

Caso clinico Ruolo dell'ecografia parenchimale in un caso d'incerta interpretazione

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Caso clinico – ottobre 2011

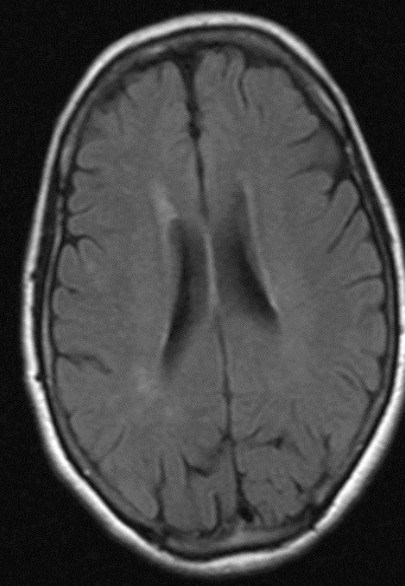
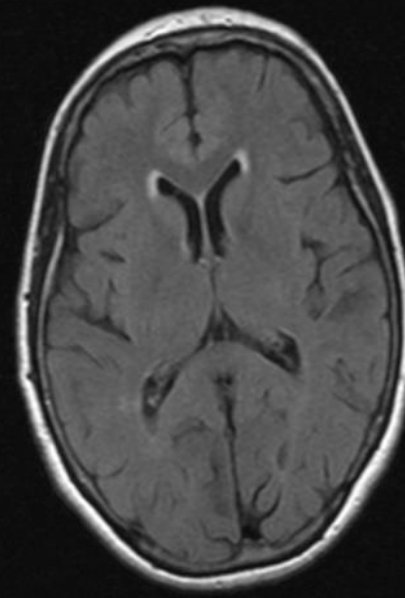
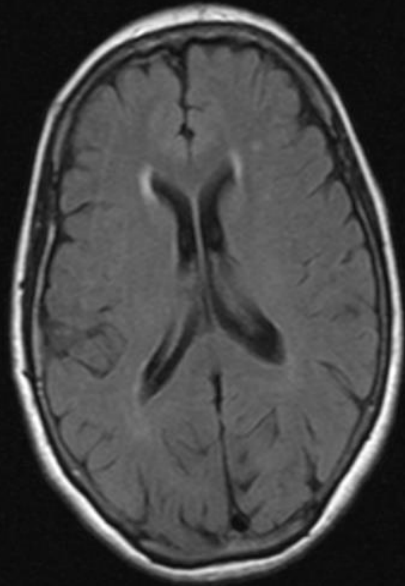
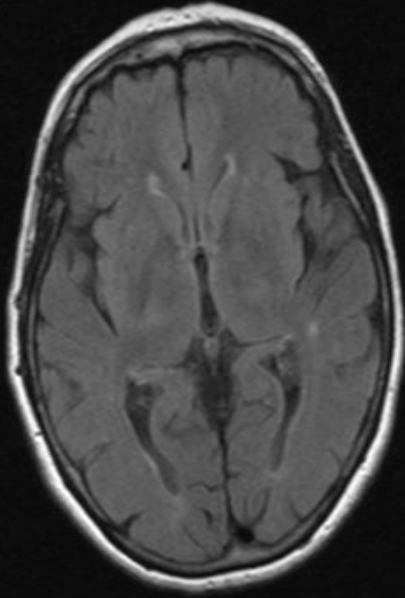
- Donna 74 anni, giunge a visita neurologica per comparsa da alcuni mesi di cefalea frontale, instabilità posturale, stato ansioso e sensazione di tremolio interno
- AF: padre con tremore in età senile
- APR: poliartrosi, ipertensione arteriosa in compenso farmacologico.
- EON: lieve ipomimia con note di bradipsichismo, sfumato ipertono plastico, non evidenza di tremore né ipocinesia.
- TC encefalo negativa
- Prescritta amitriptilina a basse dosi con modesto beneficio

- Febbraio 2014: controllo per comparsa di tremore agli arti superiori, soprattutto alla mano dx, dolore alla spalla dx, insonnia, accentuazione del disturbo d'ansia con aspetti somatoformi
- EON: lieve tremore posturale AASS, tremore a riposo Asdx, lieve ipertono plastico dx > sx, ipocinesia lieve al finger-tapping dx > sx
- Sospesa amitriptilina per intolleranza
- Prescritto trazodone

Bilancio cognitivo («lieve deficit di attenzione sostenuta e divisa»)

SPECT cerebrale - DAT-scan (integrità delle vie nigro-striatali)

- Controllo ad un anno (maggio 2015): si osserva un peggioramento dell'ipertono plastico e dell'ipocinesia, una netta riduzione del pendolarismo a dx, tremore AASS posturale, ed a riposo a dx.
- RMN encefalo: «piccole plurime alterazioni microgliotiche della sostanza bianca periventricolare sopratentoriale su verosimile base vascolare cronica».
- Inizia Levodopa/Benserazide 200+50 mg cp ¼ x 3/die con modesto beneficio.
- Ad un controllo dopo 6 mesi (dicembre 2015) viene aggiunta Selegilina 5 mg/die

