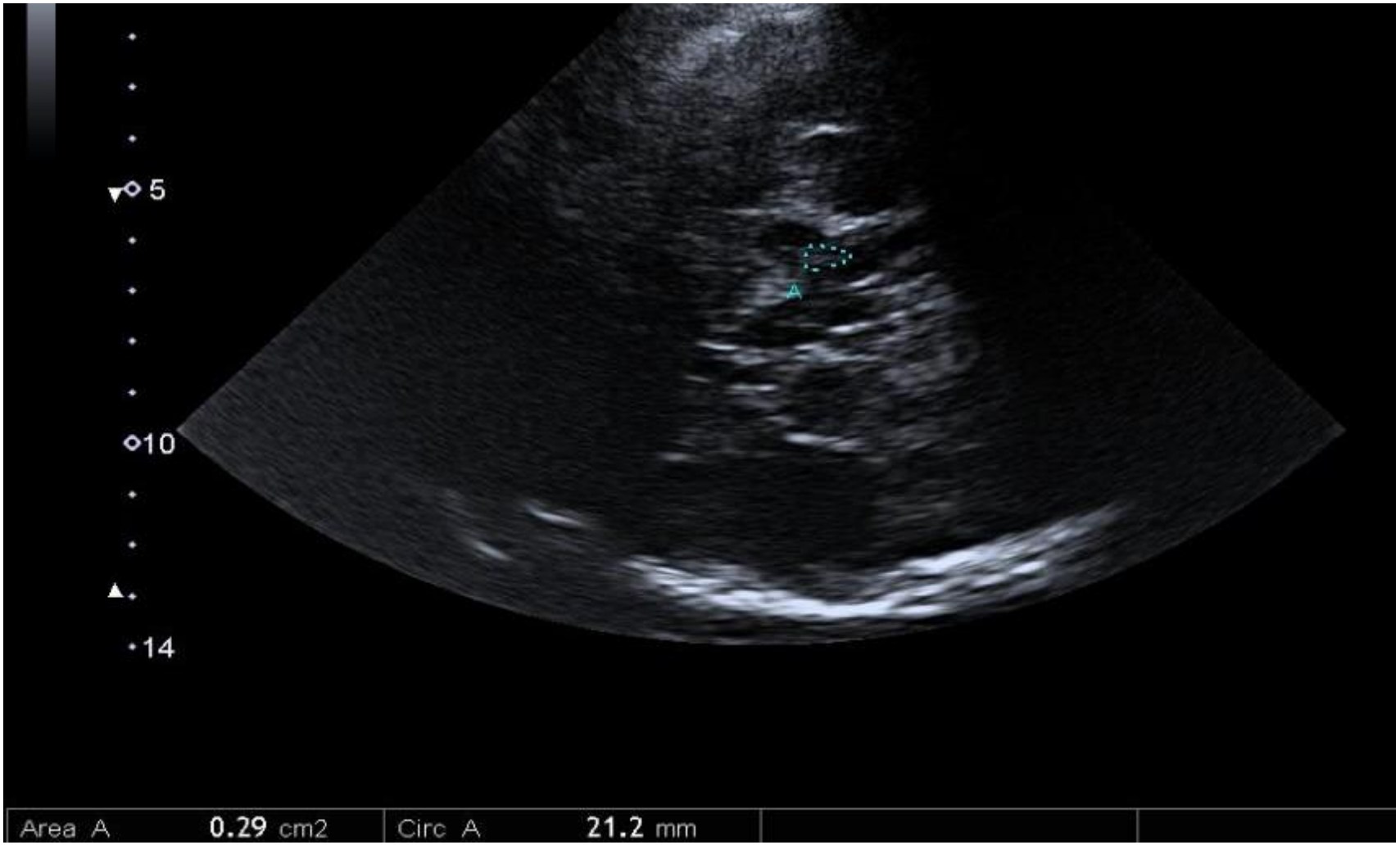
[18]*Department of Neurology, Christian-Albrechts University, Kiel, Germany*

PSP-P



Transcranial Sonography Findings in Depression in Association With Psychiatric and Neurologic Diseases: A Review

Christos Krogias, Uwe Walter

From the Department of Neurology, St. Josef-Hospital, Medical Faculty, Ruhr University Bochum, Bochum, Germany (CK); and Department of Neurology, University of Rostock, Rostock, Germany (UW).

ABSTRACT

The transcranial sonography (TCS) finding of reduced echogenicity of brainstem raphe (hypoechogenic BR) has been associated with depressive states. Here, we review the TCS studies in subjects with depressive disorders and with depression related to degenerative brain diseases, and compare the frequency and clinical correlates of hypoechogenic BR in these reports. Summarizing the data published so far, hypoechogenic BR is present in 67% (range, 37-95%) of depressed but only in 15% (5-36%) of nondepressed subjects without history of neurodegenerative disease. The finding of hypoechogenic BR in these subjects is associated with a relative risk of 3.03 (95% CI, 2.44-3.75; $P < .001$) of being diagnosed with depression. In patients with Parkinson's disease, hypoechogenic BR is present in 63% (35-92%) of depressed but only in 27% (10-62%) of nondepressed patients, resulting in a relative risk of 2.18 (95% CI, 1.80-2.66; $P < .001$) of being diagnosed with depression. Hypoechogenic BR is associated with depression in a number of neurological disorders such Huntington's disease, idiopathic Rapid Eye Movement (REM) sleep behavior disorder, myotonic dystrophies, and cerebral small vessel disease. Although some studies did not show any relationship between BR echogenicity and severity of depression, others suggest an association with higher severity of depression, or even with suicidal ideation. In one study BR hypoechogenicity was found to be associated with better responsivity to serotonin reuptake inhibitors. Further studies are warranted to compare the TCS findings of BR alteration with post-mortem histopathological findings, and with genetic variants related to cerebral serotonin metabolism.

Keywords: Brainstem raphe, depression, serotonin, *Substantia nigra*, ultrasound.

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TCS APPLICATIONS IN DBS

- **Two pilot studies have demonstrated that the intraoperative visualization with TCS and the TCS-assisted insertion of deep brain stimulation electrodes are feasible and safe.**
- **The main advantage of the intraoperative TCS monitoring was that the distance of the DBS electrode tip to an artery at the anatomic target.**
- **Moreover TCS can be recommended for the postoperative monitoring of DBS electrode position.**

TC CRANIO SMDC

Esame TC eseguito in urgenza nelle condizioni di base.

Si apprezza estesa ipodensità fronto-parieto-temporo-occipitale destra da edema interdigitato che occupa estesamente la corona radiata omolaterale determinando effetto massa sul ventricolo laterale destro (marcatamente compresso) sulla testa del caudato e sul talamo con shift della linea mediana verso sinistra di circa 1cm. Non distinguibili perchè interessate dall'edema la capsula interna ed i nuclei della base di destra. Non franche iperdensità ematiche nel contesto. Necessaria sistematizzazione neuroradiologica con eventuale RM in elezione.

RAPHE HYPOECHOGENICITY

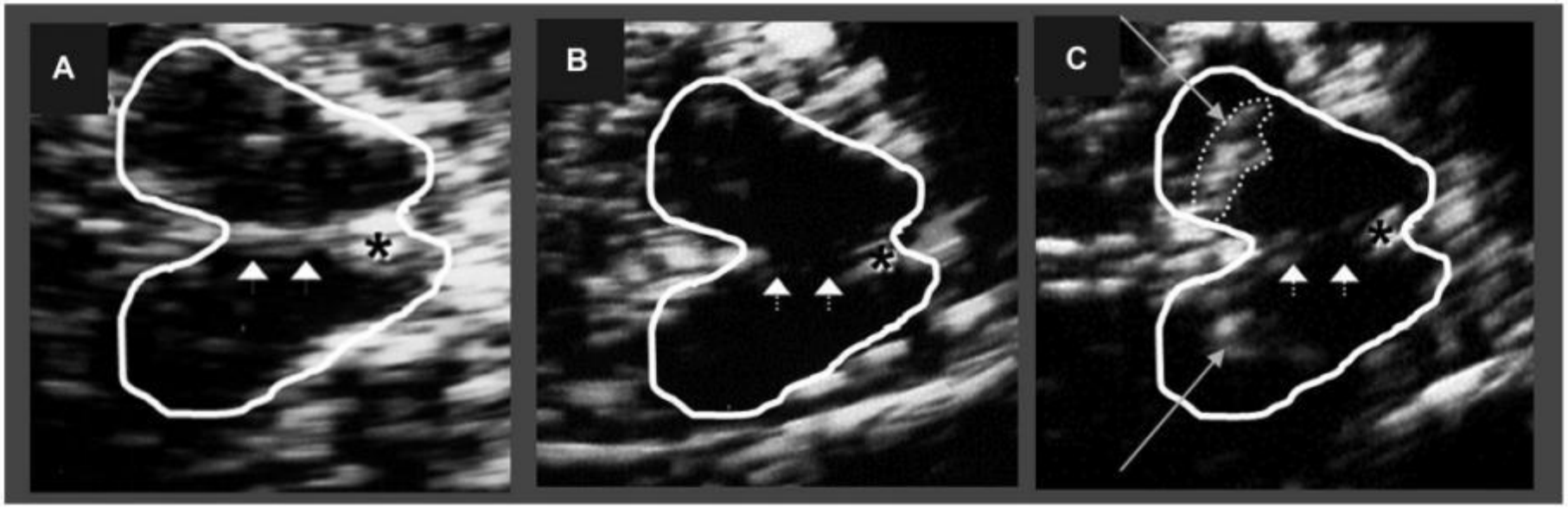


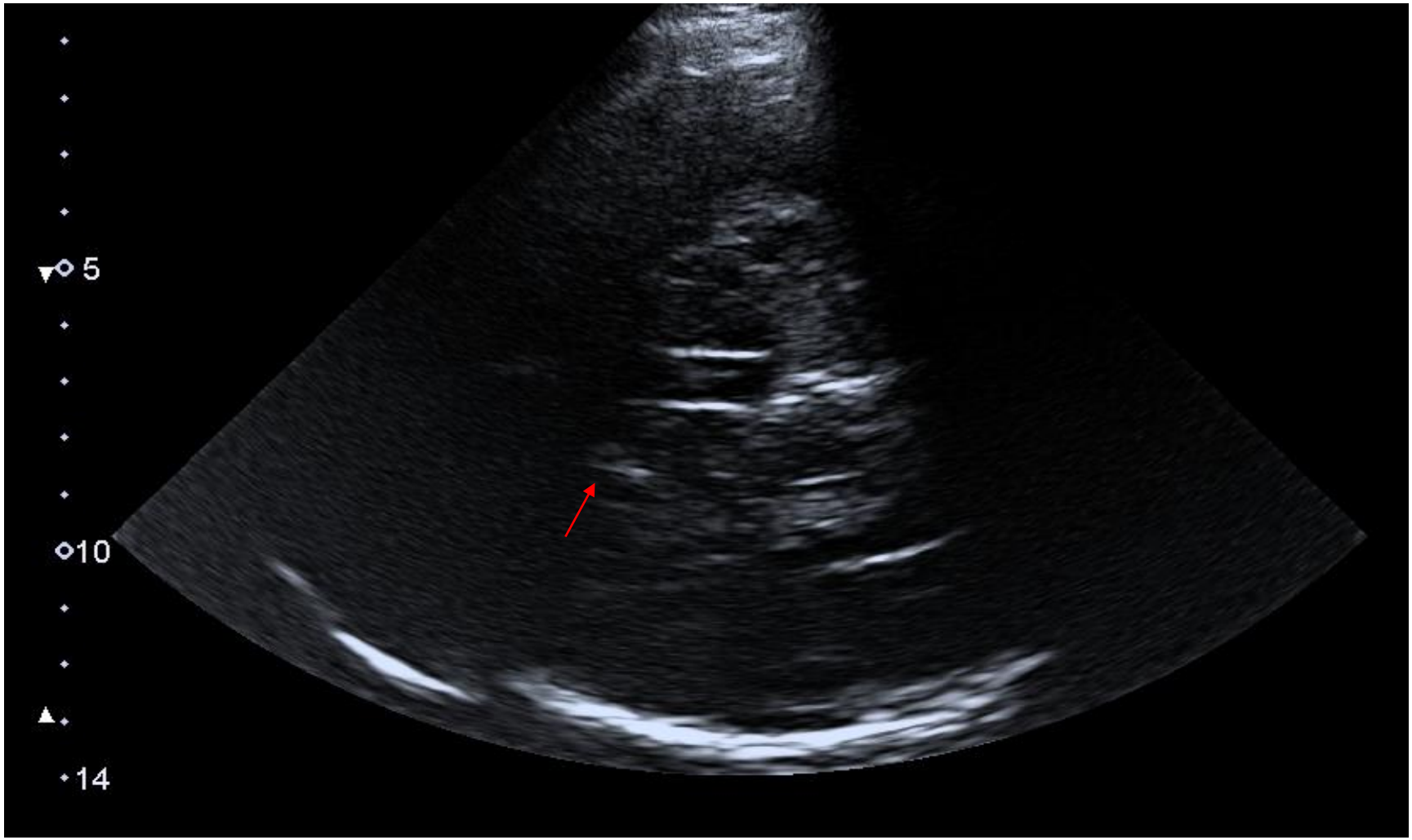
TABLE 1. LRs of risk and prodromal markers

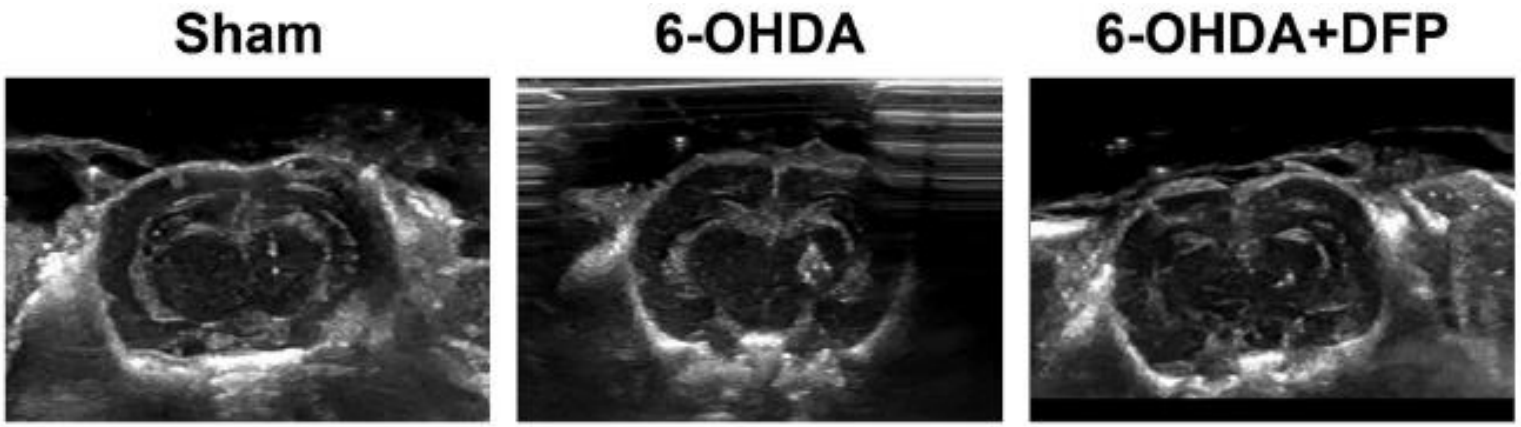
		LR+	LR-
Risk markers	Male sex	1.2 (male)	0.8 (female)
	Regular pesticide exposure	1.5	NA
	Occupational solvent exposure	1.5	NA
	Nonuse of caffeine	1.35	0.88
	Nonsmoking		
	Current smoker	NA	0.51
	Never smoker	1.2	NA
	Former smoker	NA	0.91
	First-degree relative with PD	2.5	NA
	or	LR+ dependent on age-related penetrance, see Table 2	NA
	Known gene mutation (with intermediate-strength penetrance)		
	or	1.57 (highest quartile of PRS scores)	0.45 (lowest quartile)
	Polygenic risk score (PRS)		
	SN hyperechogenicity	3.4	0.38
	Diabetes mellitus (type II)	1.5	0.97
	Physical inactivity	1.3	0.91
	Low plasma urate levels	1.8 (in men)	0.88 (in men)

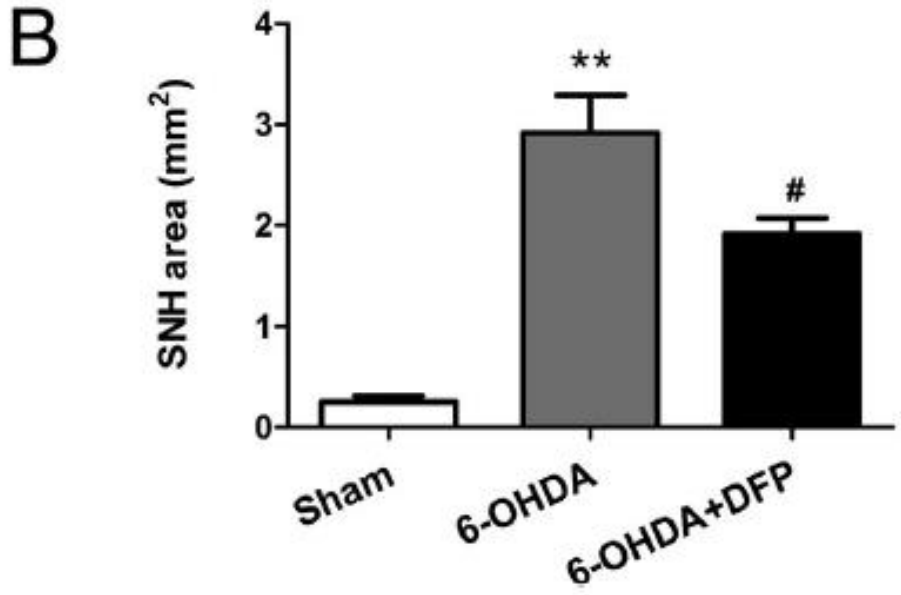
CASO CLINICO

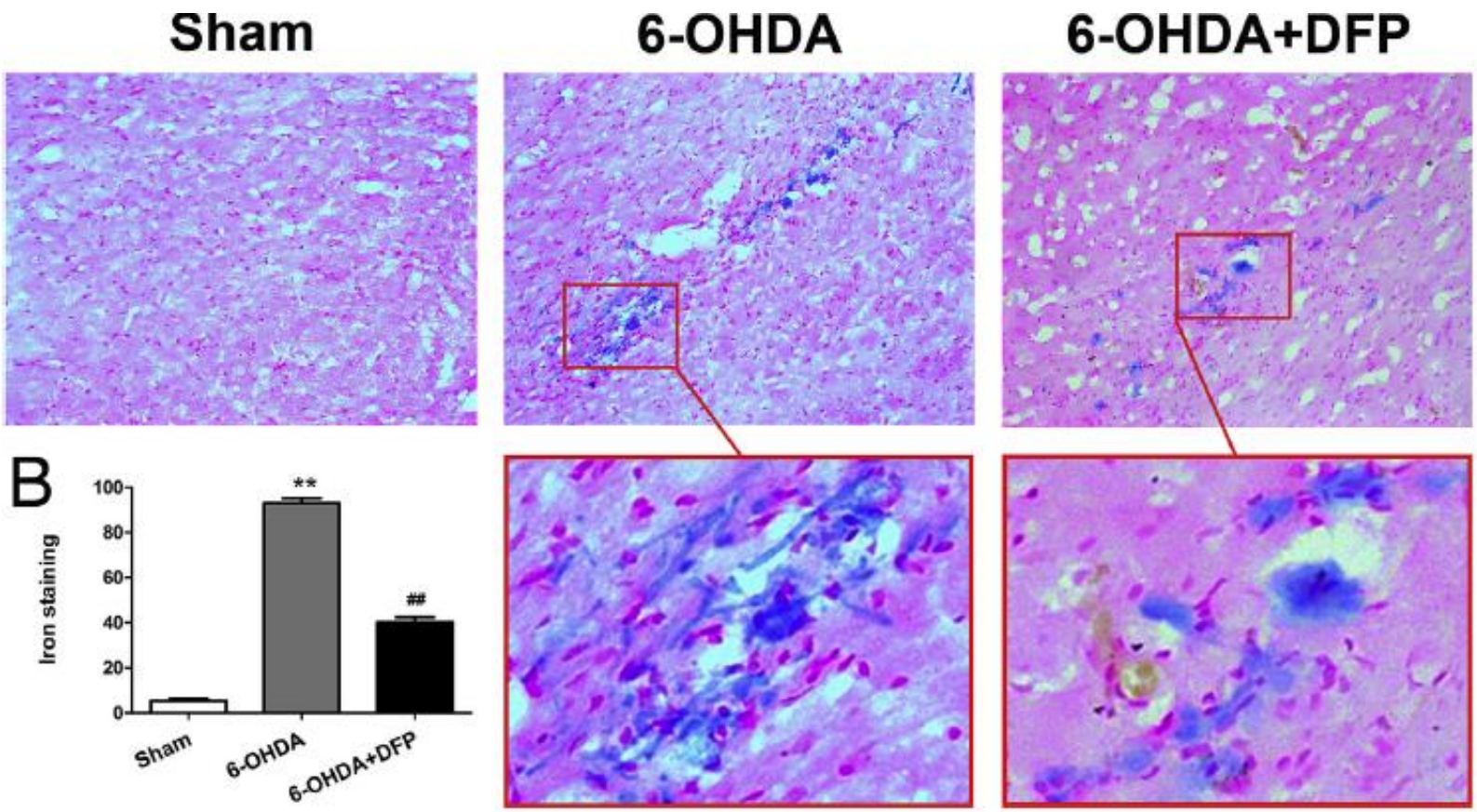
- **Uomo 24 anni riferisce sensazione di tremore interno all'arto superiore sinistro da circa 3 mesi.**
- **Obiettivamente si evidenzia lievissimo tremore posturale medio-distale con componente telecinetica.**
- **Si concorda per controllo clinico tra 6 mesi**
- **Si decide di eseguire TCS.**