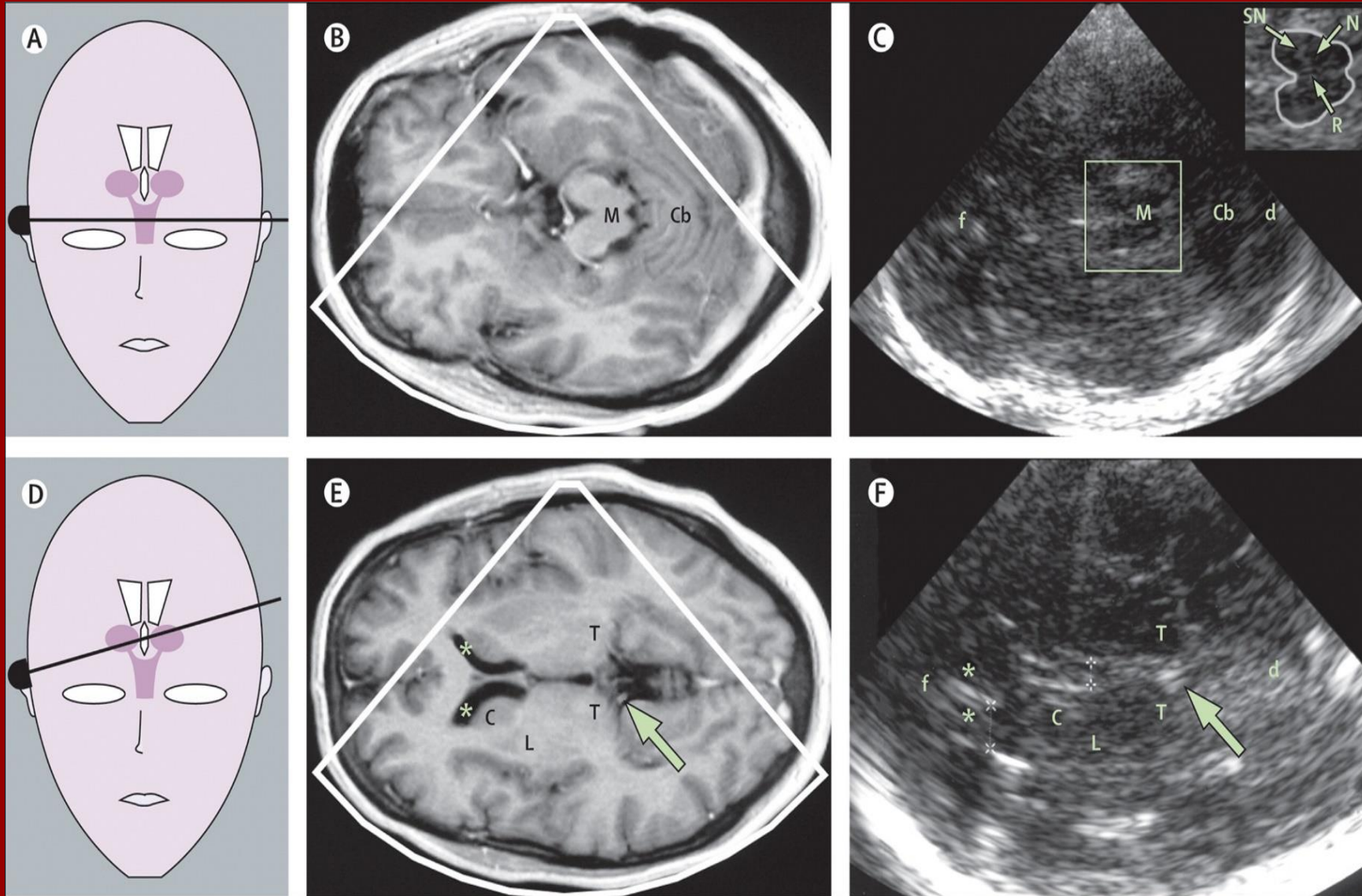


Novembre 2016: la paziente ha sospeso la terapia di sua iniziativa per scarsa compliance («sensazione di testa confusa»). Riferisce un peggioramento clinico generale.

UPDRS parte III: 18

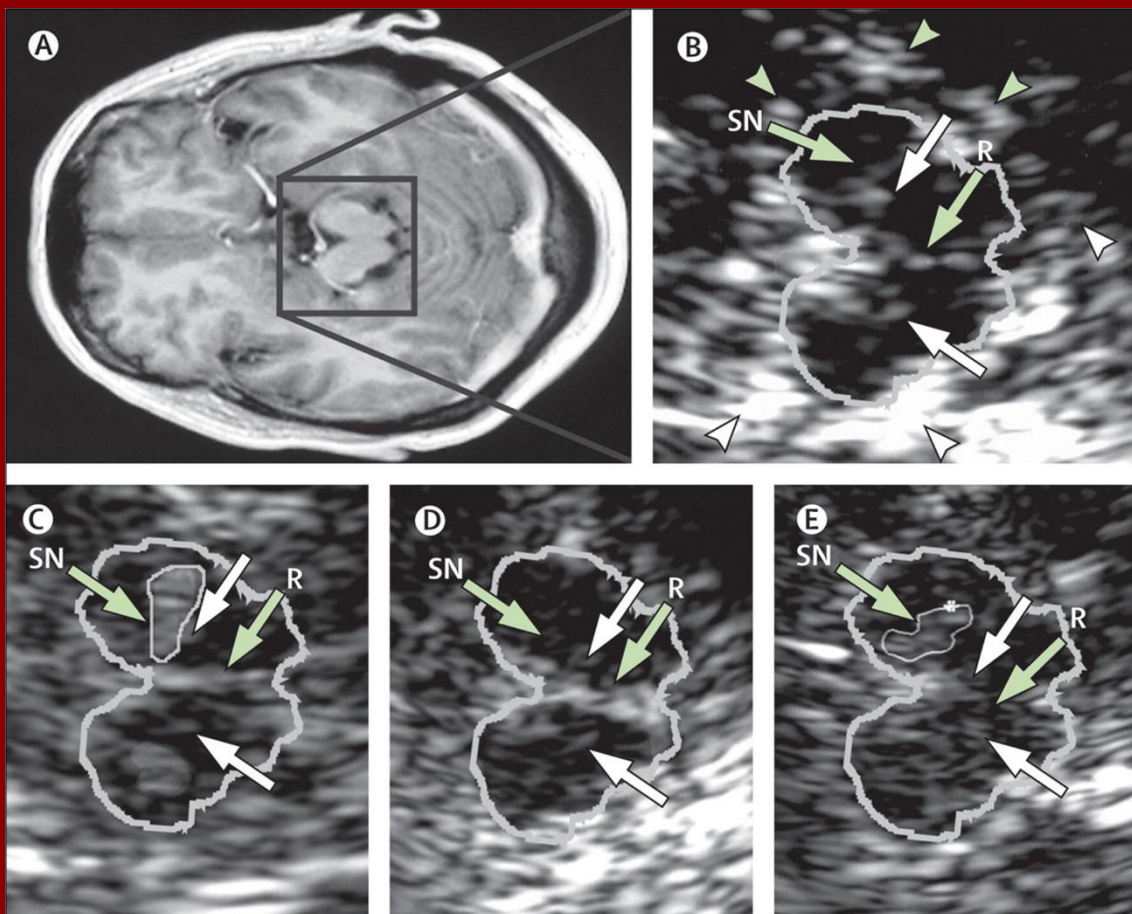
- **Ipotesi diagnostiche**
- **Tremore Essenziale?**
- **Parkinsonismo vascolare?**
- **Tremore Distonico?**
- **SWEDD?**

Esegue studio ecografico del parenchima cerebrale



Iperrecogenicità della SN > 0,20-0,25 cm² marker di PD

Una recente metanalisi ha dimostrato un'elevata accuratezza diagnostica (83% di sensibilità e 87% di specificità) nella dd tra soggetti sani e malati*



*Li DH et al. – Sci Rep. 2016; 6:20863

- **Hyperechogenicity of substantia nigra for differential diagnosis of Parkinson's disease: A meta-analysis**

A. Shafieesabet et al. – Parkinsonism Relat Dis 2017 Sep;42:1-11

- **SN hyperechogenicity has 75% sensitivity and 70% specificity to differentiate idiopathic PD from AP.**
- **Sensitivity and specificity to distinguish idiopathic PD from ET was calculated as 78% and 85%, respectively.**

- **Usefulness of Cardiac MIBG Scintigraphy, Olfactory Testing and Substantia Nigra Hyperechogenicity as Additional Diagnostic Markers for Distinguishing between Parkinson's Disease and Atypical Parkinsonian Syndromes.**

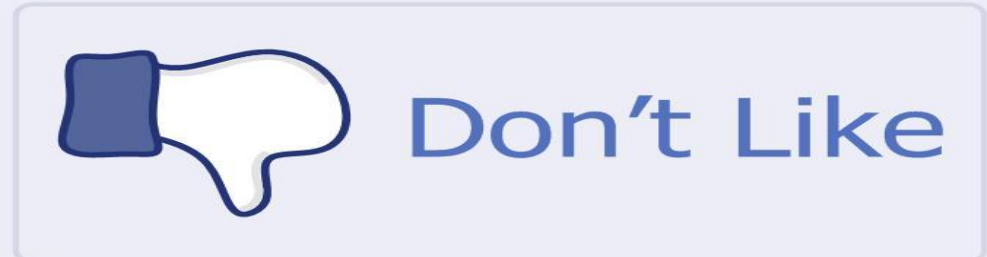
H. Fujita et al. – Plos One 2016 Nov 3;11(11):e0165869

- **Combined use of cardiac MIBG scintigraphy, olfactory testing and SN hyperechogenicity on TCS can support clinical diagnosis between PD and AP**
- **1/3 specificity 63% - sensitivity 86%**
- **2/3 specificity 96 % - sensitivity 58%**
- **3/3 specificity 100% - sensitivity 25%**

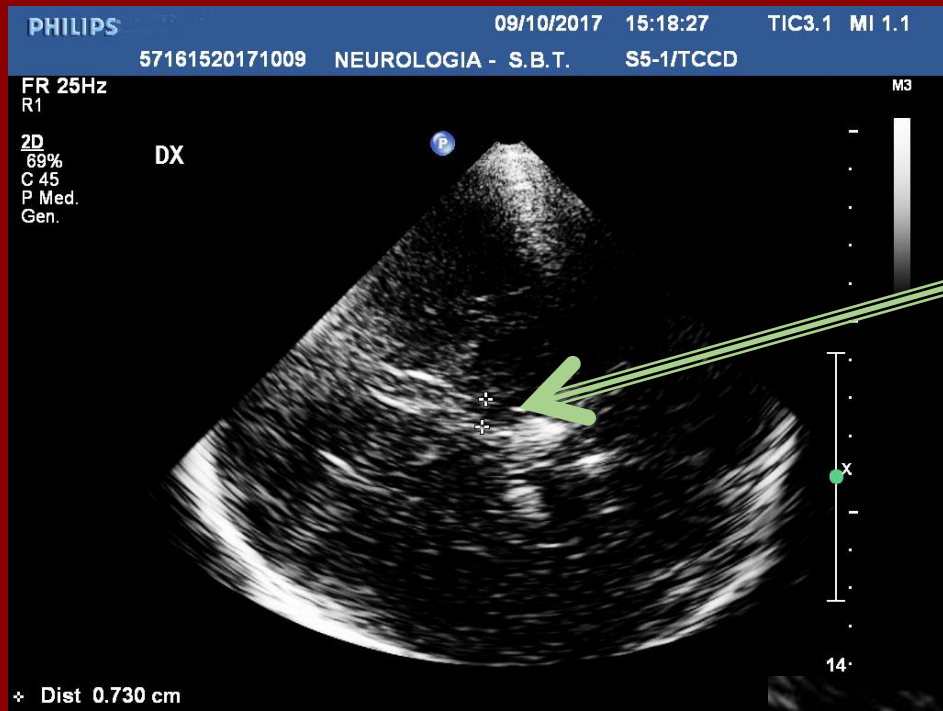
Vantaggi e limiti della metodica



- Bassi costi
- Sicuro e ripetibile
- Rapido e eseguibile in qualsiasi struttura
- Sensibile e specifico

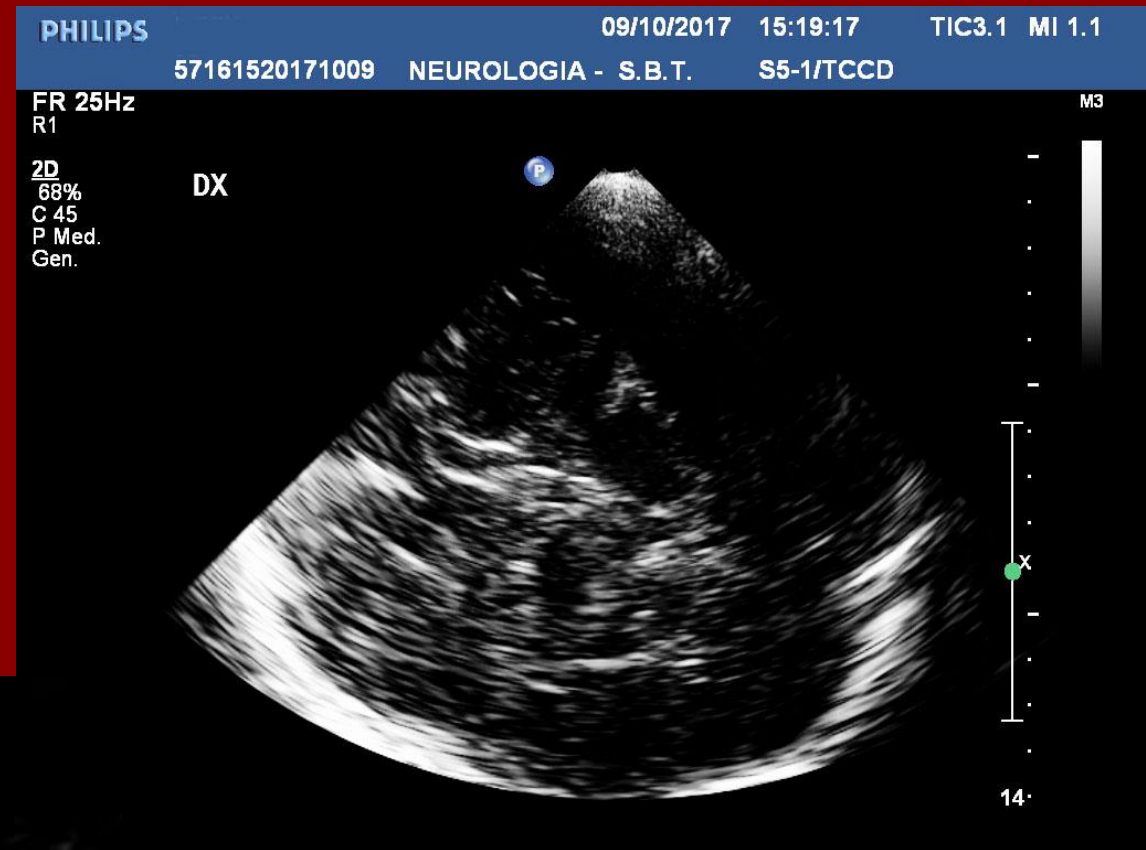
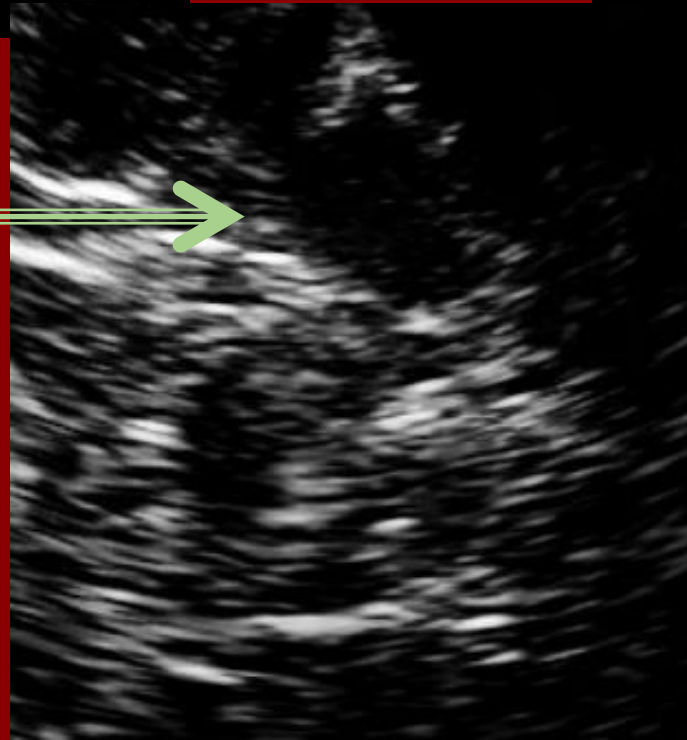