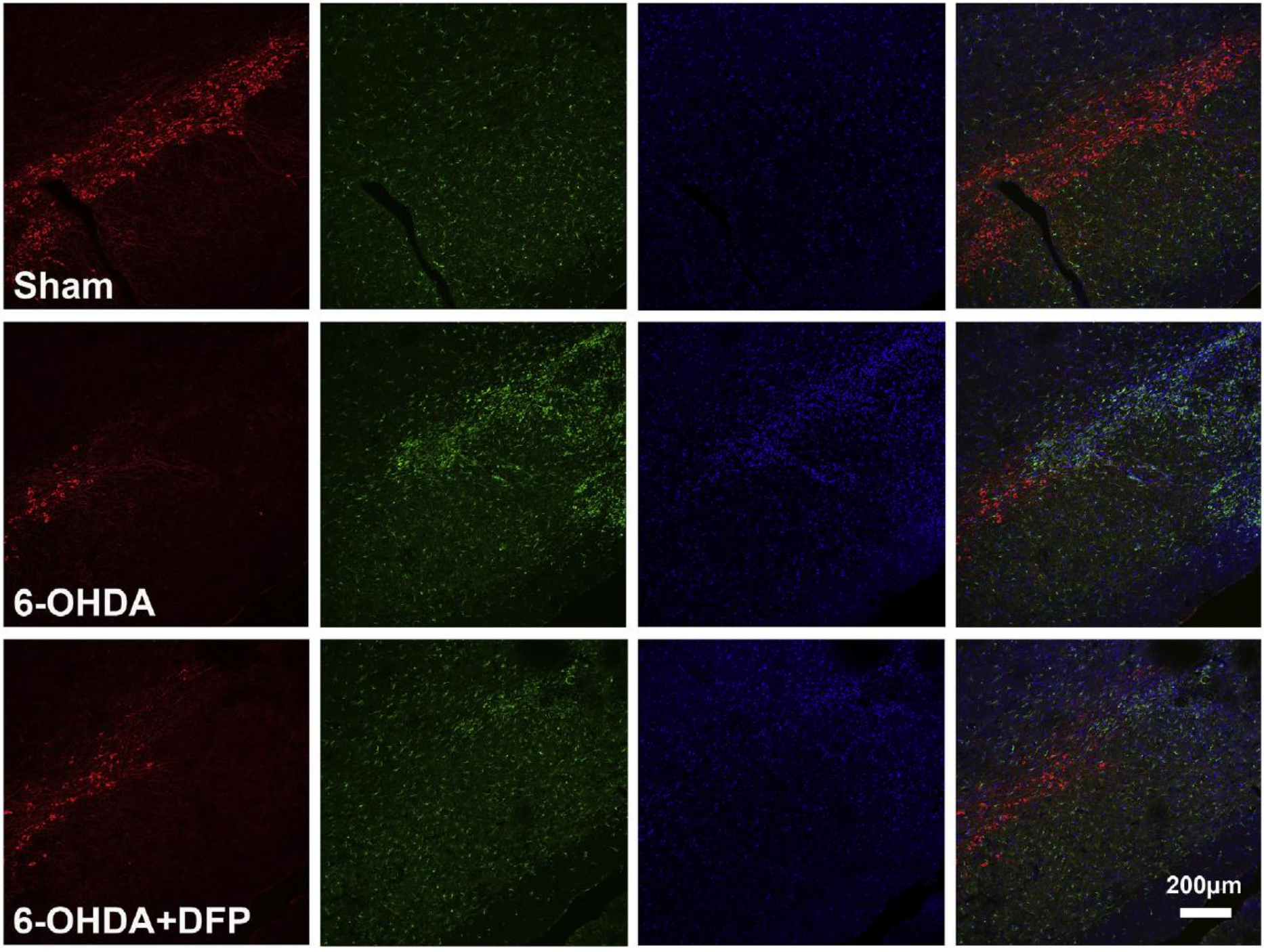
PSP-P




Sham
6-OHDA
6-OHDA+DFP


B
SNH area (mm2)
4
3
2
1
0
**
#
Sham
6-OHDA
6-OHDA+DFP


Sham
6-OHDA
6-OHDA+DFP
B
Iron staining
100
80
60
40
20
0
**
##
Sham
6-OHDA
6-OHDA+DFP


Sham
6-OHDA
6-OHDA+DFP
200μm

REVIEW

CME

MDS Research Criteria for Prodromal Parkinson's Disease

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Substantia Nigra Hypoechogenicity: Definition and Findings in Restless Legs Syndrome

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Abstract: Pathological studies demonstrate a decreased iron content in the substantia nigra (SN) contributing to the pathophysiology of restless legs syndrome (RLS). SN echogenicity as measured by transcranial sonography (TCS) correlates with the SN iron content. The objective of this study was to determine a critical value to define SN hypoechogenicity as a potential marker for RLS. There were 49 RLS patients (39 idiopathic, 10 secondary) and 49 age- and sex-matched controls who underwent TCS by 2 independent and blinded examiners to determine the area of SN echogenicity. We found that SN echogenicity is significantly decreased in RLS patients compared to healthy controls ($P < 0.001$). SN hypoechogenicity (sum area of SN echogenicity of both sides < 0.2 cm^2) is more common in idiopathic than in secondary RLS patients. The area under curve for idiopathic RLS versus controls (receiver operating characteristics) is 0.91, specificity is 0.90, and sensitivity is 0.82. TCS provides an interesting additional instrument in the diagnosis of RLS. Therefore, SN hypoechogenicity (SN sum area < 0.2 cm^2), which is supposed to indicate a decreased SN iron content, is a marker for RLS. Further studies are needed to investigate its significance for the pathophysiology of this frequent movement disorder and possible clinical applications. © 2006 Movement Disorder Society

Key words: restless legs syndrome; substantia nigra iron content; transcranial sonography; substantia nigra; brain iron homeostasis

Table 2 Prodromal Markers of PD

	LR +	LR −
Risk markers		
Male sex	1.2 (male)	0.8 (female)
Regular pesticide exposure	1.5	n/a
Occupational solvent exposure	1.5	n/a
Nonuse of caffeine	1.35	0.88
Smoking		
Current smoker	n/a	0.45
Never smoker	1.25	n/a
Former smoker	n/a	0.8
Sibling had PD with age onset <50	7.5	n/a
Any other first degree relative with PD	2.5	n/a
Known gene mutation	Berg et al. (2015)	n/a
Substantia nigra hyperechogenicity	4.7	0.45

LIMITATIONS AND ADVANTAGES

- **The main limitation is the dependence of image quality from temporal acoustic bone and/or the sonographer's experience.**
- **The midbrain structures are not or only partial assessable in 5-10% of white individuals while the basal ganglia in 10-20%.**
- **The advantages are wide availability, the same sensitivity of functional neuroimaging without invasiveness, low costs and short investigation times.**

Contents lists available at ScienceDirect

Parkinsonism and Related Disorders

journal homepage: www.elsevier.com/locate/parkreldis

Iron accumulation and microglia activation contribute to substantia nigra hyperechogenicity in the 6-OHDA-induced rat model of Parkinson's disease

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6-Hydroxydopamine
Deferiprone

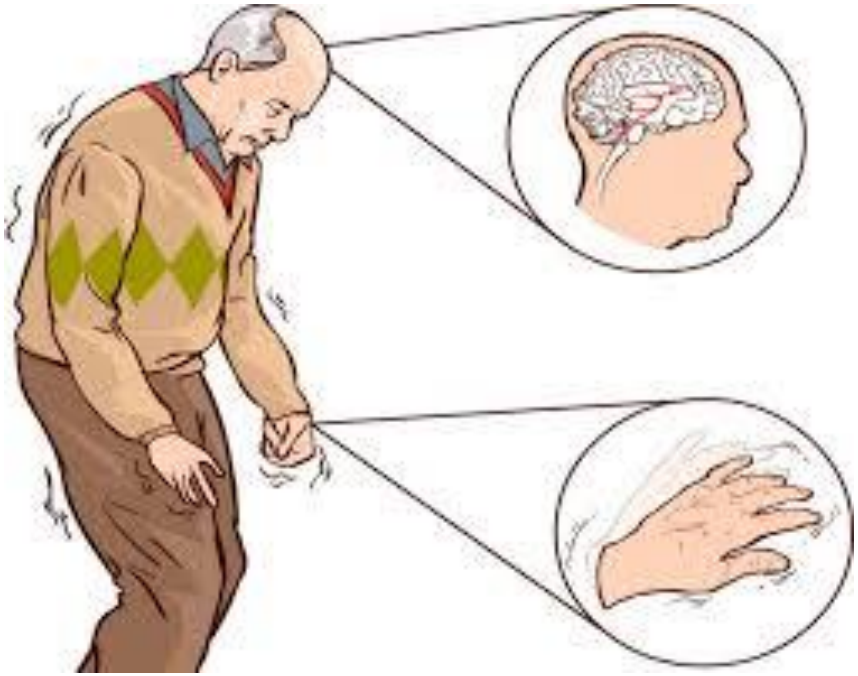
ABSTRACT

Introduction: This study aims to explain the mechanisms for the formation of sonographic features of Parkinson's disease (PD) using a 6-hydroxydopamine (6-OHDA) rat model of PD. The iron chelator deferiprone (DFP) was used in the PD model rat to examine the relationship between iron and the echo signal.

Methods: Rat models were created using stereotactic injections of 6-OHDA. DFP was administered intragastrically. Transcranial sonography (TCS) was performed to observe the substantia nigra (SN) echo signal of the brain. Immunofluorescence and iron staining were performed to observe the histological characteristics of the hyperechogenic area. The imaging findings were compared with the histopathological findings.

Results: The PD model rat presented a large area of hyperechogenicity in the SN. Ferric ion accumulation and microglia proliferation occurred in the hyperechogenic area. DFP inhibited dopaminergic (DA) neuron necrosis, ferric ion accumulation and microglia proliferation and reduced the hyperechogenic area of the SN.

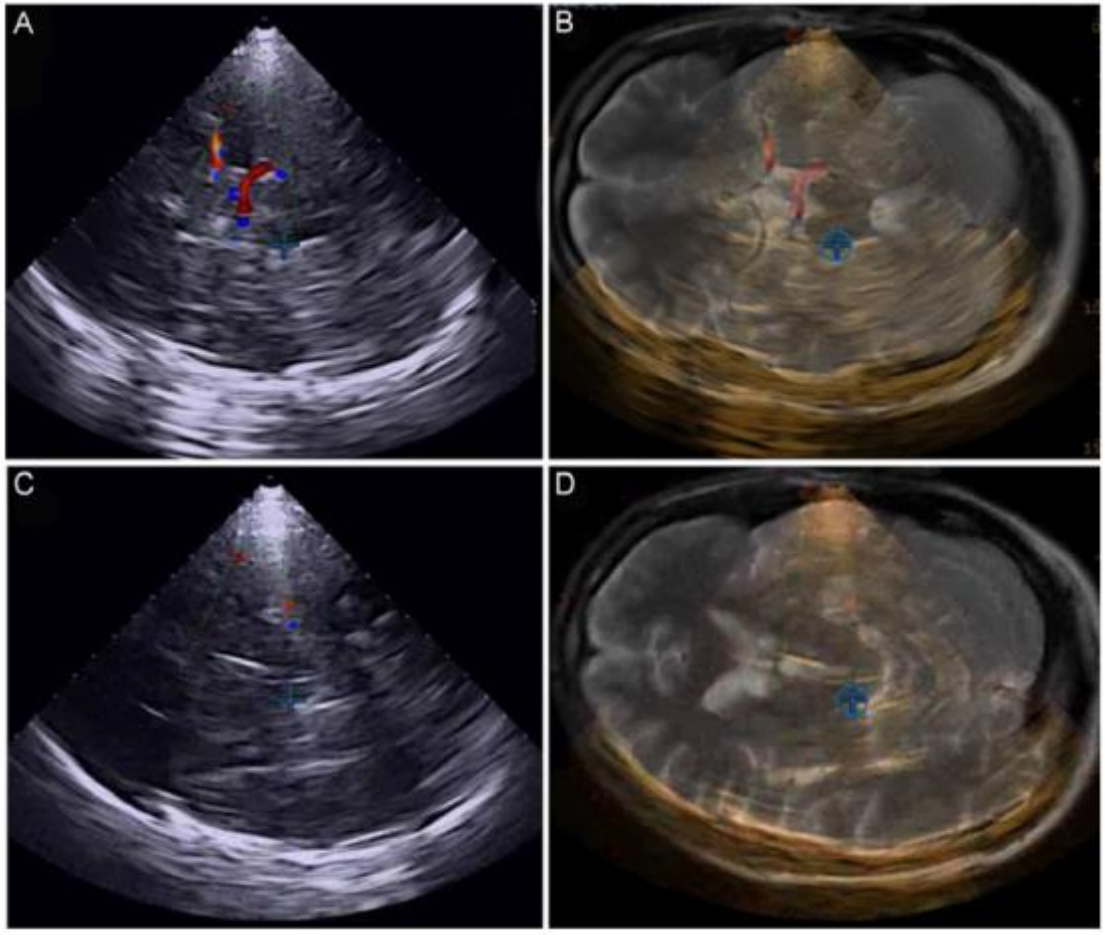
Conclusions: Both iron aggregation and gliosis contribute to the formation of substantia nigra hyperechogenicity (SNH) in PD. DFP exhibits a neuroprotective effect by inhibiting SNH. Iron deposit and the SNH are correlated with DA neuron necrosis.



- From 1995 the applications of TCS in neurologic disorders have been expanded.

TCS can be used not only as diagnostic tool in Parkinson disease but also in other movement disorders and in selected cases coming from Emergency. For example in patients with headache, head trauma and ataxia screening with TCS allows to detect hydrocephalus, brain tumors, subdural hematoma and midbrain cavernoma.