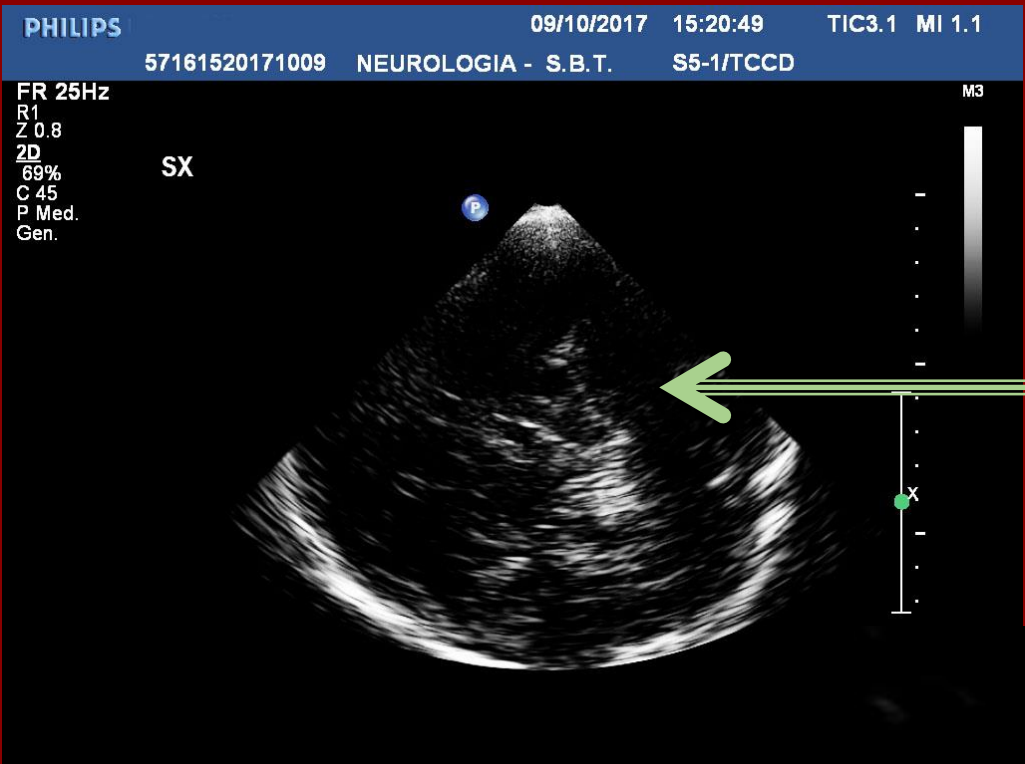
- Operatore-dipendente
- Macchina-dipendente
- Finestra acustica



III Ventricolo
0,73 cm

Peduncolo
mesencefalico dx





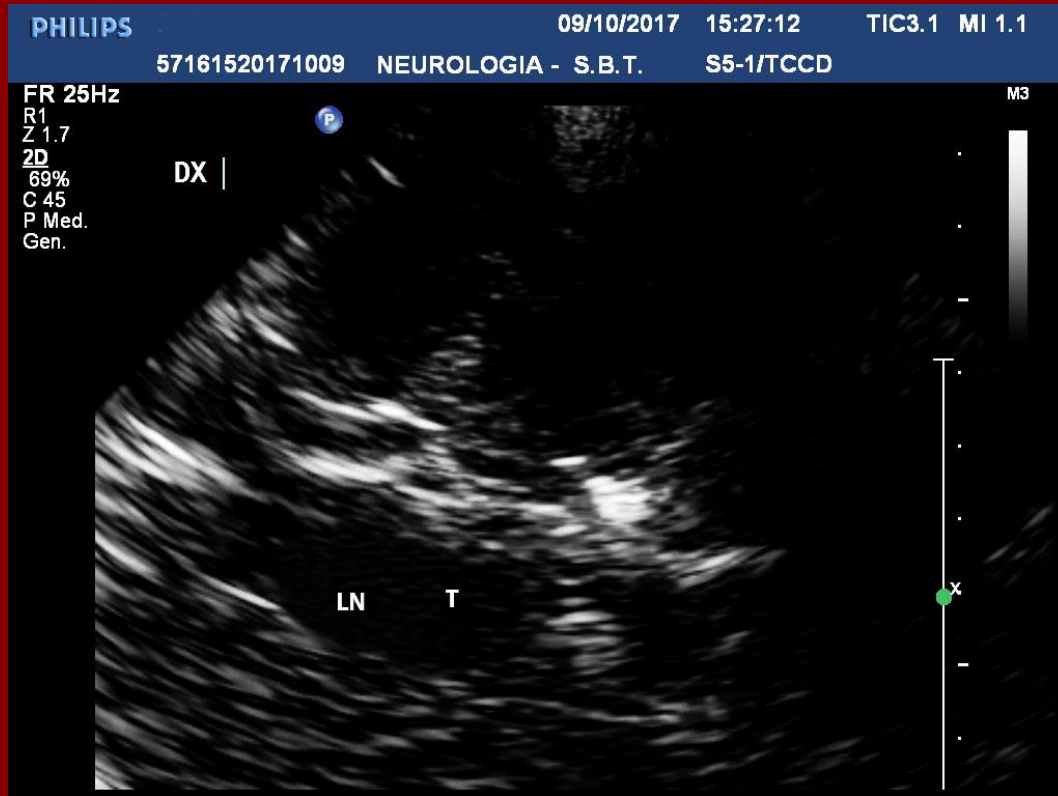
Peduncolo
mesencefalico sn



SN iperecogena sn
Area 0,35 cm²



Assente iperecogenicità bilaterale del Talamo (T) e Nucleo Lenticolare(LN)



Eco parenchima suggestivo per PD

Is Transcranial Sonography Useful to Distinguish Scans Without Evidence of Dopaminergic Deficit Patients From Parkinson's Disease?