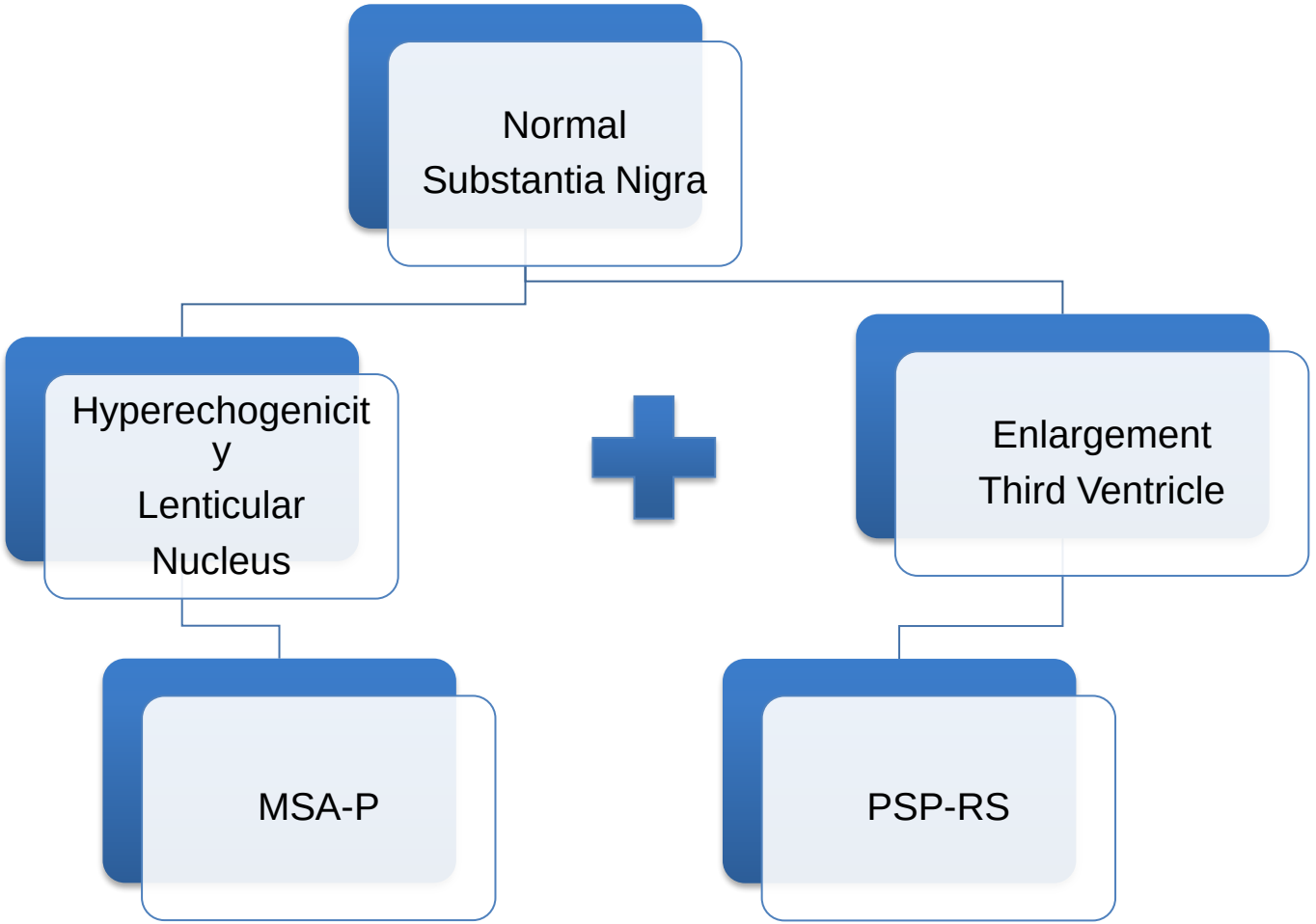
TCS APPLICATIONS IN DBS



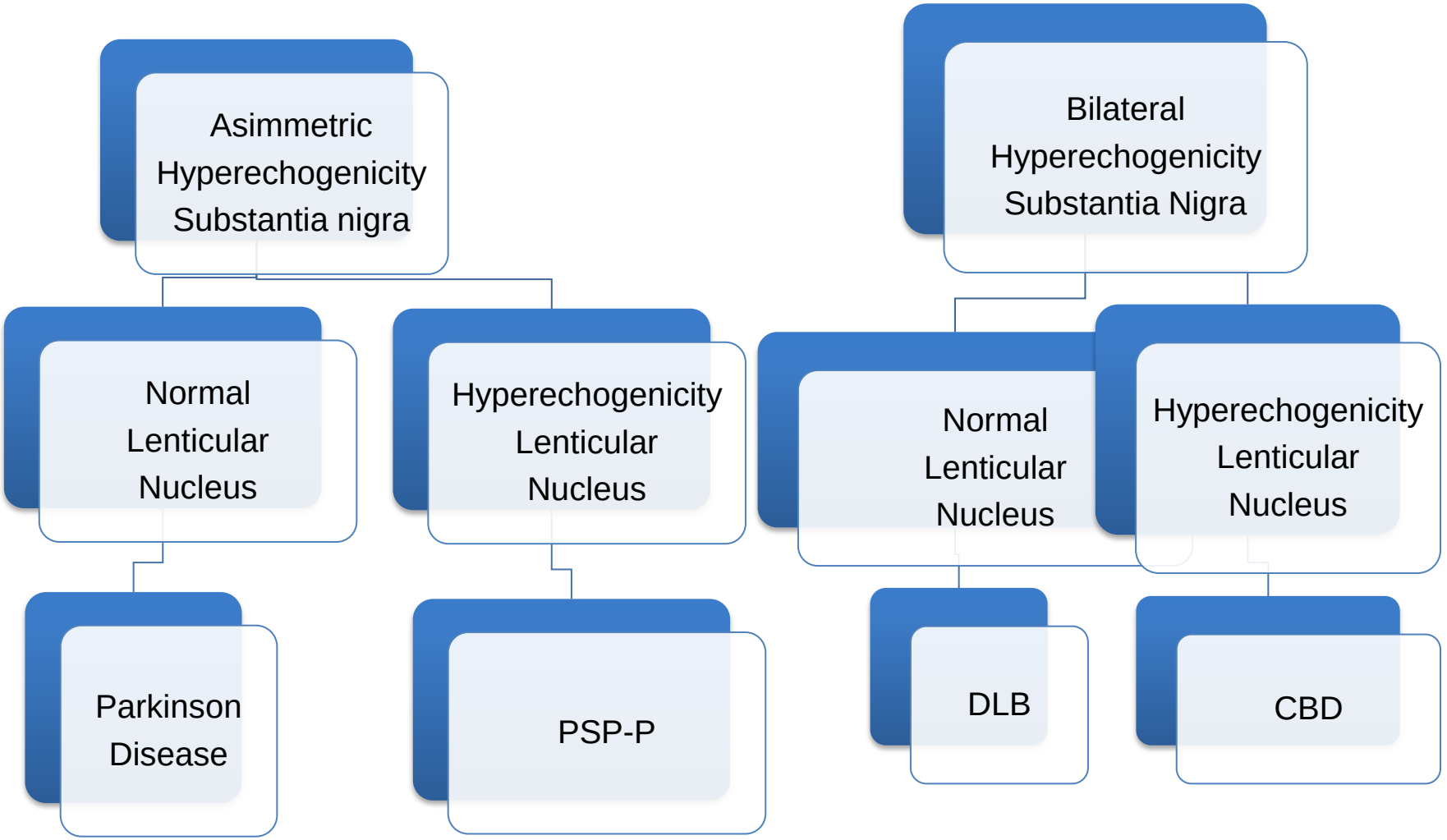
TCS IN SYNUCLEINOPATHIES

- DLB could be misdiagnosed with PD and PDD.
- All these entities share the characteristic feature of SN hyperechogenicity but a specific finding, the more pronounced and symmetry of the TCS findings, distinguishes DLB from PD and PDD.
- A right-left asymmetry index > 1.15 of SN echogenic sizes indicates IPD rather than DLB.

DIAGNOSTIC ALGORITHM

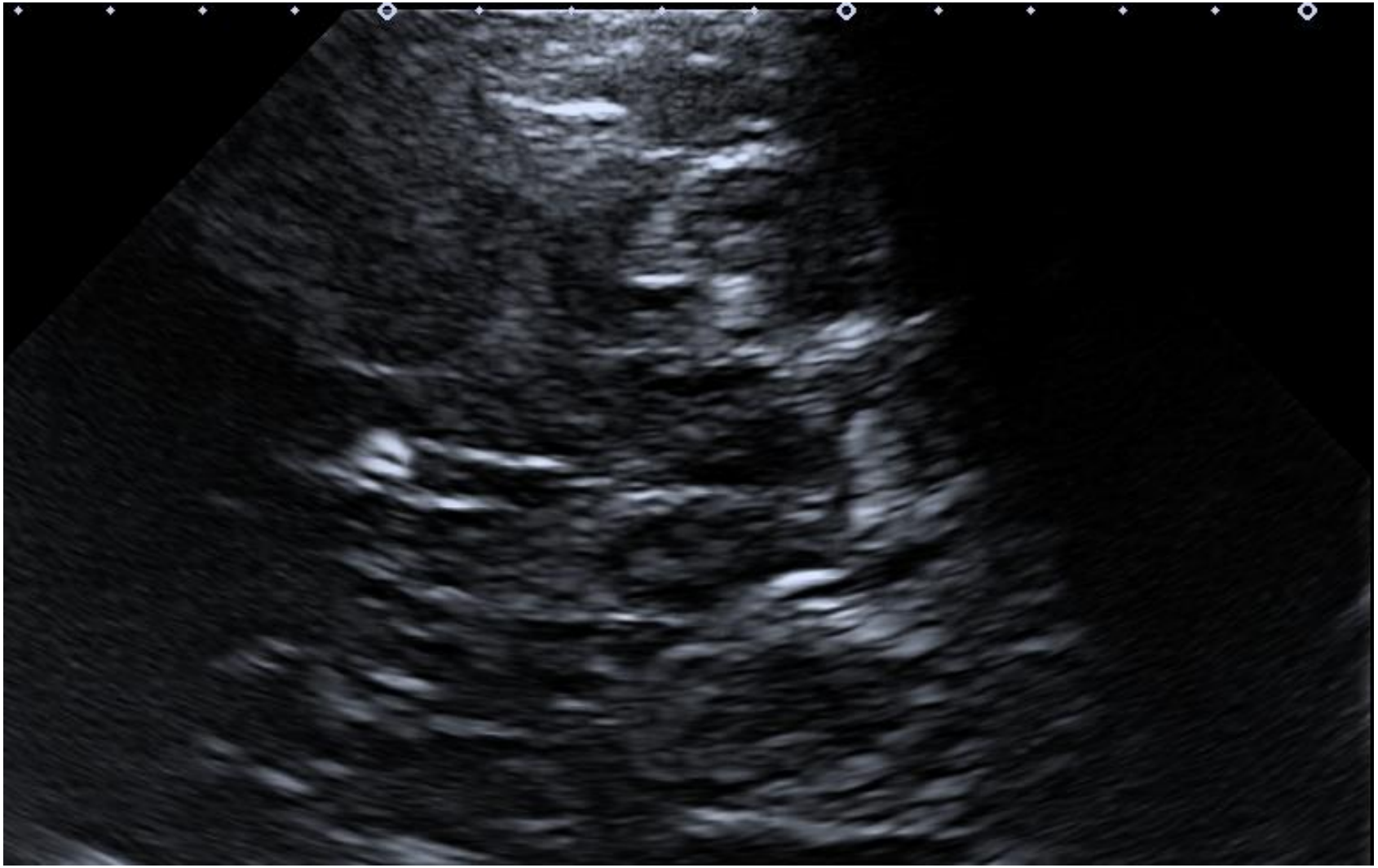


DIAGNOSTIC ALGORITHM



TCS IN atypical PARKINSONISM

- **In the early stages of aPS a large number of patients are erroneously diagnosed even by experienced movement disorder specialists.**
- **Specificity of DAT-SPECT is not sufficiently high.**
- **In the latter stages MRI, Mibg cardiac scintigraphy and [18F] PET can be helpful for differential diagnosis of IPD from MSA, PSP and CBD but not from DLB.**



PSP-RS

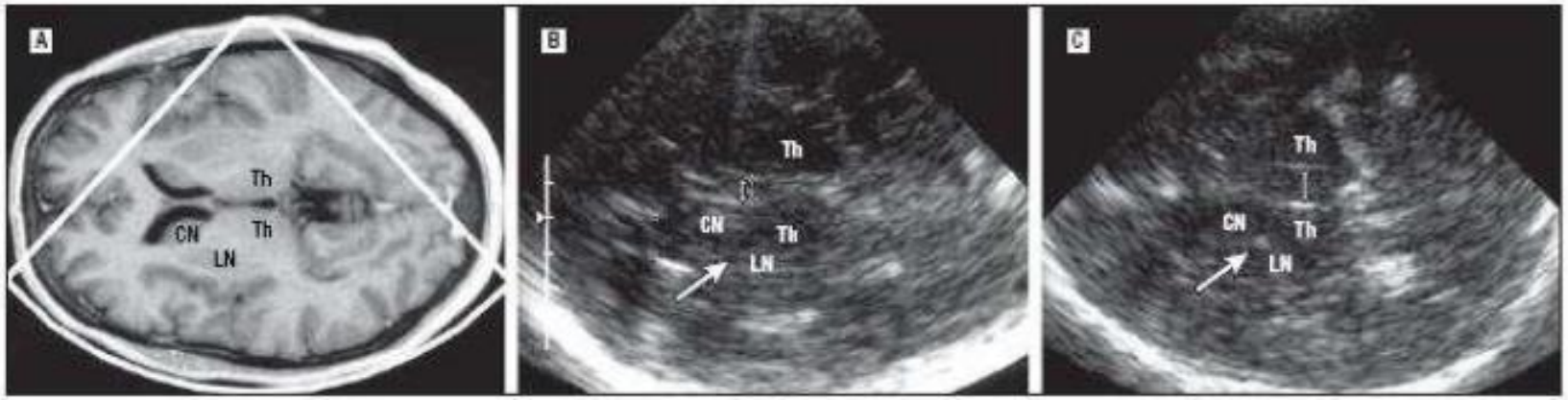
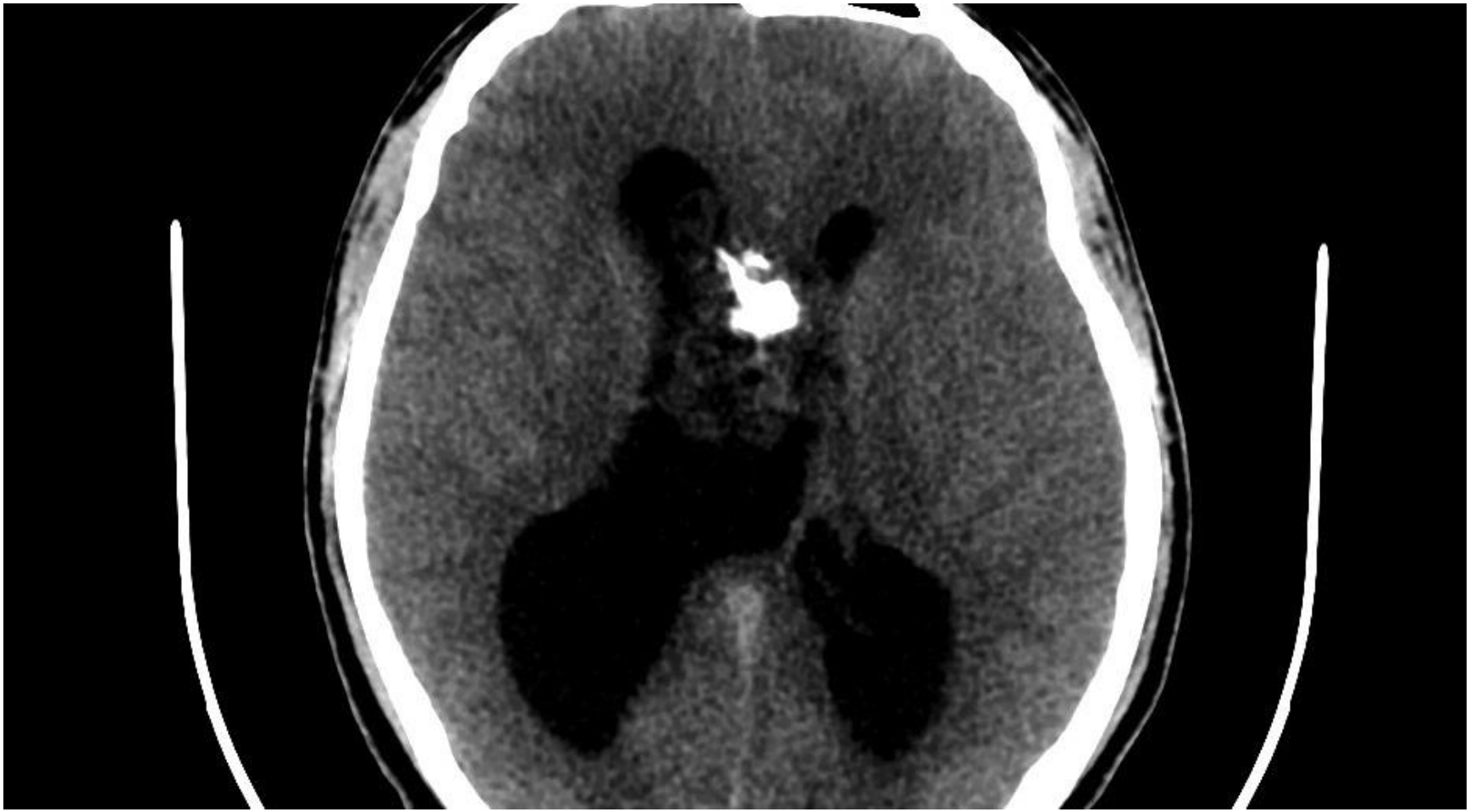


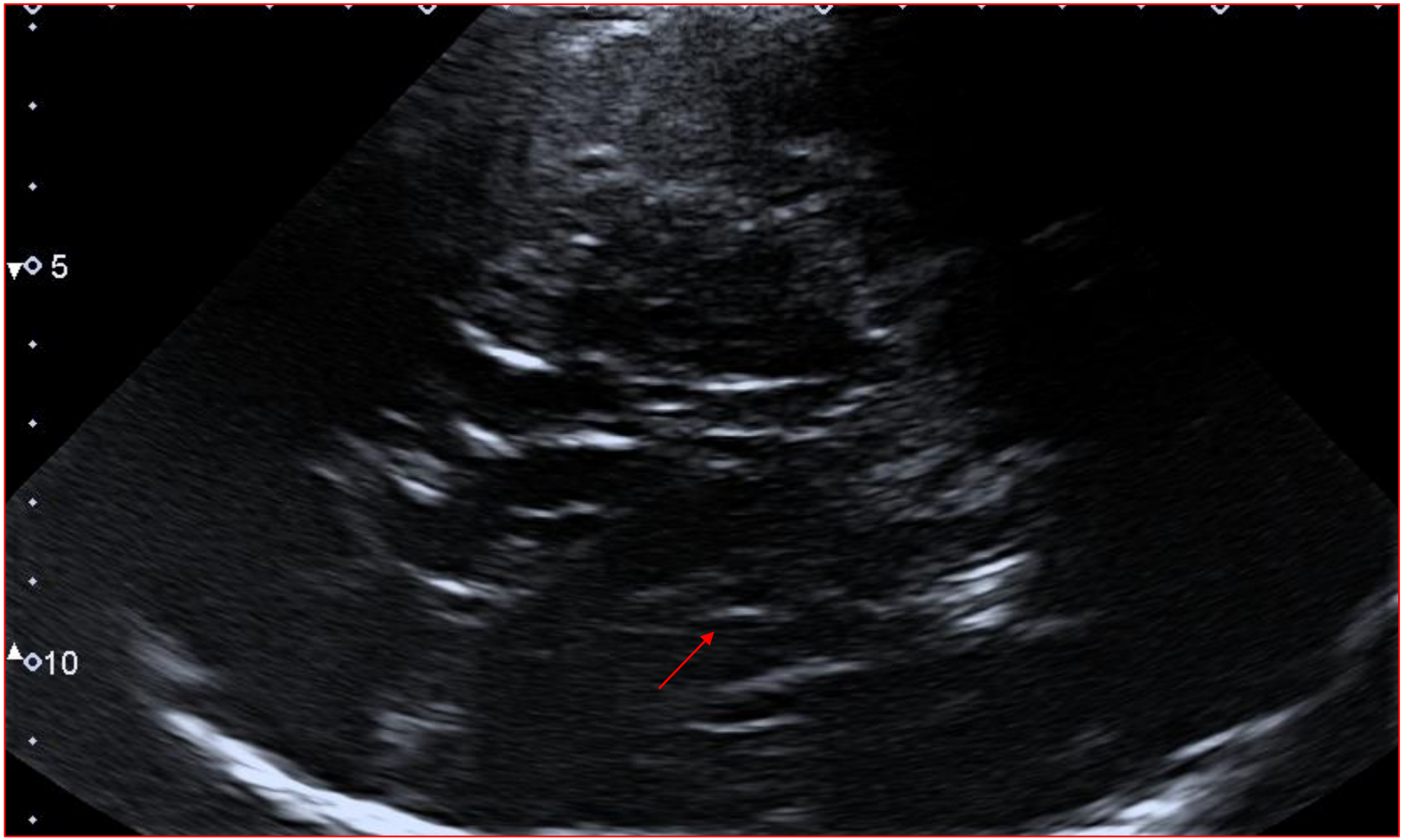
Figure 3. MRI and TCS of the brain and the thalamus level in one patient with IPD (A-B) and in one patient with PSP (C). The TCS image shows normal width of the third ventricle (double arrow) and lenticular nucleus (**LN**) in IPD while dilatation of the third ventricle and **LN** hyperechogenicity in the region of the globus pallidus internus (**CN** indicates caudate nucleus; **Th**, thalamus); (with permission from AMA) [23].



TCS IN SYNUCLEINOPATHIES

- MSA is an adult-onset, sporadic, progressive disorder with parkinsonism, cerebellar ataxia, autonomic failure, urogenital dysfunction and corticospinal involvement.
- TCS shows a normal SN echogenicity and LN hyperechogenicity in MSA-P.
- In MSA-c enlargement of fourth ventricle could be found.