H. Stockner et al. - Movement Disorders, Vol. 27, No. 9, 2012

14 SWEDD vs 19 PD

There was a significantly increased area of echogenicity in the PD group ($0.24 \pm 0.06 \text{ cm}^2$), compared to the group of patients with SWEDD ($0.13 \pm 0.06 \text{ cm}^2$; $P < 0.001$). One (9.1%) of these patients, compared to 14 (82.5%) of the PD patients, was found to have hyperechogenicity ($P < 0.001$).

STOCKNER ET AL.

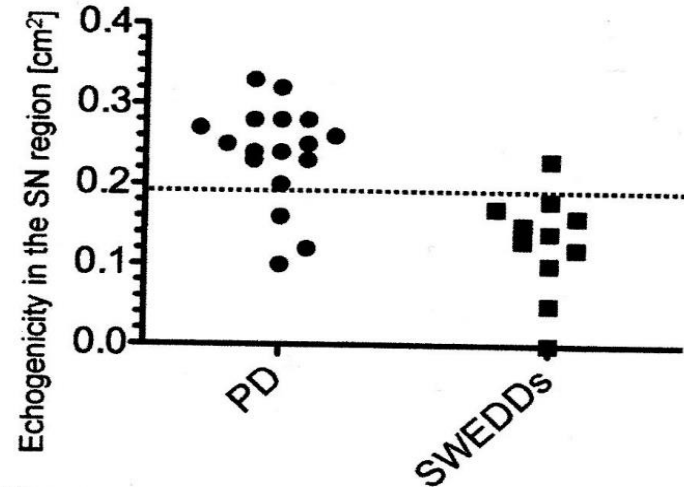


FIG. 1. Significantly increased area of midbrain echogenicity in the PD group compared with the SWEDD group ($P < 0.001$) (broken line: value set at 0.20 cm^2 to define hyperechogenicity).

Transcranial sonography in dopa-responsive dystonia

M. Svetela et al, Eur J Neurol. 2017 Jan;24(1):161-166

SN hyperechogenicity was present in 63.6% of patients with DRD, which was significantly different in comparison to patients with dystonia (20%) and HCs (6.7%), but not in comparison to the PD group (87.3%). Also, values of the maximal areas of substantia nigra hyperechogenicity in patients with DRD were higher in comparison to HCs, but significantly lower than among the PD group.

Sonographic alteration of substantia nigra is related to parkinsonism-predominant course of X-linked dystonia-parkinsonism

U. Walter et al. Parkinsonism Relat Disord 2017 Apr;37:43-49

Early alteration of the substantia nigra in XDP mutation carriers prone to develop parkinsonism. Thus, substantia-nigra hyperechogenicity may be regarded as a preclinical risk marker of parkinsonism-predominant XDP

SWEDD?

(Scans Without Evidence of Dopaminergic Deficit) Marek et al. – Neurology 2003

Downloaded from <http://jnnp.bmj.com/> on September 14, 2017 - Published by group.bmj.com



REVIEW

What do patients with scans without evidence of dopaminergic deficit (SWEDD) have? New evidence and continuing controversies

Roberto Erro,^{1,2} Susanne A Schneider,^{1,3} Maria Stamelou,^{4,5} Niall P Quinn,¹ Kailash P Bhatia¹

Movement disorders

Study (reference)	Number of SWEDD cases (%)
Elldopa1	21/142 (14.7)
InSPECT2	15/112 (13.3)
PRECEPT3	90/799 (11.3)
REAL-PET4	21/186 (11.2)
CALM-PD5	3/82 (3.6)
European FP-CIT study6	10/51 (19.6)

Table 1

Frequency of scans without evidence for dopaminergic deficit (SWEDD) cases in some of the drug trials or imaging studies for Parkinson's disease (PD)

Alternative conditions to Parkinson's disease (PD) accounting for some of the SWEDD cases

Essential Tremor

Dystonia (including monogenic forms)

Fragile X premutation

Iatrogenic/Tardive

Symptomatic (vascular/brain neoplasm, toxic)

Psychogenic

Supranigral parkinsonism

Soft extrapyramidal signs of the elderly

Revisione del DAT-scan dal 2003 al 2013 di 410 pz consecutivi affetti da parkinsonismo (80% PD)

Individuati 10 casi di possibile SWEDD (2,4%) confermati sia dall'analisi qualitativa/visiva sia da quella semiquantitativa

I 10 pz avevano una diagnosi clinica di PD (5), MSA (1), PSP (2) e CBD (2)

Ad una ri-analisi semiquantitativa solo 2 su 10 risultavano normali

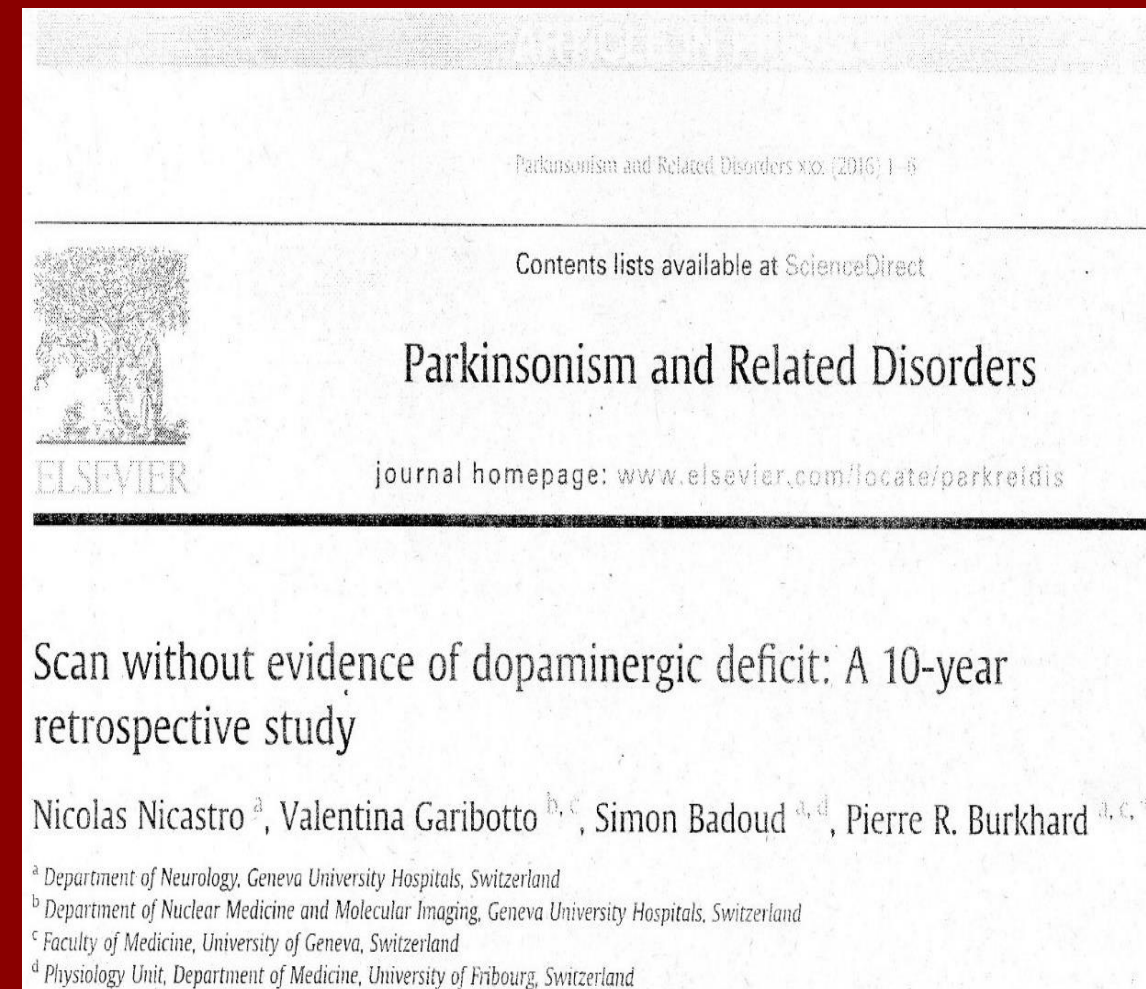
Ad un riesame visivo solo 1 (CBD) su 10 risultava normale e coincideva con uno dei due normali all'analisi semiquantitativa