CBD



SUBSTANTIA NIGRA

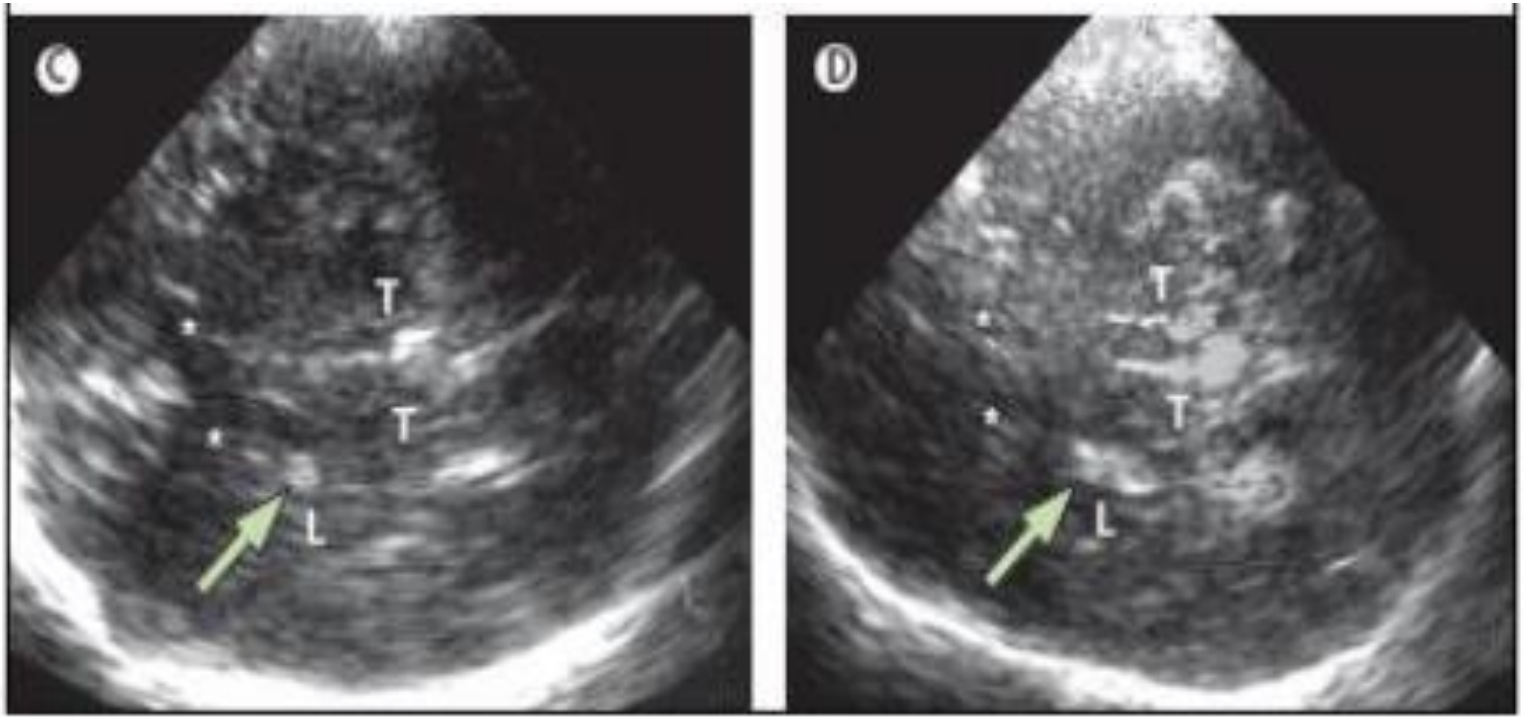
- **Assessment three times ispilaterally to insonation.**
- **TCS needs to be performed on both sides.**
- **Cut-off value is defined by the 90% percentile of measures in normal population.**
- **Normal echogenic: measured area is below the 75^{th} percentile.**
- **Moderately hyperechogenic: measure area is between the 75^{th} and 90^{th} percentile.**
- **Markedly hyperechogenic: measure area is above the 90^{th} percentile.**

TCS IN TAUOPATHIES

- **PSP-P shows asymmetrical onset and moderate initial response to levodopa.**
- **TCS findings are asymmetric hyperechogenicity of substantia nigra, hyperechogenicity of LN and normal width of third ventricle.**
- **90% patients with CBD had marked bilateral SN hyperechogenicity. LN hyperechogenicity is frequently present.**

TCS IN TAUOPATHIES

- The most common PSP variant is PSP-RS.
- It is characterized by an insidious symmetric akinetic-rigid syndrome with vertigal gaze palsy, early backwards falls and frontal dysfunction.
- TCS findings are isoechogenic SN, hyperechogenic LN and increased width of third ventricle.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RED NUCLEUS

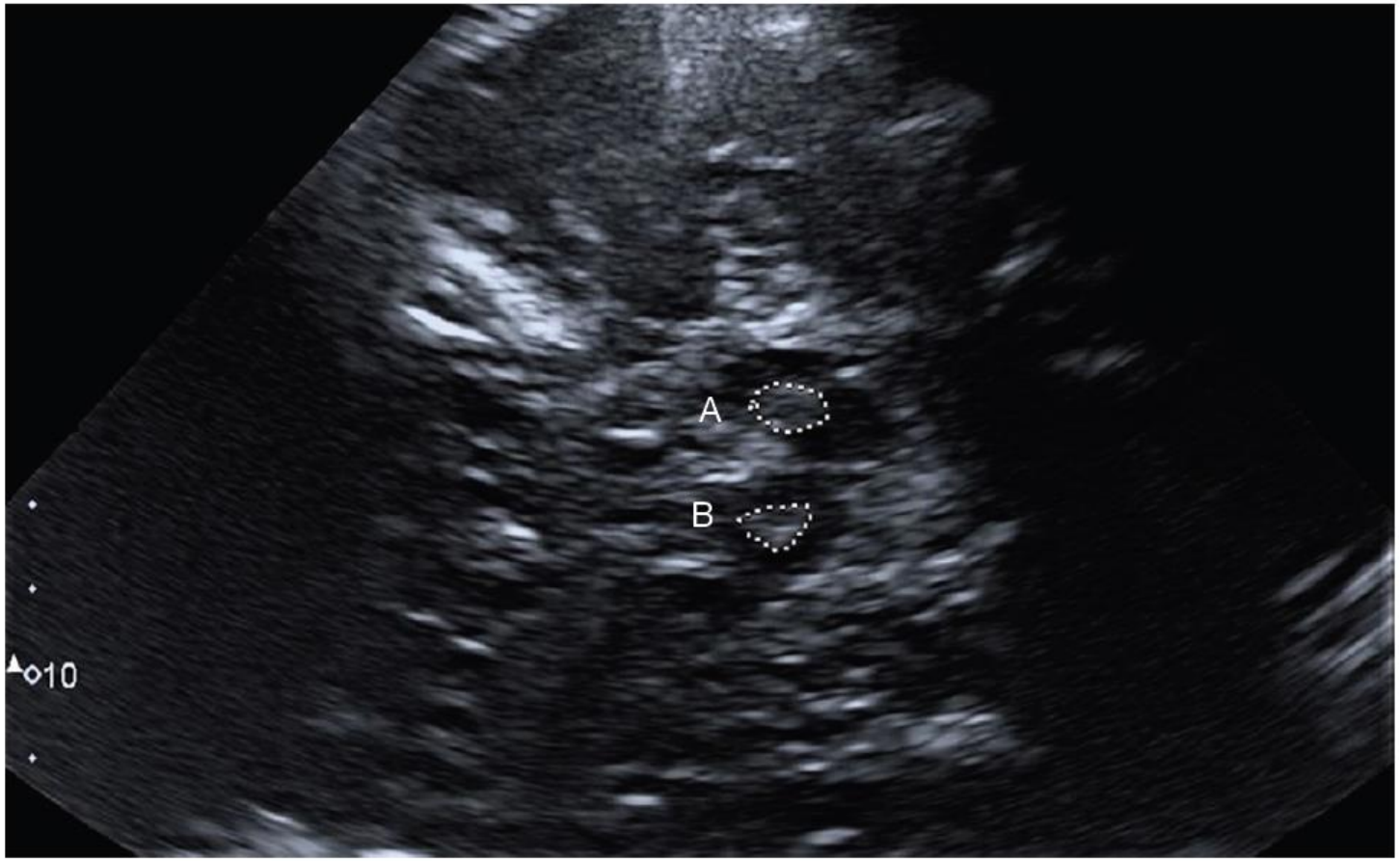
- **It's visualized as two small hyperechogenic dots near the SN and brainstem raphe.**
- **The clear differentiation between red nucleus and SN is essential for the correct assessment of SN echogenicity.**
- **Hyperechogenicity has been associated with restless legs syndrome**

HUNTINGTON'S DISEASE

- Distinct TCS findings are related to all of the three symptom domains (motor, cognitive and psychiatric).
- SN hyperechogenicity is related to a higher clinical disease severity and correlates with CAG repeats number in the huntingtin gene.
- Hyperechogenicity of caudate nucleus has also been described (80%).
- A poorer cognitive performance correlates with larger width of third ventricle and frontal horn.
- Depressive symptoms are associated with abnormal echogenicity of brainstem raphe.

BRAINSTEM RAPHE

- In 90-95% of the normal population the brainstem raphe is depicted as a highly echogenic line with an echogenicity identical to the red nucleus.
- In 5-10% of healthy population but 50-70% of depressive subjects a reduced echogenicity of BR can be detected.
- Hypoechogenicity should be rated only if it appears interrupted or not visible at both sides of investigation.


A
B
10

THALAMUS

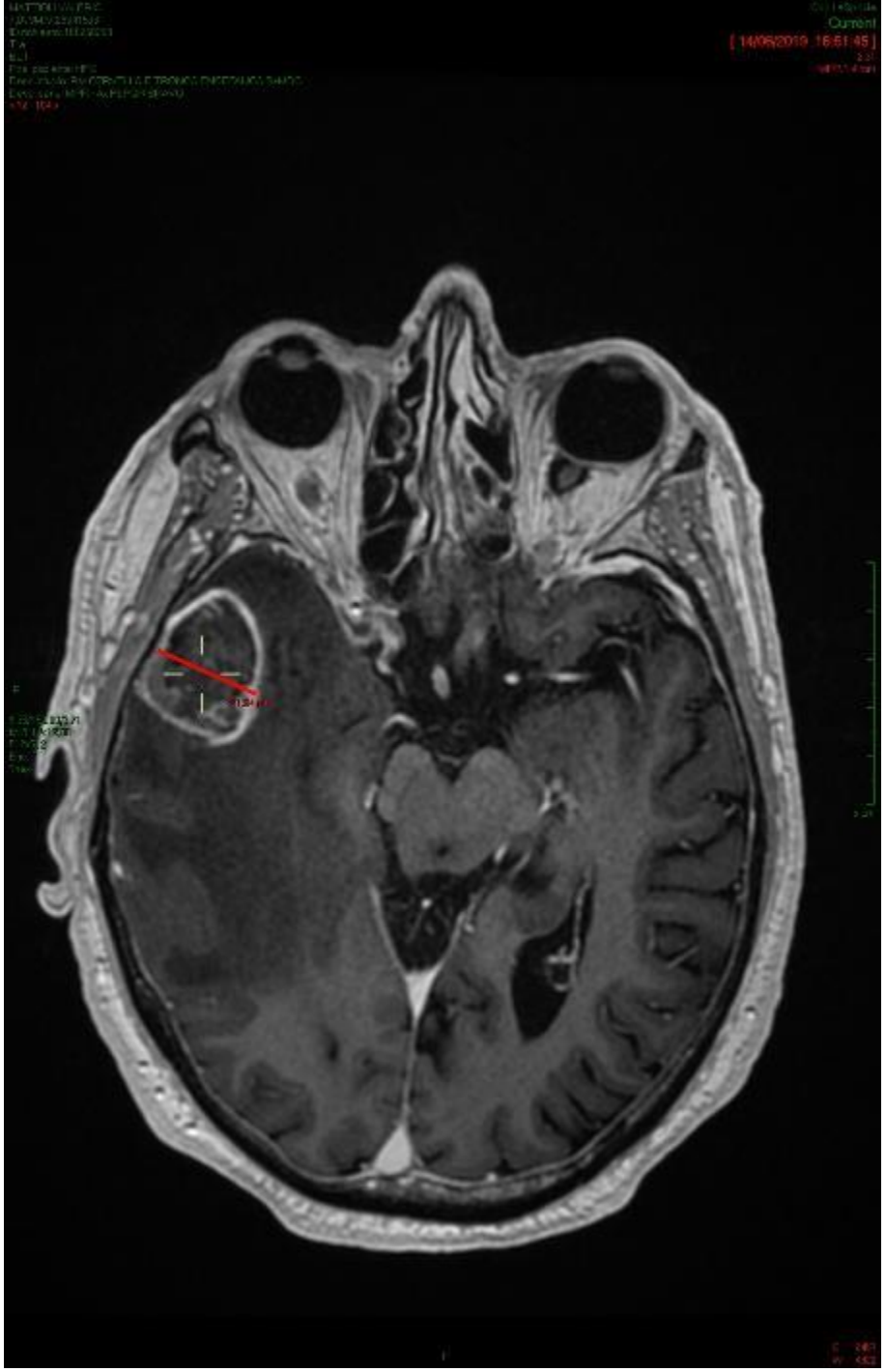
- **Normally the thalamus is an ovalar structure of low echogenicity displayed laterally to the third ventricle.**
- **Thalamus has not a diagnostic relevance but it's important to localize lenticular nucleus and caudate nucleus.**

LENTICULAR NUCLEUS

- **Normally it is isoechogenic to the surrounding brain parenchyma.**
- **An increased echogenicity of lenticular nucleus is abnormal and it has been described in aPS, Wilson's disease, idiopathic dystonia.**

CAUDATE NUCLEUS

- **It's normally isoechogenic to the surrounding parenchyma.**
- **Caudate nucleus hyperechogenicity is frequently seen in Huntington's disease and in advanced stages of PD.**
- **This finding is related to an increased risk of psychosis.**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BRIEF REPORTS

Substantia Nigra Hyperechogenicity and Parkinson's Disease Risk in Patients with Essential Tremor

Fabienne S. Sprenger, MD,[1] Isabel Wurster, MD,[2] Klaus Seppi, MD,[1]* Heike Stockner, MD,[1] Christoph Scherfler, MD,[1] Martin Sojer, MD,[1] Christof Schmidauer, MD,[1] Daniela Berg, MD,[2] and Werner Poewe, MD[1]*

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patients with essential tremor have an increased risk for Parkinson's disease compared with the general population.[3-6] Hyperechogenicity in the area of the substantia nigra, determined by transcranial sonography, has been proposed as a risk marker for Parkinson's disease, and previous studies have identified substantia nigra hyperechogenicity in 13% to 16% of individuals with clinically defined essential tremor[7-10] and in 10% of healthy controls.[11] In this prospective follow-up cohort study, we sought to assess the incidence of new-onset Parkinson's disease in patients with essential tremor ("PD-on-ET") in relation to their baseline echogenic status over an average of 6.16 years of follow-up.

FOURTH VENTRICLE

- It can be displayed usually as a comma-shaped structure if there is no cerebellar atrophy.
- If a relevant cerebellar atrophy is present the enlarged fourth ventricle can be identified as a hypo-anechogenic circular structure in the immediate dorsal vicinity of the mesencephalon.
- It is abnormal when the area is > 0.6 cm^2

DENTATE NUCLEUS

- **It's a slightly hyperechogenic structure compared to the surrounding tissue.**
- **In patients with advanced spinocerebellar atrophy the echogenicity of the dentate nucleus appears to be brighter compared with healthy controls.**

Neurological Sciences (2018) 39:1887–1894
https://doi.org/10.1007/s10072-018-3514-z

ORIGINAL ARTICLE

The predictive power of transcranial sonography in movement disorders: a longitudinal cohort study

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Received: 1 February 2018 / Accepted: 30 July 2018 / Published online: 7 August 2018

Abstract

Transcranial sonography (TCS) is a noninvasive, easily performed, and commonly available neuroimaging technique useful for the study of brain parenchyma in movement disorders. This tool has been increasingly used in the diagnosis of Parkinson's disease and atypical parkinsonism. The aim of the study was to evaluate the applicability of this technique as supportive tool in the early diagnosis of movement disorders. We performed TCS on 315 individuals which were diagnosed as healthy controls or affected by idiopathic Parkinson's disease, monogenetic subtypes of Parkinson's disease, atypical parkinsonism, and Dementia with Lewy bodies. Five TCS diagnostic patterns were defined on the basis of substantia nigra's and lenticular nuclei's echogenicity. TCS evaluations were performed by two blinded neuro-sonographers. Clinical diagnosis on all individuals was performed at baseline and at 4-year follow-up. The concordance rate between TCS patterns and clinical diagnosis and the specificity of TCS pattern to discriminate each group of individuals were compared at baseline and at follow-up. The concordance rate between TCS patterns and clinical diagnosis of all individuals was 84% at baseline and increased at follow-up (91%) significantly ($p = 0.01$). The specificity of TCS pattern in the comparison between patients diagnosed as affected by idiopathic Parkinson's disease and atypical parkinsonism showed a significant increase at follow-up ($p = 0.03$). Our study strongly confirms the role of TCS as a noninvasive and cost-effective tool in early diagnosis of movement disorders.

Keywords Transcranial sonography · Substantia nigra · Lenticular nuclei · Idiopathic Parkinson's disease · Atypical parkinsonism · Dementia with Lewy bodies

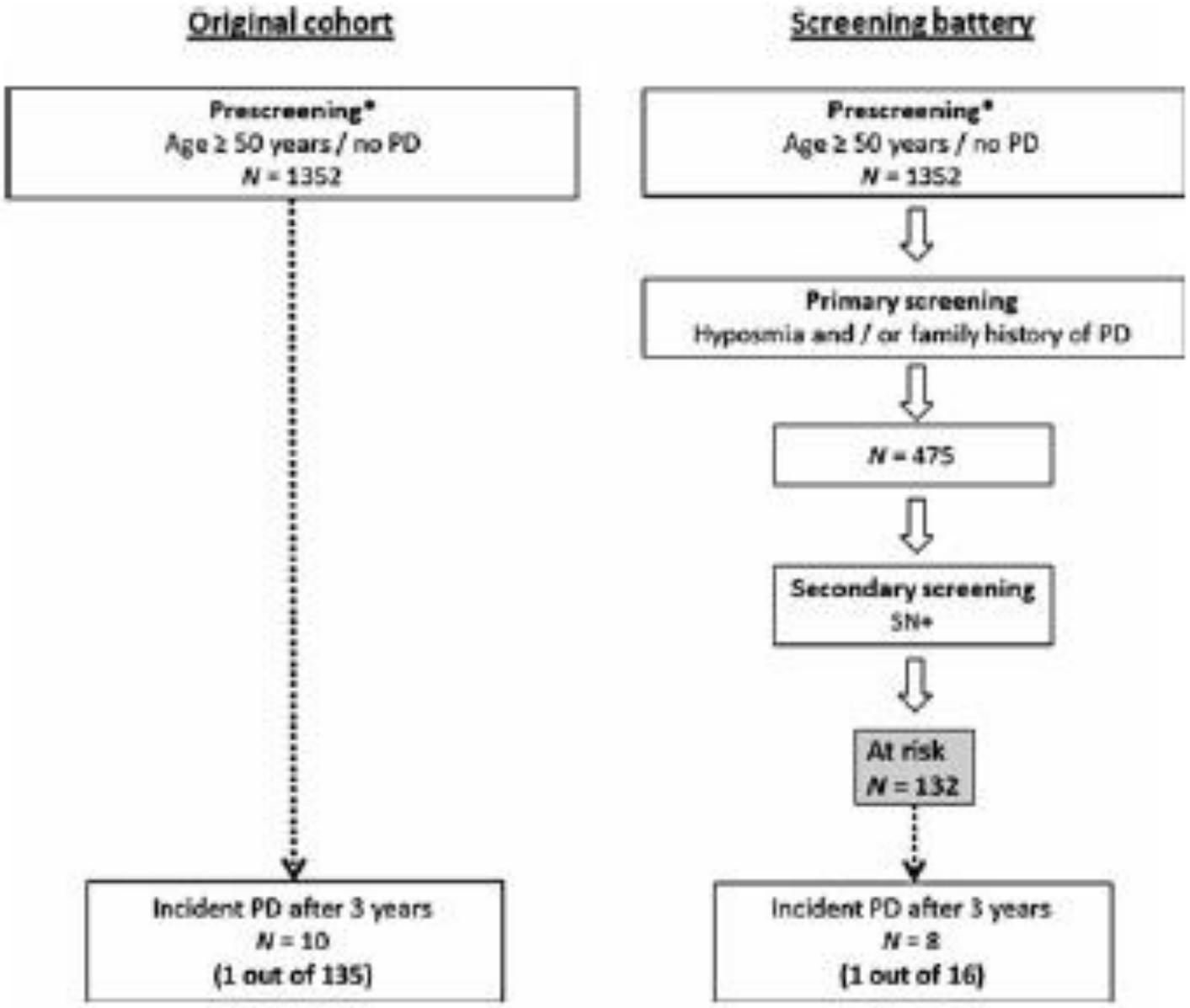
doi:10.1093/brain/awx053 BRAIN 2017: 140; 1371–1383 | 1371

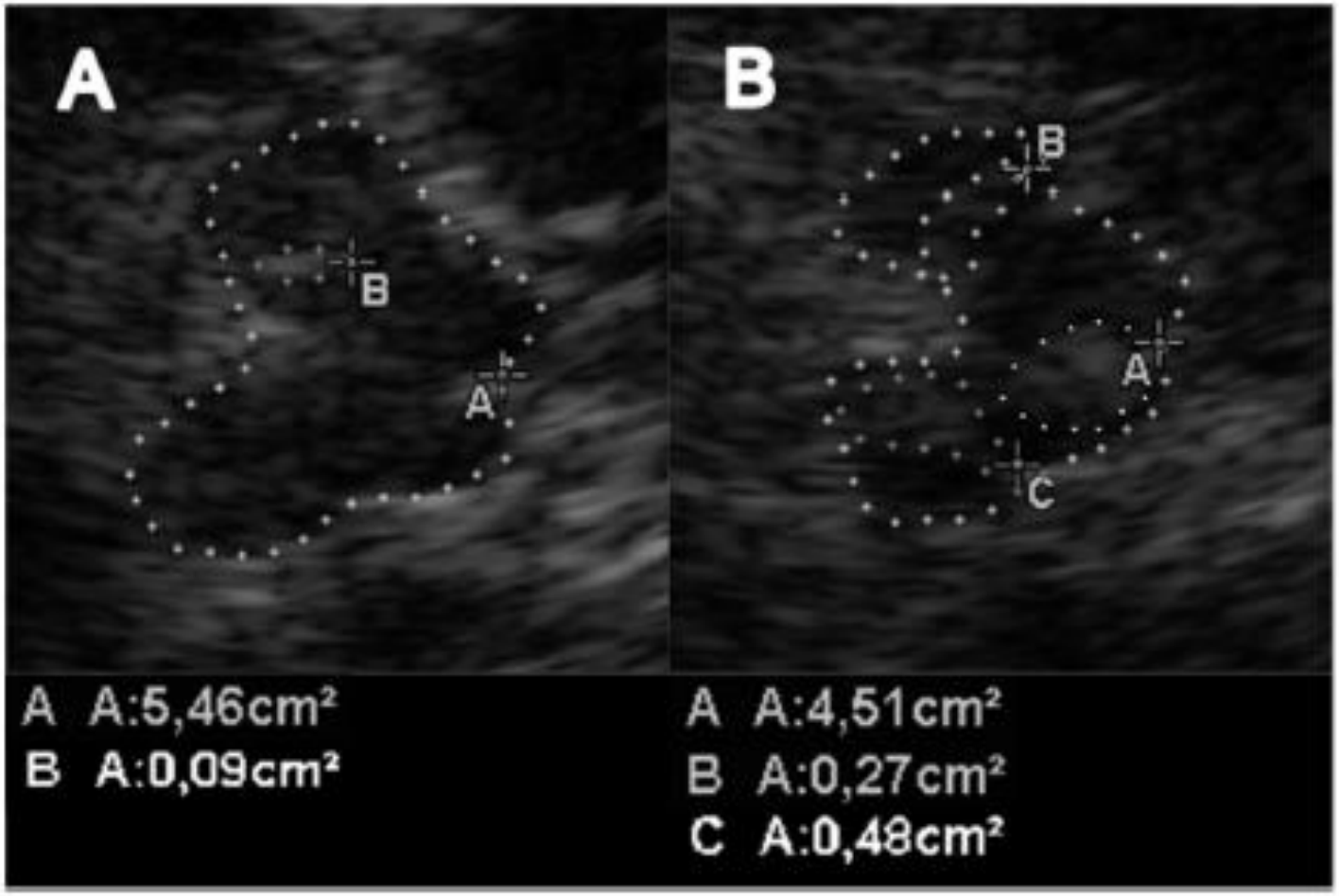
BRAIN
A JOURNAL OF NEUROLOGY

Neuroimaging and clinical features in adults with a 22q11.2 deletion at risk of Parkinson's disease

Nancy J. Butcher,[1,2] Connie Marras,[3,4] Margarita Pondal,[3] Pablo Rusjan,[5,6] Erik Boot,[6,7] Leigh Christopher,[2,3,5,8] Gabriela M. Repetto,[9] Rosemarie Fritsch,[10] Eva W. C. Chow,[1,6] Mario Masellis,[11] Antonio P. Strafella,[2,3,4,5,8,12] Anthony E. Lang[2,3,4,12,13] and Anne S. Bassett[1,2,6,7,14,15]

The recurrent 22q11.2 deletion is a genetic risk factor for early-onset Parkinson's disease. Adults with the associated 22q11.2 deletion syndrome (22q11.2DS) may exhibit phenotypes that could help identify those at highest risk and reveal disease trajectories. We investigated clinical and neuroimaging features relevant to Parkinson's disease in 26 adults: 13 with 22q11.2DS at genetic risk of Parkinson's disease (mean age = 41.5 years, standard deviation = 9.7), 12 healthy age and sex-matched controls, and a 22q11.2DS patient with L-DOPA-responsive early-onset Parkinson's disease. Neuroimaging included transcranial sonography and positron emission tomography using ^{11}C-dihydrotetrabenazine (^{11}C-DTBZ), a radioligand that binds to the presynaptic vesicular monoamine transporter. The 22q11.2DS group without Parkinson's disease demonstrated significant motor and olfactory deficits relative to controls. Eight (61.5%) were clinically classified with parkinsonism. Transcranial sonography showed a significantly larger mean area of substantia nigra echogenicity in the 22q11.2DS risk group compared with controls ($P = 0.03$). The 22q11.2DS


Original cohort
Prescreening*
Age ≥ 50 years / no PD
N = 1352
Incident PD after 3 years
N = 10
(1 out of 135)
Screening battery
Prescreening*
Age ≥ 50 years / no PD
N = 1352
Primary screening
Hyposmia and / or family history of PD
N = 475
Secondary screening
SN+
At risk
N = 132
Incident PD after 3 years
N = 8
(1 out of 16)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A A:5,46cm²
B A:0,09cm²
A A:4,51cm²
B A:0,27cm²
C A:0,48cm²

DIAGNOSTIC STRUCTURES

- SN
- Raphe
- Red nucleus
- Thalamus
- Lenticular nucleus
- Caudate nucleus
- Widths of third and fourth ventricles
- Width frontal hornes of lateral ventricle
- Dentate nucleus

Radiology

MR Imaging of the Substantia Nigra at 7 T Enables Diagnosis of Parkinson Disease[1]

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Ilaria Pesaresi, MD
Mauro Costagli, PhD
Laura Biagi, PhD
Roberto Ceravolo, MD
Ubaldo Bonuccelli, MD
Michela Tosetti, PhD

Purpose: To evaluate the anatomy of the substantia nigra (SN) in healthy subjects by performing 7-T magnetic resonance (MR) imaging of the SN, and to prospectively define the accuracy of 7-T MR imaging in distinguishing Parkinson disease (PD) patients from healthy subjects on an individual basis.

Materials and Methods: The 7-T MR imaging protocol was approved by the Italian Ministry of Health and by the local competent ethics

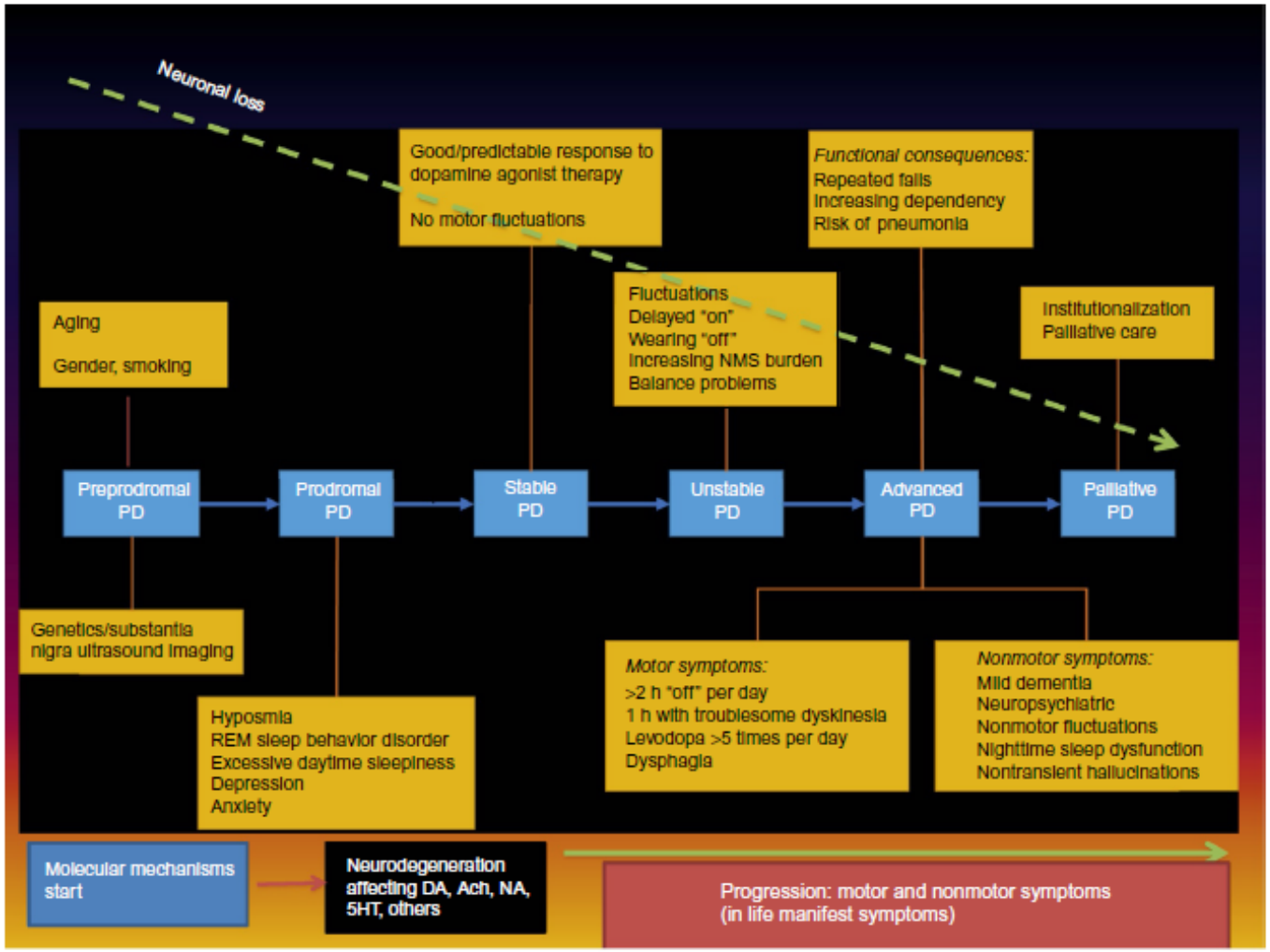
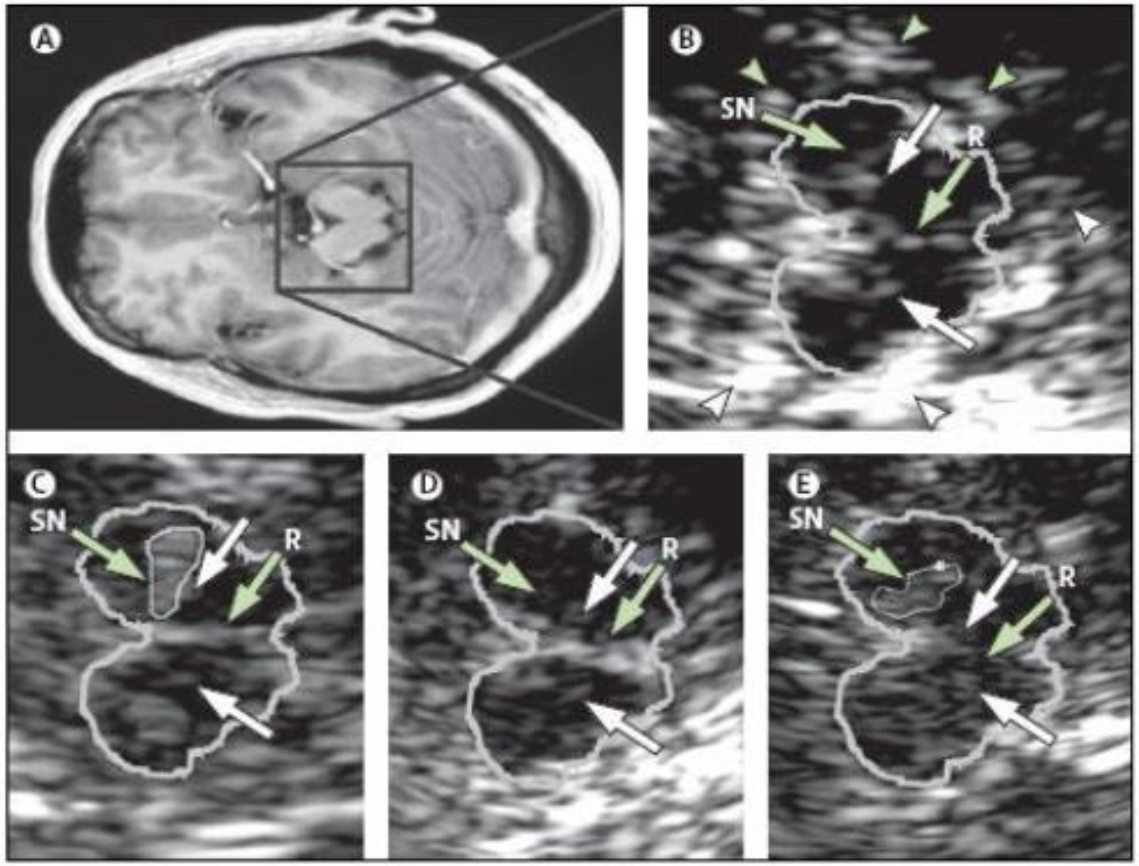


Fig. 1 The proposed natural history pattern of Parkinson's disease. It is to be noted that the neuronal loss in PD is unlikely to follow a linear pattern (as suggested in the figure) and the relevant line is a schematic representation. *Ach*, acetylcholine; *DA*, dopamine; *NA*, noradrenaline; *5HT*, serotonin. *Adapted from Chaudhuri, K. R., & Fung, V. S. C. (2016).* Fast facts: Parkinson's disease *(4th ed.) (p. 9). Oxford: Health Press Limited.*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HYPERECHOGENICITY?

- A characteristic enlargement of the echogenic signals at the anatomic area of the substantia nigra.
- An increased brightness of the lenticular nucleus, caudate nucleus, red nucleus, dentate nucleus.

EUROPEAN JOURNAL OF NEUROLOGY

ORIGINAL ARTICLE

Accuracy of transcranial brain parenchyma sonography in the diagnosis of dementia with Lewy bodies

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Keywords:
Alzheimer disease, dementia with Lewy bodies, sonography, substantia nigra

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doi:10.1111/ene.13028

Background and purpose: Transcranial sonography (TCS) of the brain parenchyma is used to visualize alterations in the substantia nigra (SN) and it is applied for early diagnosis of Parkinson's disease. Our aim was to explore specific echogenic alterations of the SN in dementia with Lewy bodies (DLB) compared to Alzheimer's disease (AD).

Methods: Seventy-one subjects underwent TCS: 22 DLB, 28 AD and 21 healthy elderly controls. Cognitive impairment, extrapyramidal signs, visual hallucinations, fluctuations and rapid eye movement sleep behaviour symptoms were investigated. TCS assessed SN hyperechogenicity and symmetry.

Results: Transcranial sonography revealed SN hyperechogenicity in 100% of DLB compared to 50% of AD and 30% of controls. Mean SN echogenic area (cm^2) was 0.22 ± 0.03 in DLB, 0.15 ± 0.03 in AD and 0.14 ± 0.03 in controls ($P < 0.0001$). More than 50% of DLB presented a marked hyperechogenicity (cutoff value >0.22 cm^2) compared to only 10% of AD ($P < 0.0003$). DLB had symmetrical SN enlargement, whereas AD were mostly asymmetrical ($P = 0.015$). A combination of SN echogenic area and asymmetry index had a sensitivity of 88.9% and a specificity of 81.2% in discriminating DLB from AD (positive predictive value 85.7%, negative predictive value 85.7%). No association was found between SN hyperechogenicity and Unified Parkinson's Disease Rating Scale part III, Mini Mental State Examination or the presence of visual hallucinations.

Conclusions: Transcranial sonography may be a valid supportive tool in the diagnostic workup of neurodegenerative dementia helping clinicians to distinguish DLB from AD even at the early stages.

Psychiatry and Clinical Neurosciences 2017; 71: 238–246 doi:10.1111/pcn.12483

Regular Article

Transcranial sonography in idiopathic REM sleep behavior disorder and multiple system atrophy

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Departments of [1]Neurology and [2]Senior Official Ward, China–Japan Friendship Hospital, Beijing, China

Aim: We investigated preclinical abnormalities as revealed by transcranial sonography (TCS) in patients with idiopathic rapid eye movement sleep behavior disorder (iRBD) compared with those revealed in patients with multiple system atrophy (MSA) or Parkinson's disease (PD) and in normal controls.

Methods: Twenty-two patients with iRBD, 21 patients with MSA, 22 patients with PD, and 21 normal controls were included in this study. All participants underwent one night of video-polysomnography monitoring, and the sleep parameters were analyzed using Polysmith software and by visual analysis. TCS was performed following a standardized procedure. The echogenicity of the substantia nigra and basal ganglia were evaluated.

11 iRBD patients (50.0%) had hyperechogenicity in the basal ganglia, whereas hyperechogenicity in the basal ganglia was less frequent in PD patients (18.2%) and normal controls (9.5%) ($P < 0.001$). Poor sleep efficiency, less stage II sleep time, and more periodic leg movements were found in MSA and PD patients, whereas iRBD patients had almost normal sleep.

Conclusion: Some iRBD patients had basal ganglia hyperechogenicity that was similar to that observed in MSA, which may represent another possible convert direction. The present study further confirmed iRBD as a prodromal stage of synucleinopathy. TCS could detect subclinical changes and thus might provide useful markers for identifying individuals at increased risk for developing a synucleinopathy.

SUBJECTS AT RISK FOR PD

- **Five years before PD diagnosis only two high predictive factors are present.**
- **SN hyperechogenicity (80%) and hyposmia (60%) followed by depression (12.5%) and constipation (4.7%).**
- **SN hyperechogenicity was the only prodromal marker reaching sufficient sensitivity and specificity to be classified as risk factor at this stage.**
- **The authors suggested an approach to combine different markers for the identification of individuals at higher risk for PD.**

SPINOCEREBELLAR ATAXIAS

- There are two TCS case-control studies which reported hyperechogenicity of SN as a frequent finding in SCA 2, SCA 3 and SCA 17 indicating a vulnerability of the nigrostriatal system in SCA patients.
- Other possible findings are the fourth ventricle enlargement and the dentate nucleus hyperechogenicity.