Variabilità interpretativa nell'analisi visiva?

Variabili tecniche anche nell'analisi semiquantitativa?

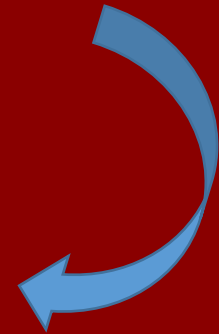
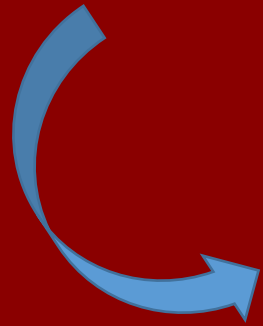
Limite dei casi controllo?

Incidenza dell'età, dei farmaci?



ERRORE DIAGNOSTICO

ERRORE TECNICO



SWEDD

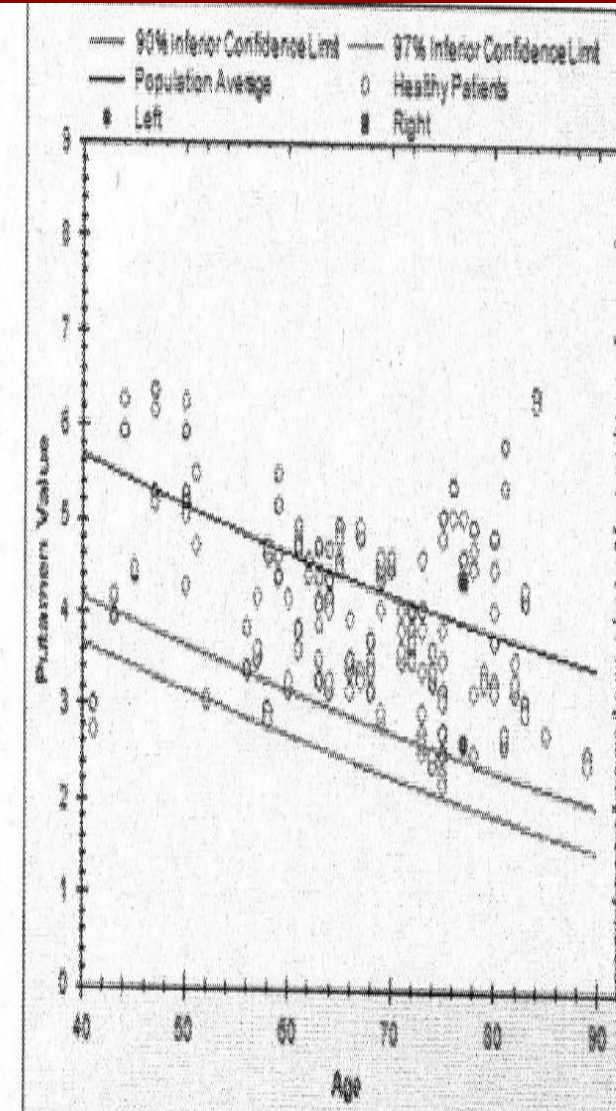
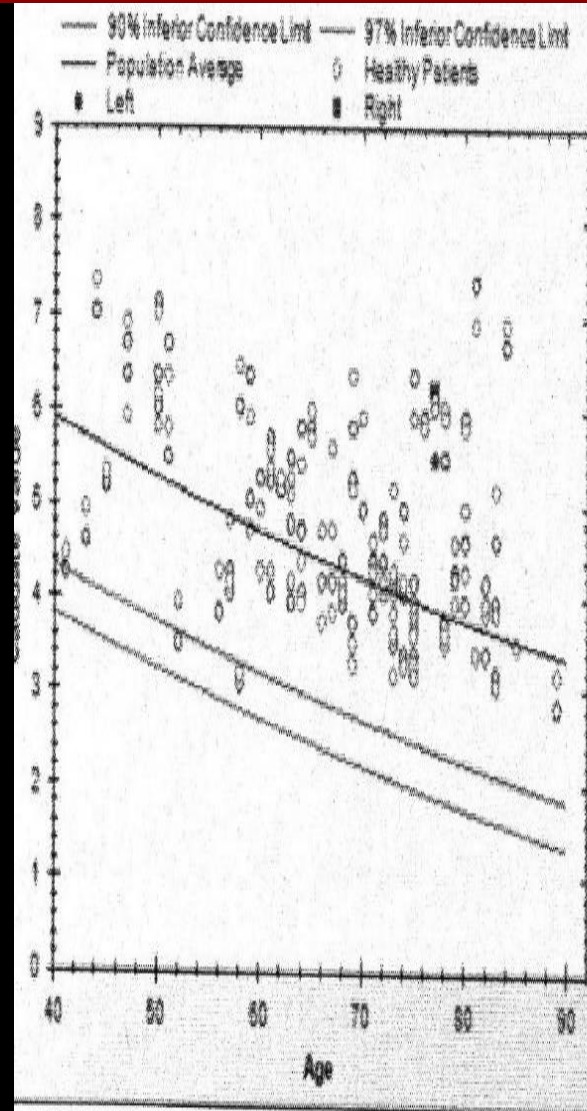
?