SYDENHAM'S CHOREA

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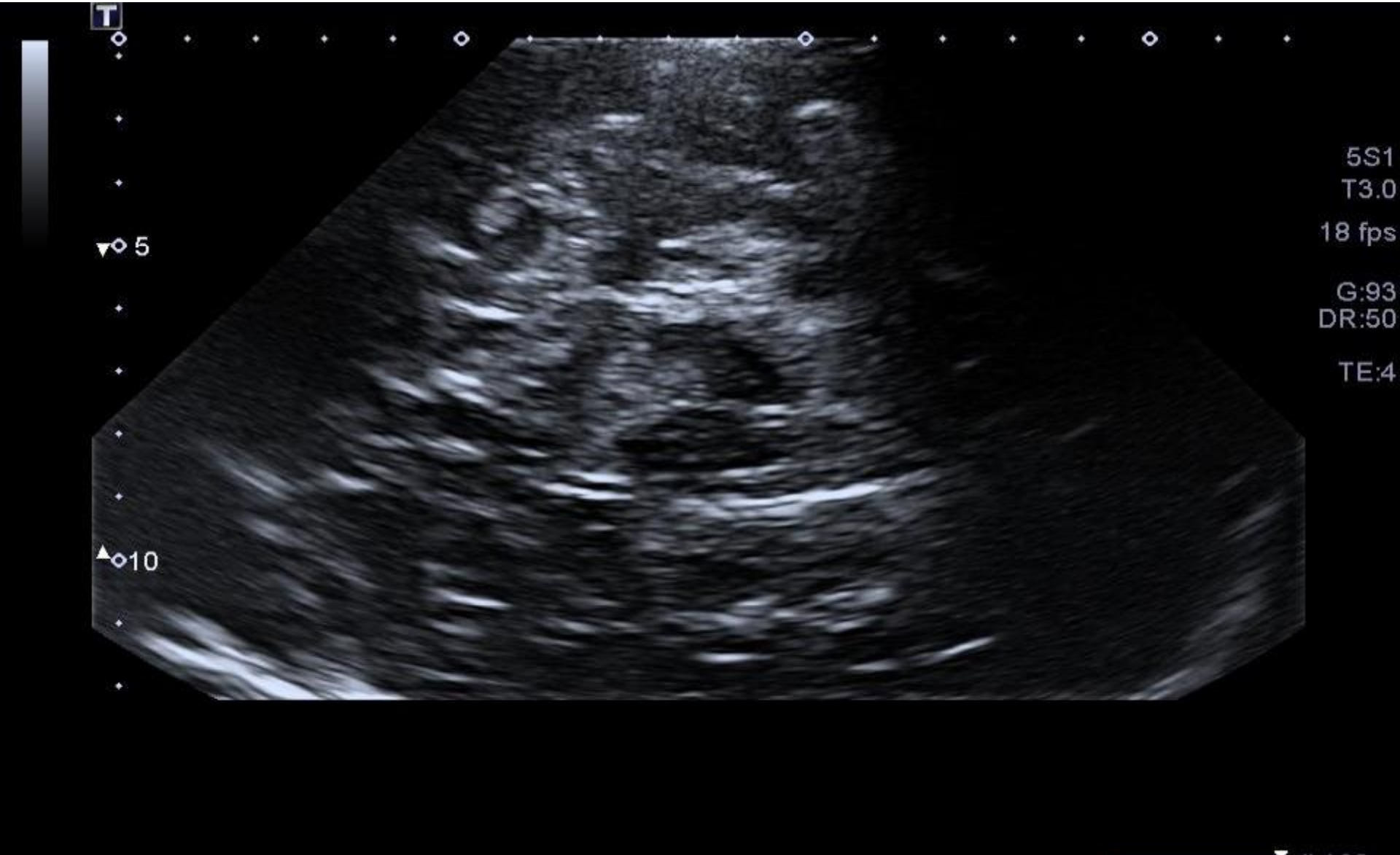
SYDENHAM'S CHOREA



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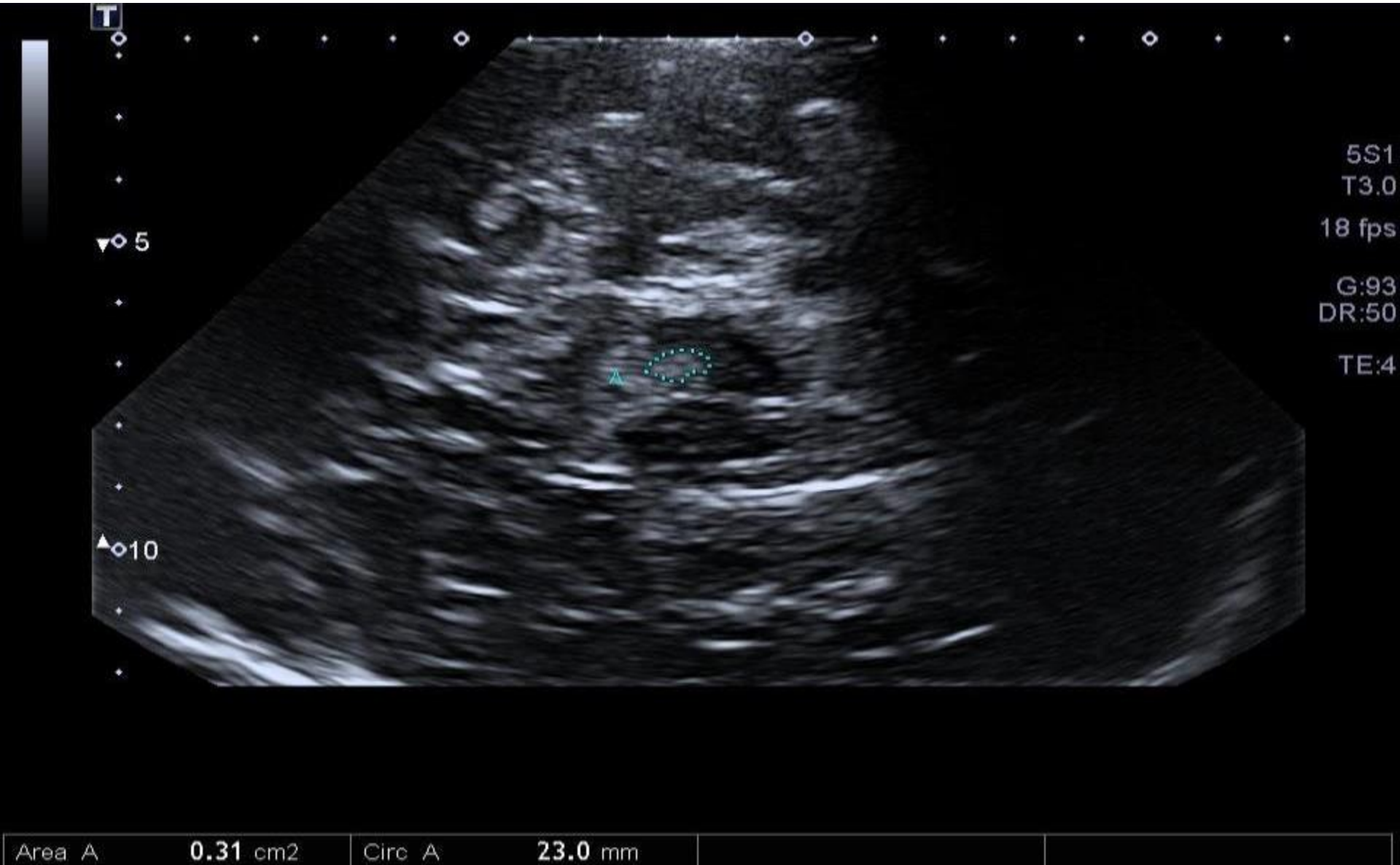

ARTICLE

Neuroimaging: Current Role in Detecting Pre-Motor Parkinson's Disease

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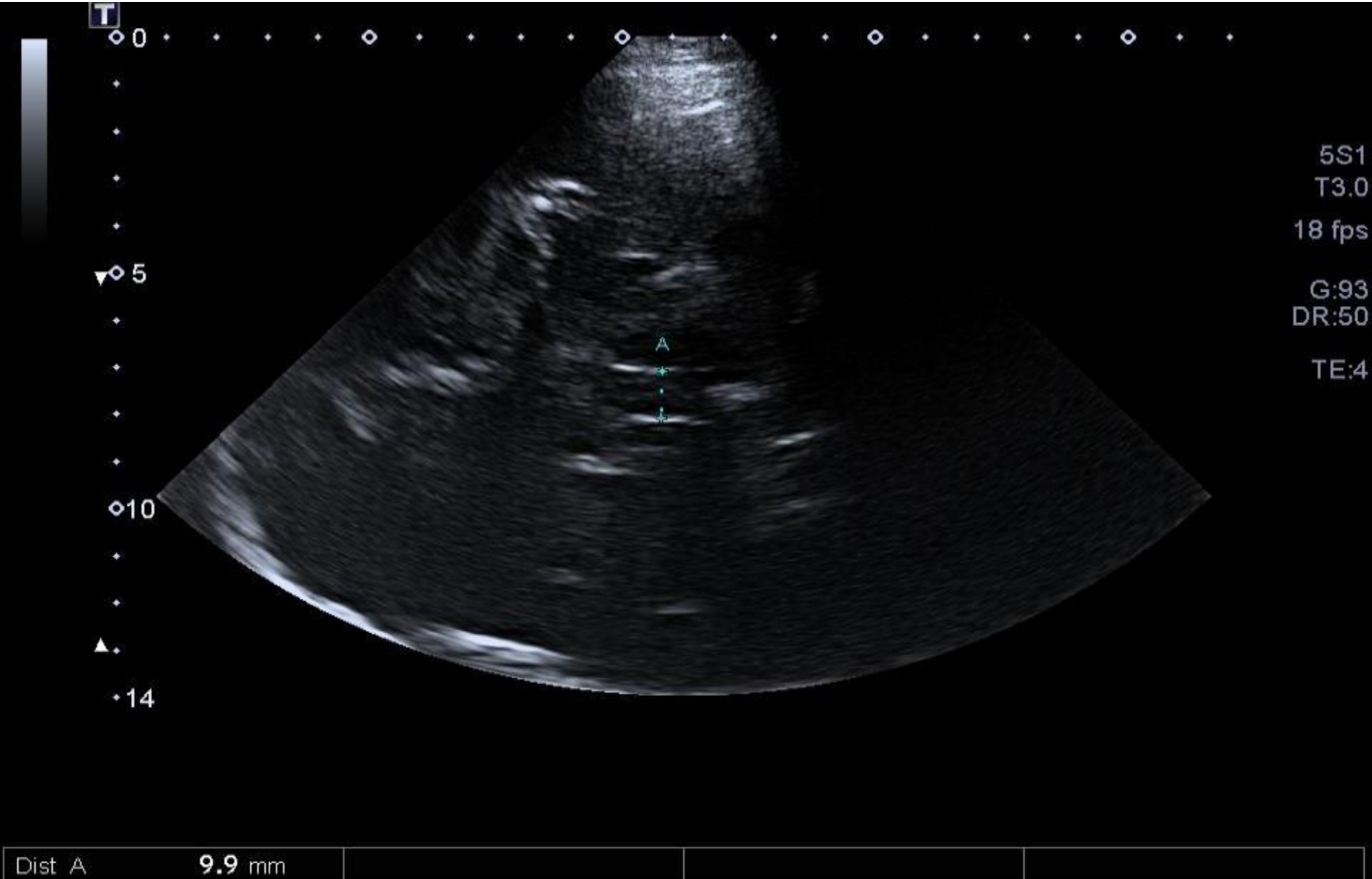
ABSTRACT: Convergent evidence suggests a pre-motor period in Parkinson's disease (PD) during which typical motor symptoms have not yet developed although dopaminergic neurons in the substantia nigra have started to degenerate. Advances in different neuroimaging techniques have allowed the detection of functional and structural changes in early PD. This review summarizes the state of the art knowledge concerning structural neuroimaging techniques including magnetic resonance imaging (MRI) and transcranial B-mode-Doppler-sonography (TCS) as well as functional neuroimaging techniques using radiotracer imaging (RTI) with different radioligands in detecting pre-motor PD.

Key Words: ultrasound; MRI; PET; SPECT; Parkinson's disease

SYDENHAM'S CHOREA



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0301-5629/$ - see front matter

http://dx.doi.org/10.1016/j.ultrasmedbio.2014.05.014

● *Original Contribution*

TRANSCRANIAL SONOGRAPHY AND ^{123}I-FP-CIT SINGLE PHOTON EMISSION COMPUTED TOMOGRAPHY IN MOVEMENT DISORDERS

PETRA BÁRTOVÁ,* OTAKAR KRAFT,† JAROMÍR BERNÁTEK,‡ MARTIN HAVEL,† PAVEL RESSNER,* KATEŘINA LANGOVÁ,§ ROMAN HERZIG,¶ and DAVID ŠKOLOUDÍK*‖

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(*Received* 7 *December* 2013; *revised* 6 *May* 2014; *in final form* 15 *May* 2014)

Abstract—Diagnosis of Parkinson's disease (PD) can be difficult in the early stages of the disease. The aim of the study described here was to assess the correlation between transcranial sonography (TCS) and ^{123}I-FP-CIT ([^{123}I] ioflupane, *N*-ω-fluoropropyl-2β-carbomethoxy-3β-(4-[^{123}I]iodophenyl)nortropane) SPECT (single photon emission computed tomography) findings and the diagnosis of PD. A total of 49 patients were enrolled in the study: 29 patients with PD, 7 patients with other parkinsonian syndromes, 11 patients with essential tremor and 2 with psychogenic movement disorder. Substantia nigra echogenicity was measured using TCS. SPECT was performed using DaTSCAN ([^{123}I]ioflupane). TCS and SPECT findings were correlated in 84% of patients, with $\kappa = 0.62$ (95% confidence interval: 0.38–0.86). TCS-measured substantia nigra echogenicity and SPECT-measured striatal binding ratio were negatively correlated ($r = -0.326$, $p = 0.003$). TCS/SPECT sensitivity, specificity and positive and negative predictive values for the diagnosis of PD were 89.7%/96.6%, 60.0%/70.0%, 76.5%/82.4% and 80.0%/93.3%, respectively. Both positive TCS and SPECT findings correlated significantly with the diagnosis of PD ($\kappa = 0.52$, 95% confidence interval: 0.27–0.76, and $\kappa = 0.69$, 95% confidence interval: 0.49–0.90, respectively).
(E-mail: petrabartova@seznam.cz)

RISK FACTORS FOR PD

- **Positive family hystory**
- **Age**
- **Gender**
- **SN hyperechogenicity**

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DOI 10.1007/s12264-017-0164-8

www.neurosci.cn
www.springer.com/12264

REVIEW

Clinical Significance of REM Sleep Behavior Disorders and Other Non-motor Symptoms of Parkinsonism

Hong Jin[1] · Jin-Ru Zhang[1] · Yun Shen[1] · Chun-Feng Liu[1,2]

Received: 24 March 2017 / Accepted: 14 May 2017 / Published online: 3 August 2017

Abstract Rapid eye movement sleep behavior disorder (RBD) is one of the most common non-motor symptoms of parkinsonism, and it may serve as a prodromal marker of neurodegenerative disease. The mechanism underlying RBD is unclear. Several prospective studies have reported that specific non-motor symptoms predict a conversion risk of developing a neurodegenerative disease, including olfactory dysfunction, abnormal color vision, autonomic dysfunction, excessive daytime sleepiness, depression, and cognitive impairment. Parkinson's disease (PD) with RBD exhibits clinical heterogeneity with respect to motor and non-motor symptoms compared with PD without RBD. In this review, we describe the main clinical and pathogenic features of RBD, focusing on its association with other non-motor symptoms of parkinsonism.

of undesirable dreams. RBD can be either idiopathic or secondary to drugs or other diseases. Idiopathic RBD (iRBD) has attracted increasing attention because patients may eventually be diagnosed with parkinsonism, such as Parkinson's disease (PD), multiple system atrophy (MSA), or dementia with Lewy bodies (DLB) [1]. The primary goals of this review are to summarize the mechanism and predictive factors underlying the conversation from RBD to parkinsonism.

The prevalence of iRBD in otherwise asymptomatic individuals has not yet been investigated, partly due to the general ignorance of the public who incorrectly believe that dream-related motor manifestations are normal. The prevalence of probable RBD is 4.6%–7.7% in the elderly Caucasian population (aged 60–97 years) as assessed by the RBD Screening Questionnaire and the Innsbruck RBD

Neurol Sci (2013) 34:935–940
DOI 10.1007/s10072-012-1164-0

ORIGINAL ARTICLE

Comparison study of olfactory function and substantia nigra hyperechogenicity in idiopathic REM sleep behavior disorder, Parkinson's disease and normal control

Hee Young Shin · Eun Youn Joo · Seong Tae Kim · Hun-Jong Dhong · Jin Whan Cho

Received: 18 December 2011 / Accepted: 26 March 2012 / Published online: 28 July 2012

Abstract Rapid eye movement (REM) sleep behavior disorder (RBD) is a preclinical feature of synucleinopathies, such as Parkinson's disease (PD).This study aimed to investigate the presence of potential early manifestations of parkinsonism, such as olfactory dysfunction and substantia nigra (SN) hyperechogenicity, in idiopathic RBD (iRBD) patients, PD patients and normal controls. We performed an olfactory function test using the cross-cultural smell identification test (CC-SIT) and midbrain transcranial

In conclusion, we found that the concomitant abnormality of olfaction and increased SN echogenicity was more frequent in iRBD compared with normal control. Olfactory dysfunction and SN hyperechogenicity could be preclinical manifestations of parkinsonism in iRBD patients.

Keywords REM sleep behavior disorder · Parkinson's disease · Olfaction · CC-SIT · Transcranial sonography

Characterization of patients with longstanding idiopathic REM sleep behavior disorder

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Monica Serradell, BSc
Maria Jose Martí, MD
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Philipp Mahlknecht, MD
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Ana Fernández-Arcos, MD
Werner Poewe, MD
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ABSTRACT

Objective: To evaluate the presence of prodromal markers of Parkinson disease (PD) in patients with longstanding idiopathic REM sleep behavior disorder (IRBD), a small subgroup of individuals with IRBD with long-term follow-up thought not to be at risk of developing PD.

Methods: Demographic, clinical, and neuroimaging markers of PD were evaluated in 20 patients with polysomnographic-confirmed longstanding IRBD and in 32 matched controls.

Results: Patients were 16 men and 4 women with mean age of 72.9 ± 8.6 years and mean follow-up from IRBD diagnosis of 12.1 ± 2.6 years. Patients more often had objective smell loss (35% vs 3.4%, $p = 0.003$), constipation (50% vs 15.6%, $p = 0.008$), and mild parkinsonian signs (45% vs 18.8%, $p = 0.042$) than controls. Unified Parkinson's Disease Rating Scale motor score was higher in patients than in controls (5.6 ± 3.5 vs 2.0 ± 2.1, $p < 0.0001$). Dopamine transporter imaging showed decreased striatal uptake in 82.4% of the patients and transcranial sonography found substantia nigra hyperechogenicity in 35.3%. α-Synuclein aggregates were found in 3 of 6 patients who underwent colon or submandibular gland biopsies. All 20 patients showed clinical, neuroimaging, or histologic markers of PD. Probability of prodromal PD (according to recent Movement Disorders Society research criteria) was higher in patients than in controls (<0.0001), and 45% of patients surpassed 80% probability.

Conclusions: Prodromal PD markers are common in individuals with longstanding IRBD, suggesting that they are affected by an underlying neurodegenerative process. This observation may be useful for the design of disease-modifying trials to prevent PD onset in IRBD. *Neurology®* 2017;89:242–248

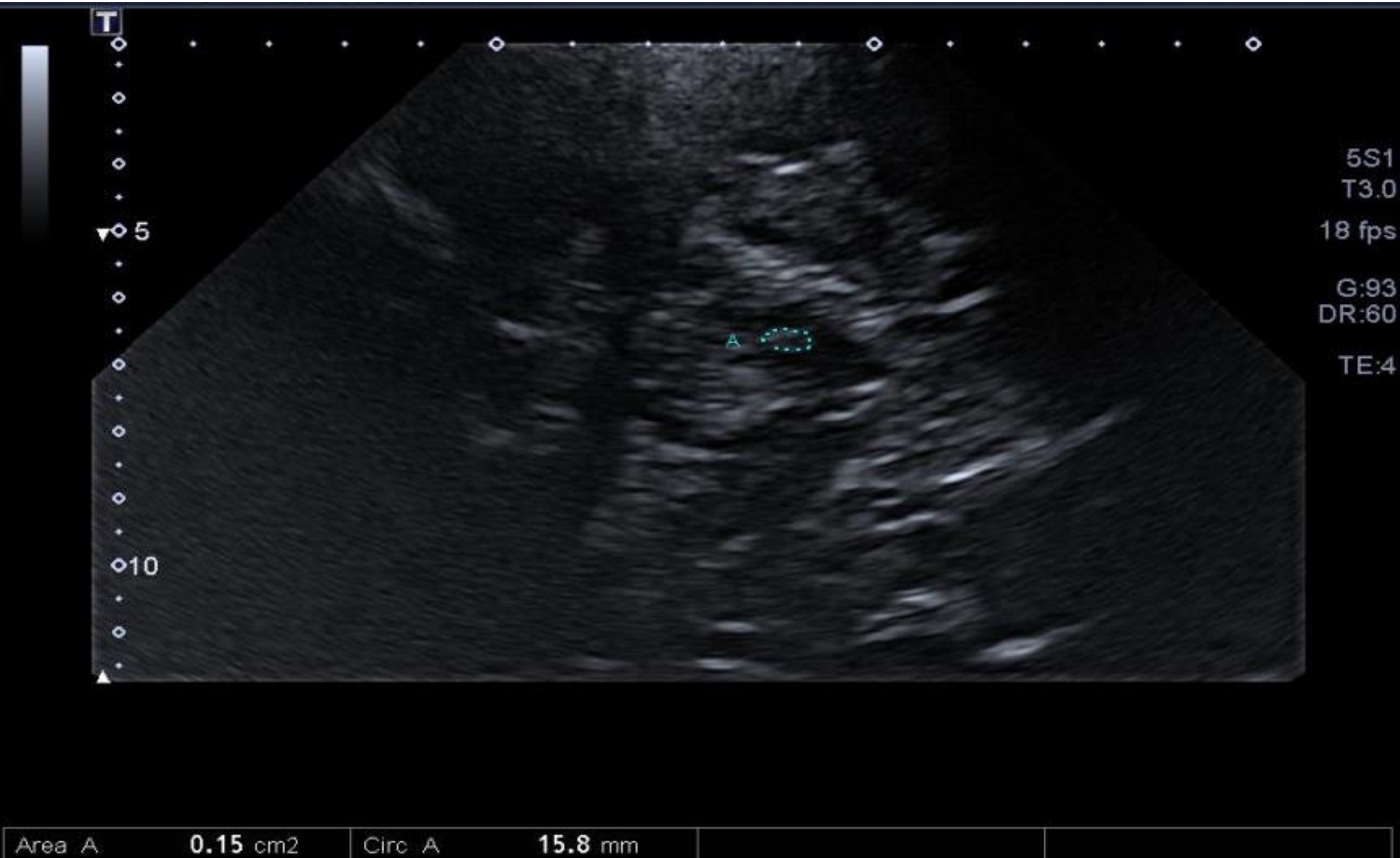
TABLE 1. LRs of risk and prodromal markers

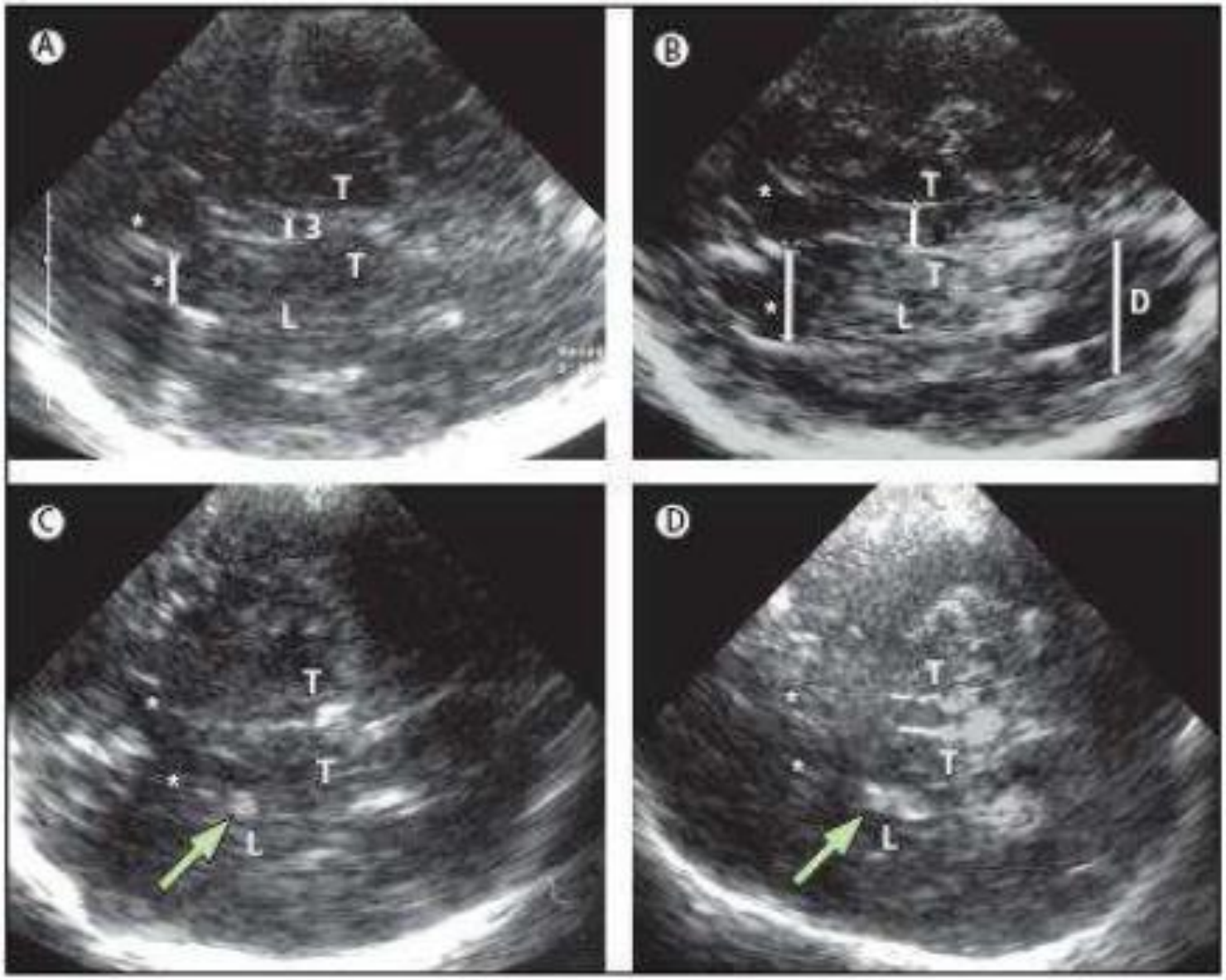
	LR^+	LR^-
Risk markers		
Male sex	1.2 (male)	0.8 (female)
Regular pesticide exposure	1.5	n/a
Occupational solvent exposure	1.5	n/a
Nonuse of caffeine	1.35	0.88
Smoking		
Current	n/a	0.45
Never	1.25	n/a
Former	n/a	0.8
Sibling had PD with age onset <50	7.5	n/a
or		
Any other first-degree relative with PD	2.5	n/a
or		
Known gene mutation	see Supporting Table II	n/a
SN hyperechogenicity	4.7	0.45
Prodromal markers		
PSG-proven RBD	130	0.62
or		
Positive RBD screen questionnaire with $>80\%$ specificity	2.3	0.76
Dopaminergic PET/SPECT clearly abnormal (e.g., $<65\%$ normal, 2 SDs below mean)	40	0.65
Possible subthreshold parkinsonism (UPDRS >3 excluding action tremor)	10	0.70
or		
Abnormal quantitative motor testing	3.5	0.60
Olfactory loss	4.0	0.43
Constipation	2.2	0.80
Excessive daytime somnolence	2.2	0.88
Symptomatic hypotension	2.1	0.87
Severe erectile dysfunction	2.0	0.90
Urinary dysfunction	1.9	0.90
Depression ($\pm$ anxiety)	1.8	0.85

ESSENTIAL TREMOR

- Usually patients affected by ET have no hyperechogenicity of the SN.
- However in a study comparing SN areas of 44 ET patients with 100 IPD and 100 controls has been demonstrated that about three or four times more patients with ET show hyperechogenicity of SN rather than healthy controls.
- This finding is consistent with the fact that the risk of developing IPD is about seven times greater in patients with ET than in the general population.

PSP-RS

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frontiers in Neurology

ORIGINAL RESEARCH
published: 07 August 2018
doi: 10.3389/fneur.2018.00645

Brainstem Raphe Alterations in TCS: A Biomarker for Depression and Apathy in Parkinson's Disease Patients

Daniel Richter[1], *Dirk Woitalla*[1,2], *Siegfried Muhlack*[1], *Ralf Gold*[1,3], *Lars Tönges*[1,3] *and Christos Krogias*[1*]

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Movement Disorders
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Midbrain Hyperechogenicity in Idiopathic REM Sleep Behavior Disorder

Heike Stockner, MD,[1] Alex Iranzo, MD,[2] Klaus Seppi, MD,[1] Mónica Serradell, BSc,[2] Viola Gschliesser, MD,[1] Martin Sojer, MD,[1] Francesc Valldeoriola, MD,[2] José L. Molinuevo, MD,[2] Birgit Frauscher, MD,[1] Christof Schmidauer, MD,[1] Joan Santamaria, MD,[2] Birgit Högl, MD,[1] Eduardo Tolosa, MD,[2] and Werner Poewe, MD[1]*; for the SINBAR (Sleep Innsbruck Barcelona) Group

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Abstract: Recent studies have reported an increased risk to develop Parkinson's disease (PD) in patients with idiopathic RBD (iRBD). Midbrain hyperechogenicity is a common transcranial sonography (TCS) finding in PD and has been suggested as a PD risk-marker in nonparkinsonian subjects. The objective of this study is to assess midbrain echogenicity by TCS in patients with iRBD and compare the findings with the healthy controls. TCS was performed in 55 iRBD patients and in 165 age and sex-matched controls. The area of echogenicity in the SN region in the iRBD group was significantly increased compared with the control group ($P < 0.001$). About 19 (37.3%) of patients with iRBD were found to have SN hyperechogenicity when compared with 16 (10.7%) of the controls ($P < 0.001$). This is the first case-control study assessing midbrain echogenicity in a large iRBD cohort compared to age- and sex-matched healthy individuals. The finding of an increased prevalence of hyperechogenicity in a subgroup of individuals with a priori increased risk for PD supports the potential role of hyperechogenicity as a risk marker for PD. The prospective follow-up of this iRBD cohort is needed to establish if those with midbrain hyperechogenicity will go on to develop clinically defined PD or not. © 2009 Movement Disorder Society

Key words: idiopathic RBD; transcranial sonography; substantia nigra; hyperechogenicity; Parkinson's disease

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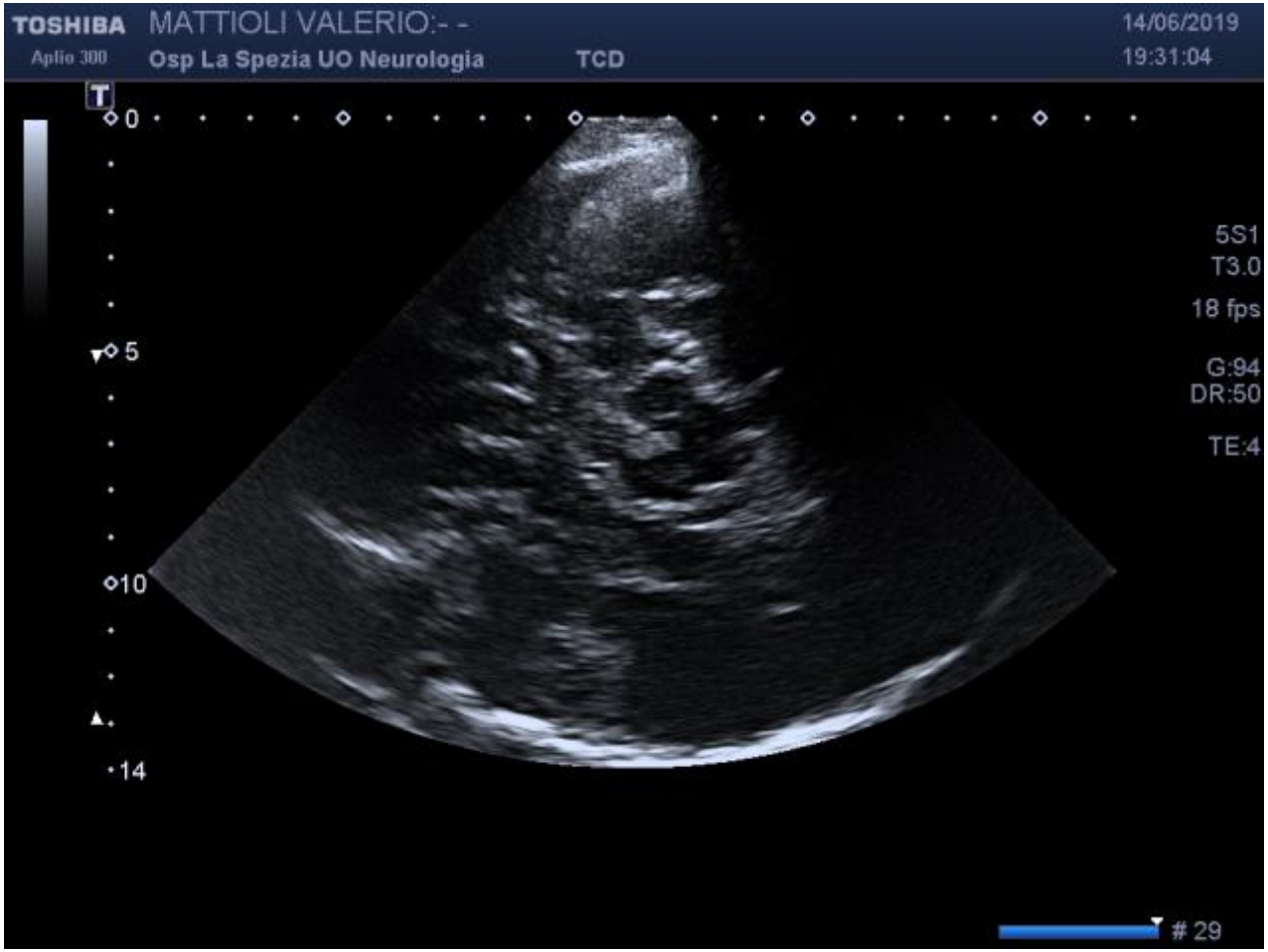
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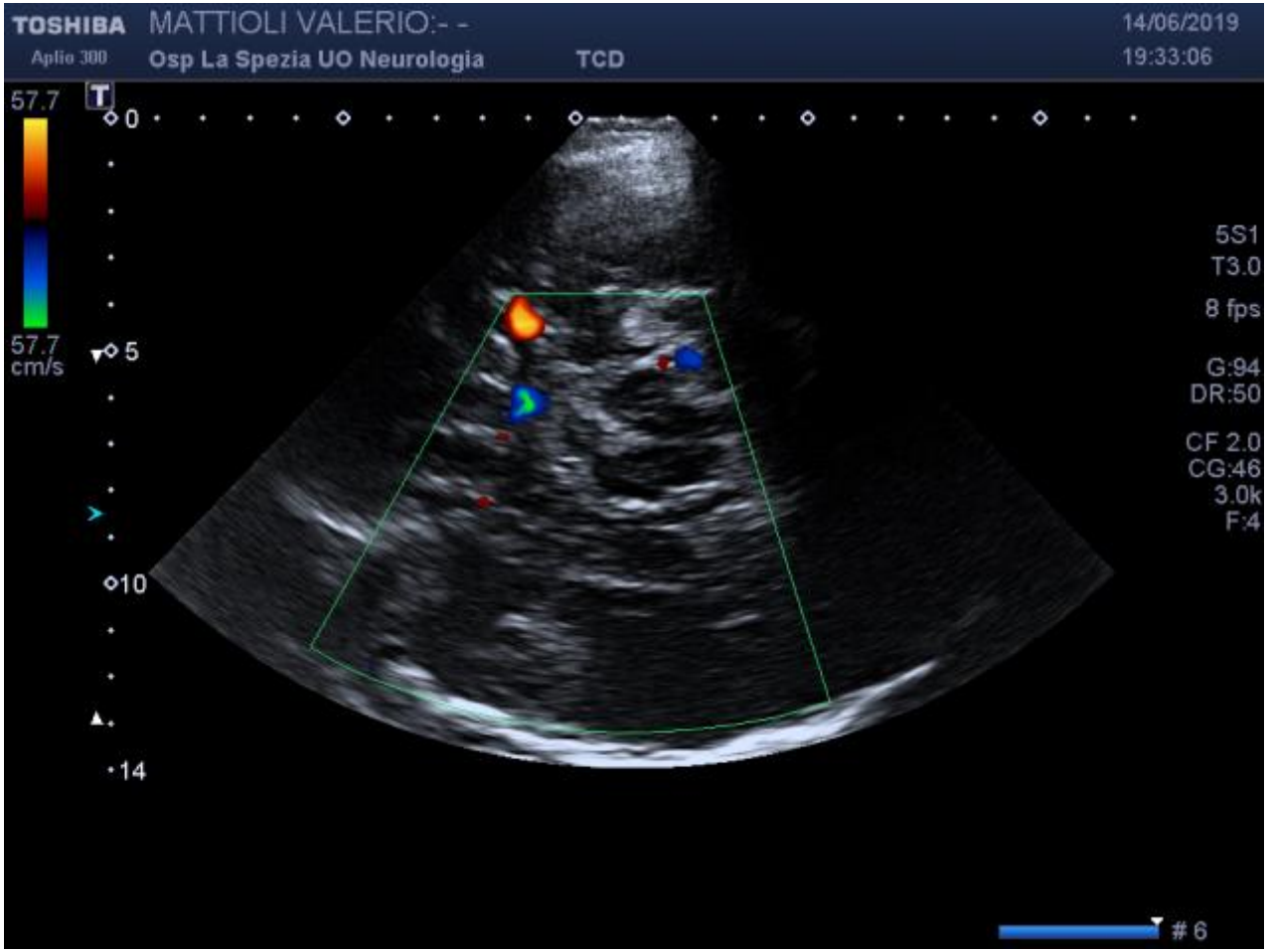
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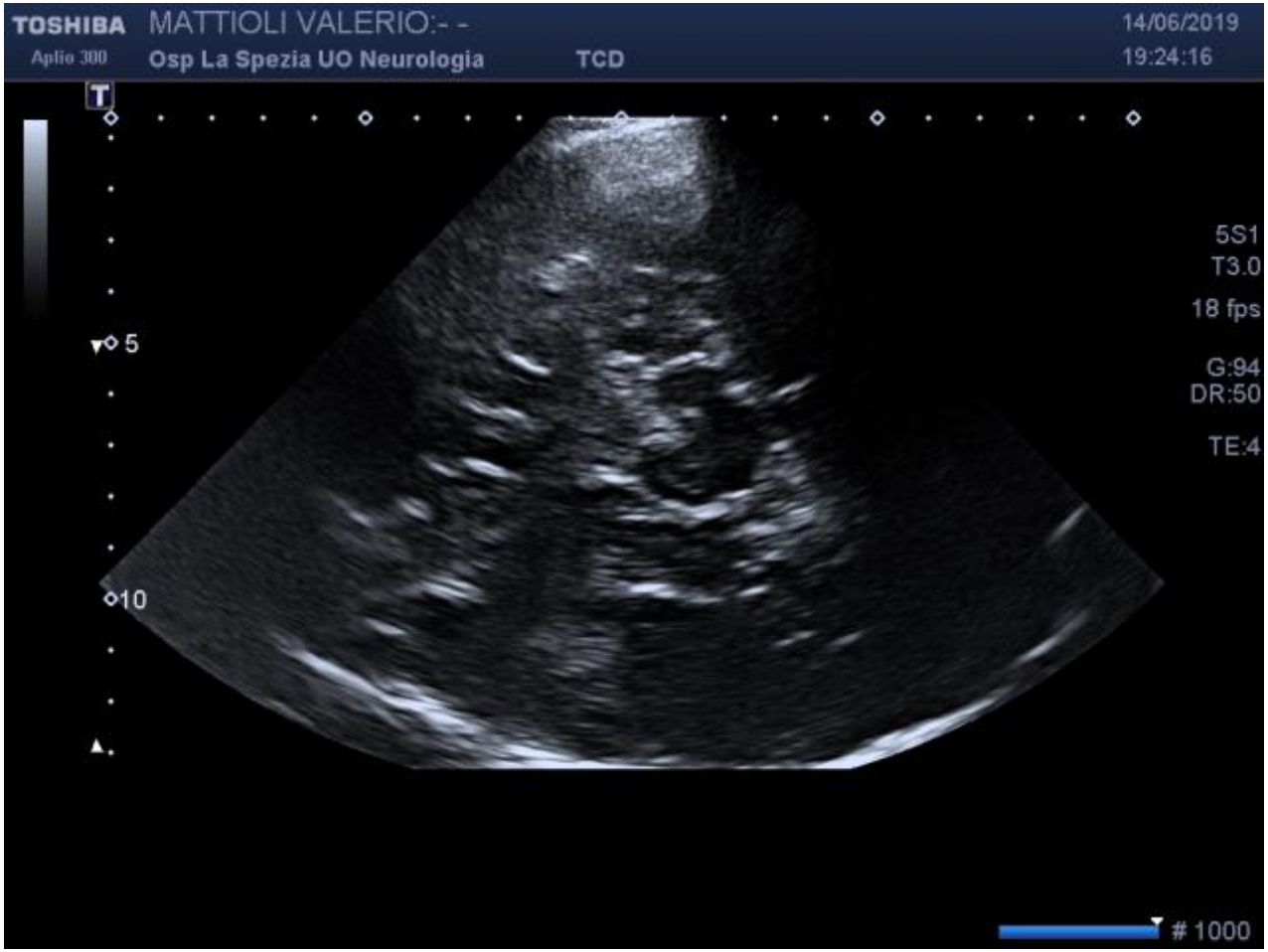
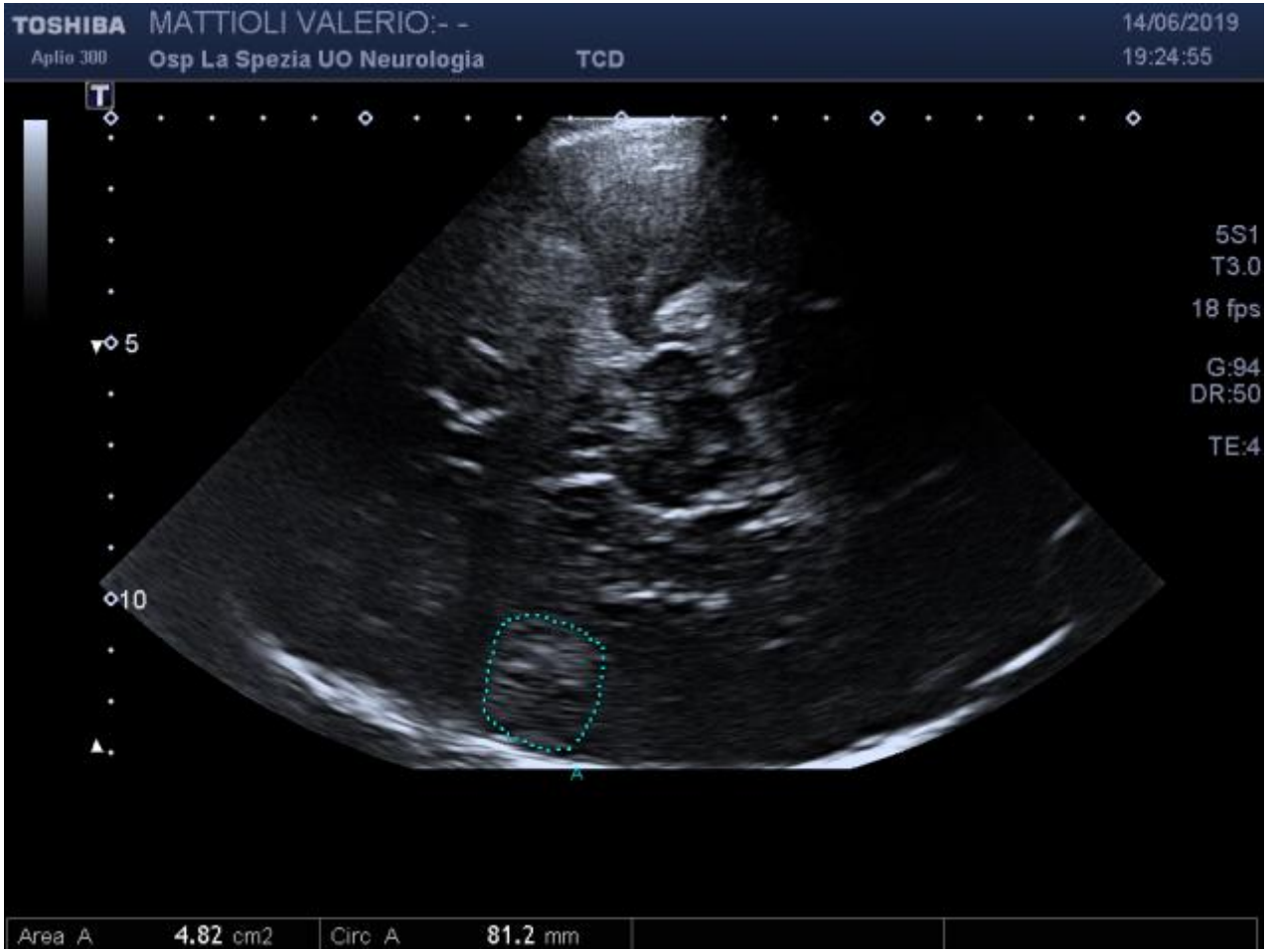
cm/s
5
10
14
5S1
T3.0
8 fps
G:94
DR:50
CF 2.0
CG:46
3.0k
F:4
6