LLRK2 gene mutation - 1 SWEDD (REAL-PET)

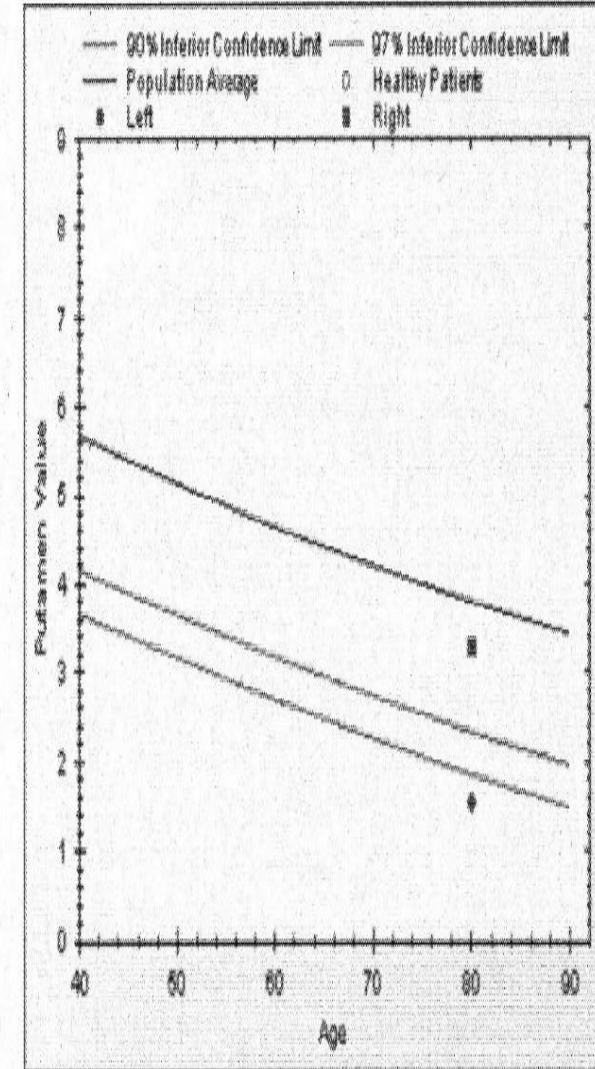
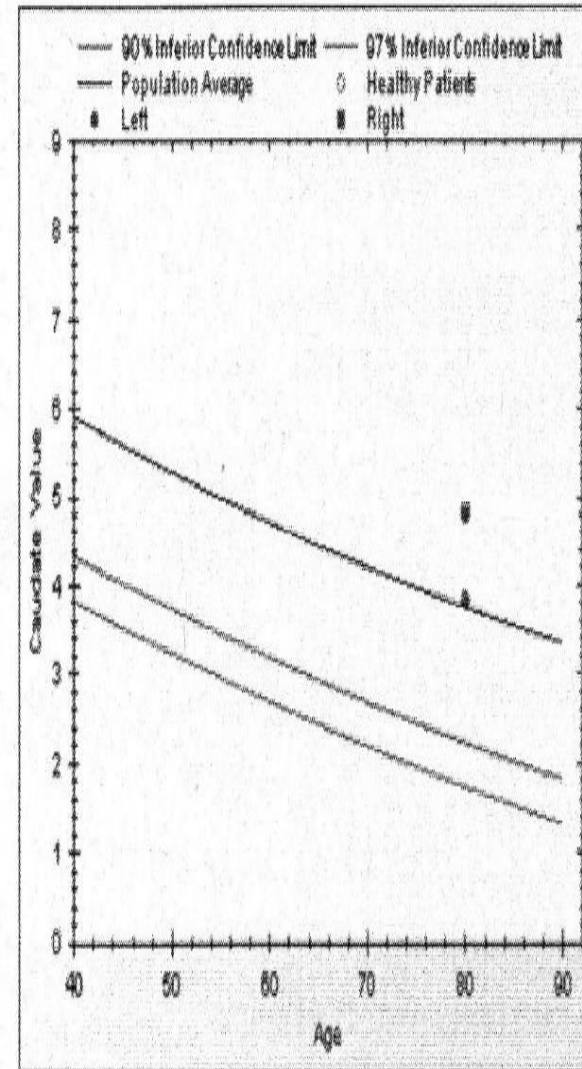
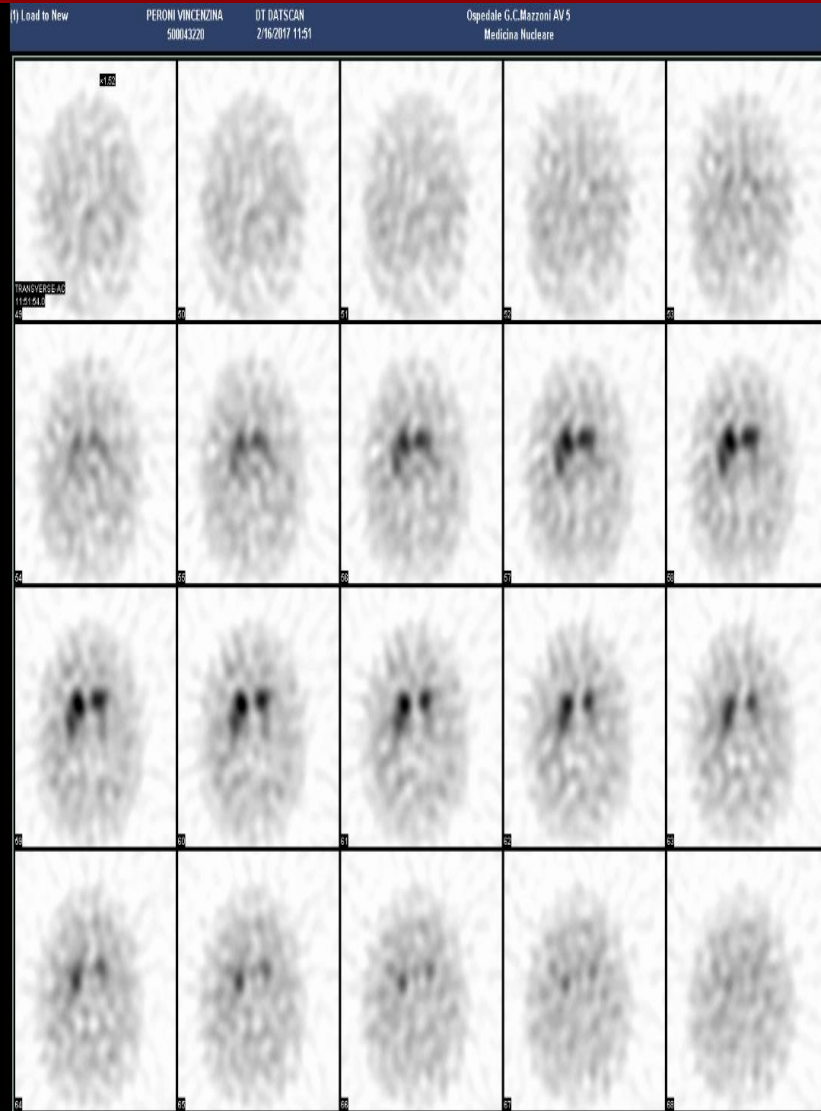
**Inizia terapia con
Pramipexolo RP
incrementato
progressivamente
fino a 1,05 mg con
miglioramento
clinico, soprattutto
dell'ipocinesia e del
tono dell'umore.
Lieve attenuazione
del tremore**