TOSHIBA
Aplio 300
MATTIOLI VALERIO:- -
Osp La Spezia UO Neurologia
TCD
14/06/2019
19:24:16
T
5
10
5S1
T3.0
18 fps
G:94
DR:50
TE:4
1000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14/06/2019
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18 fps
G:94
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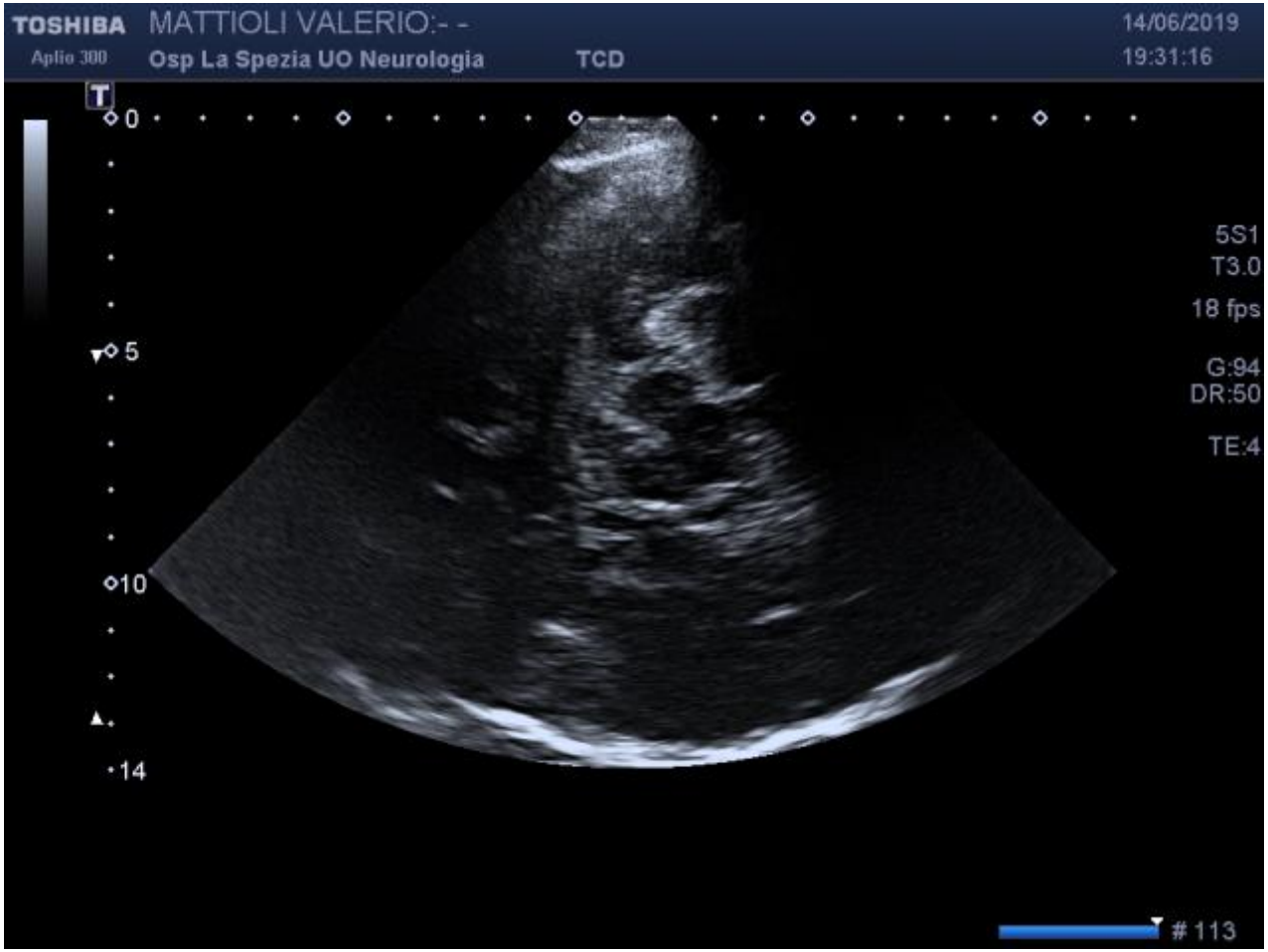
TE:4
5
10
Area A 4.82 cm2
Circ A 81.2 mm


TOSHIBA
Aplio 300
MATTIOLI VALERIO:- -
Osp La Spezia UO Neurologia
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14/06/2019
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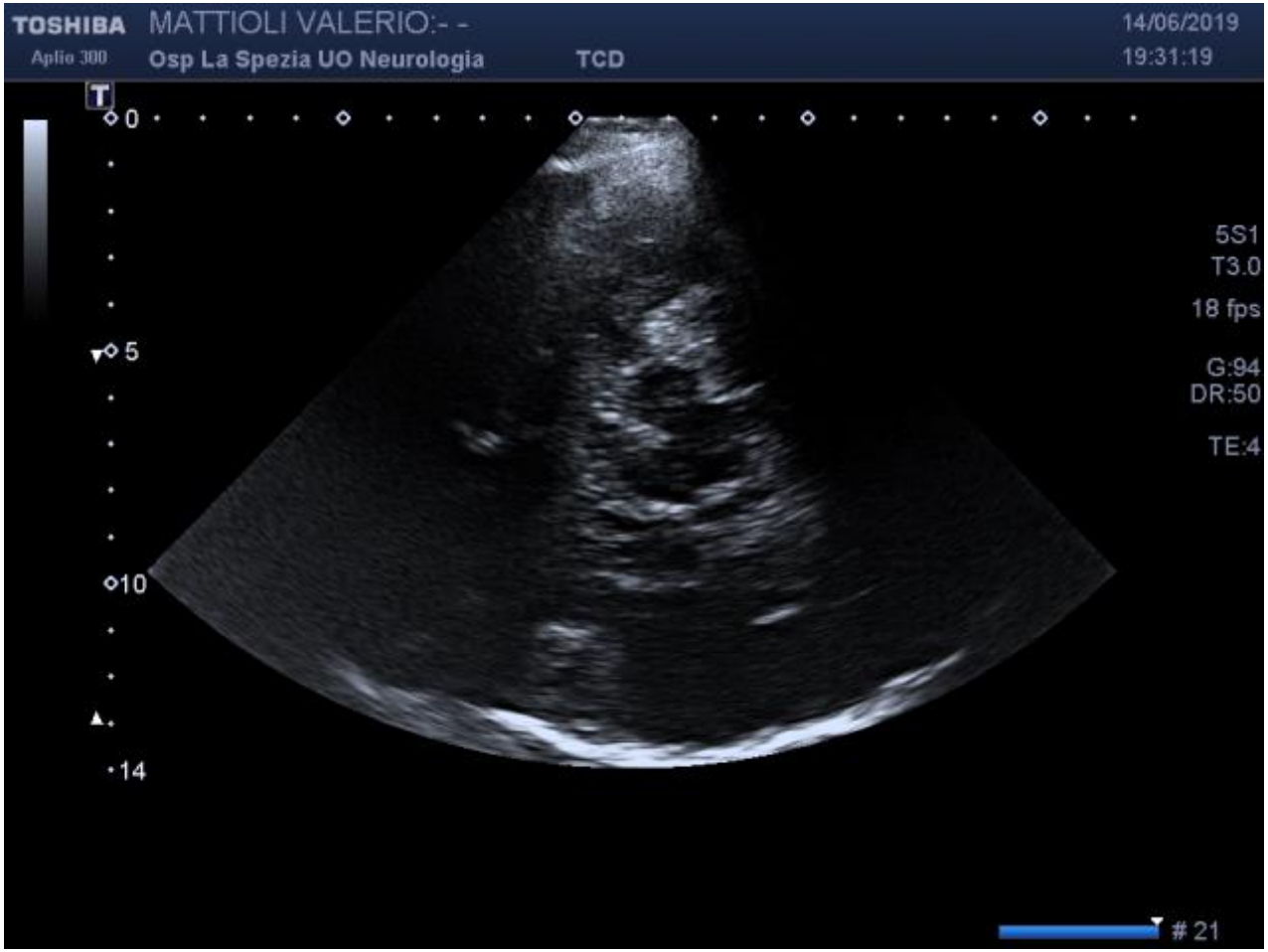
5
10
14
5S1
T3.0
18 fps
G:94
DR:50
TE:4
113


TOSHIBA
Aplio 300
MATTIOLI VALERIO:- -
Osp La Spezia UO Neurologia
TCD
14/06/2019
19:31:19
T
0
5
10
14
5S1
T3.0
18 fps
G:94
DR:50
TE:4
21

An unusual gait disorder at the Emergency Department: role of the quantitative assessment of parenchymal transcranial Doppler sonography

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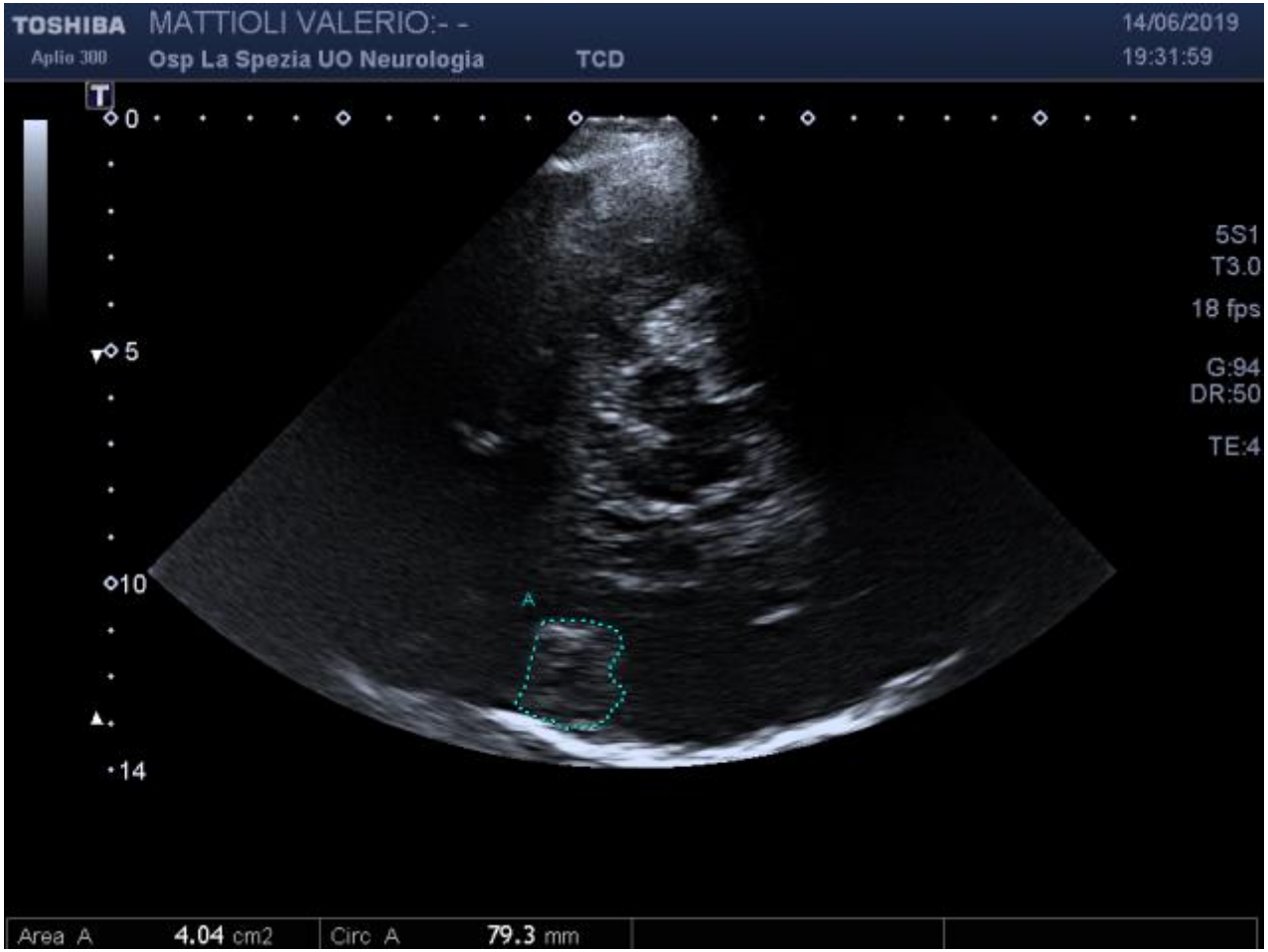
TOSHIBA
Aplio 300
MATTIOLI VALERIO:- -
Osp La Spezia UO Neurologia
TCD
14/06/2019
19:31:59
T
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5
10
14
A
5S1
T3.0
18 fps
G:94
DR:50
TE:4
Area A 4.04 cm2
Circ A 79.3 mm