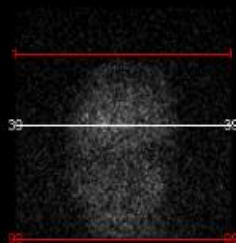
- Negatività DAT-scan rappresenta un criterio d'esclusione assoluto per diagnosi di PD secondo MDS criteria
- Se il risultato del DAT è incerto, il criterio d'esclusione non va applicato
- DAT-scan vs. diagnosi neuropatologica: 85 % sensibilità – 86% specificità nell'individuare un parkinsonismo degenerativo (Walker study – in progress)

DAT-scan 2014

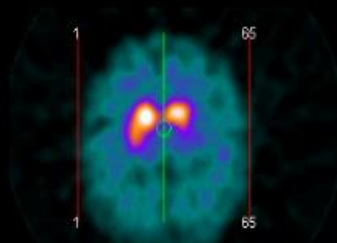


DAT-scan 2017

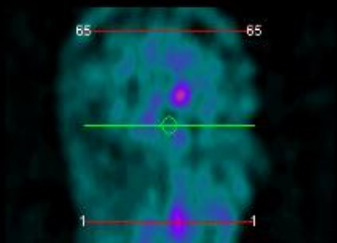




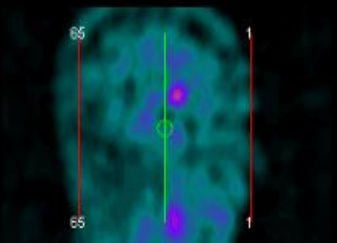
Planars -EARLY



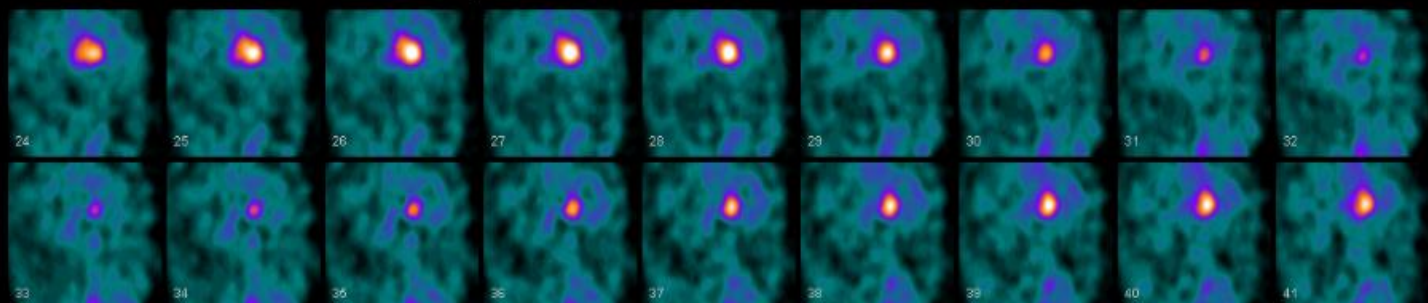
Sagittal Limits



Transverse Limits



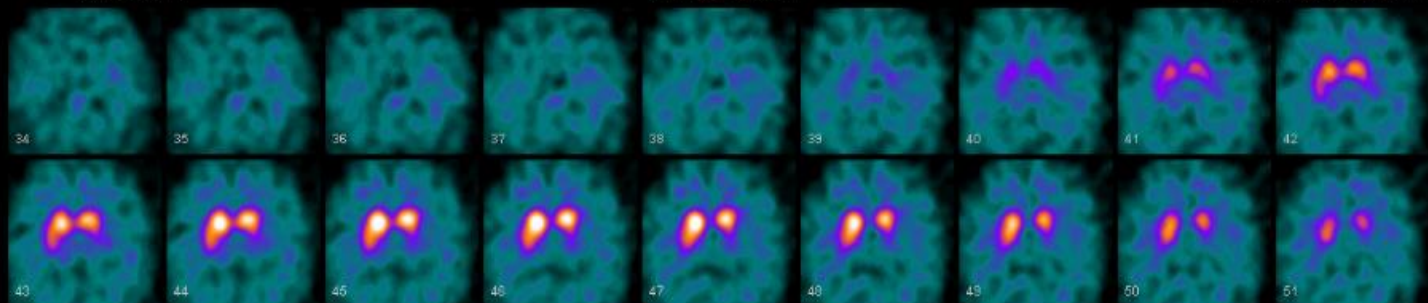
Coronal Limits



Right to Left

SAGITTAL -EARLY

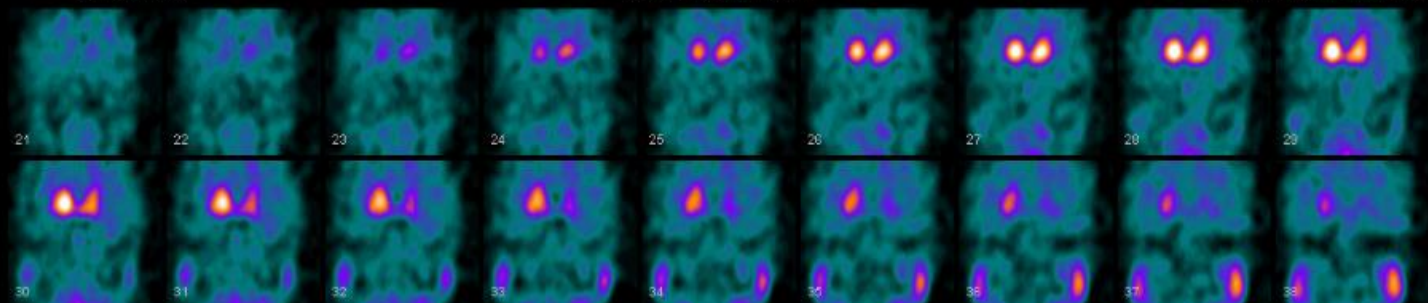
Slice thickness 2.58 mm



Feet to Head

TRANSVERSAL -EARLY

Slice thickness 2.58 mm



Anterior to Posterior

CORONAL -EARLY

Slice thickness 2.58 mm

Considerazioni...

- Lo studio ecografico del parenchima cerebrale può essere di supporto nella definizione clinica dei casi incerti.
- E' determinante il dialogo tra medico nucleare e neurologo.
- Consigli della MDS criteria task force:
- Il fatto che la negatività del DAT-scan rappresenti un criterio assoluto d'esclusività nella diagnosi, non è un suggerimento ad utilizzarlo di routine nella pratica clinica.
- L'utilizzo del DAT-scan va limitato ad un ridotto numero di casi dubbi, dal momento che non è attualmente di aiuto nel differenziare i parkinsonismi.

GRAZIE PER L'ATTENZIONE