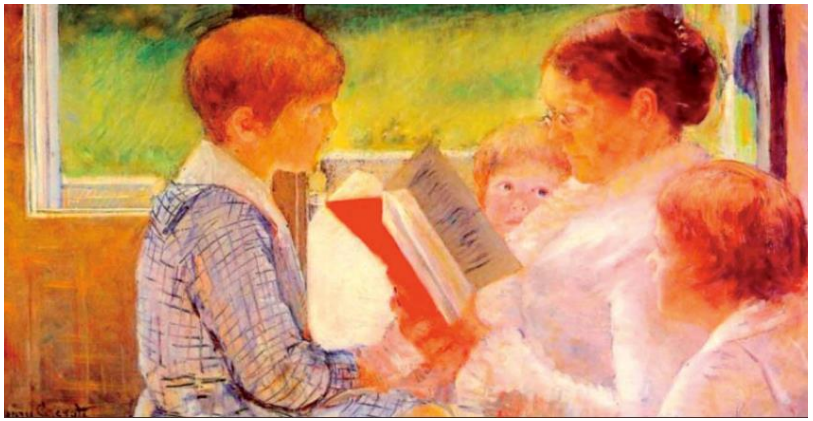
Scuola Superiore di Neurologia

V CORSO: “Neuroimmagini nella Malattia di Parkinson e Parkinsonismi”

MIBG Scintigraphy



Fabiana Novellino

CONSIGLIO NAZIONALE DELLE RICERCHE
Unità di Ricerca Neuroimmagini
Istituto Bioimmagini e Fisiologia Molecolare

Genova, 21-22 Febbraio 2017

OUTLINE OF THE PRESENTATION:

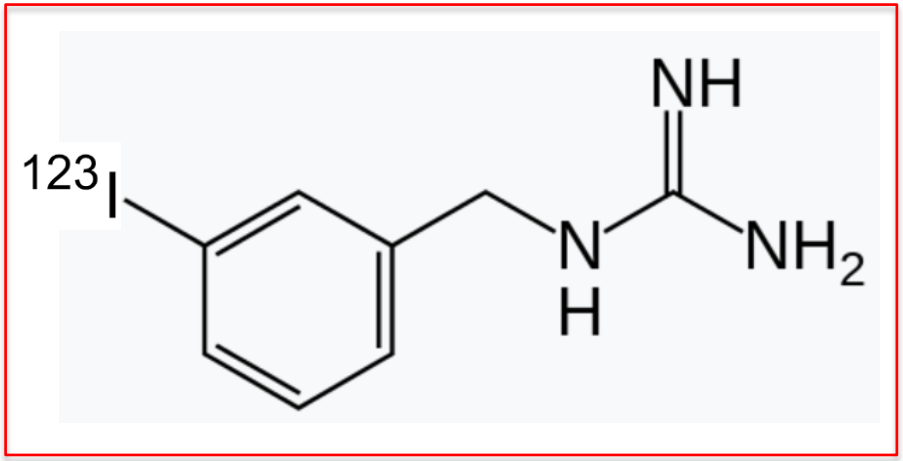
- ✓ **MIBG-Scintigraphy;**
- ✓ **MIBG-Scintigraphy in Parkinson Disease and Atypical Parkinsonism;**
- ✓ **MIBG-Scintigraphy in Preclinical and Premotor Phases of Movement Disorders;**

MIBG SCINTIGRAPHY

^{123}I-Meta-iodo-benzylguanidine (MIBG)

Analog of Guanethidine

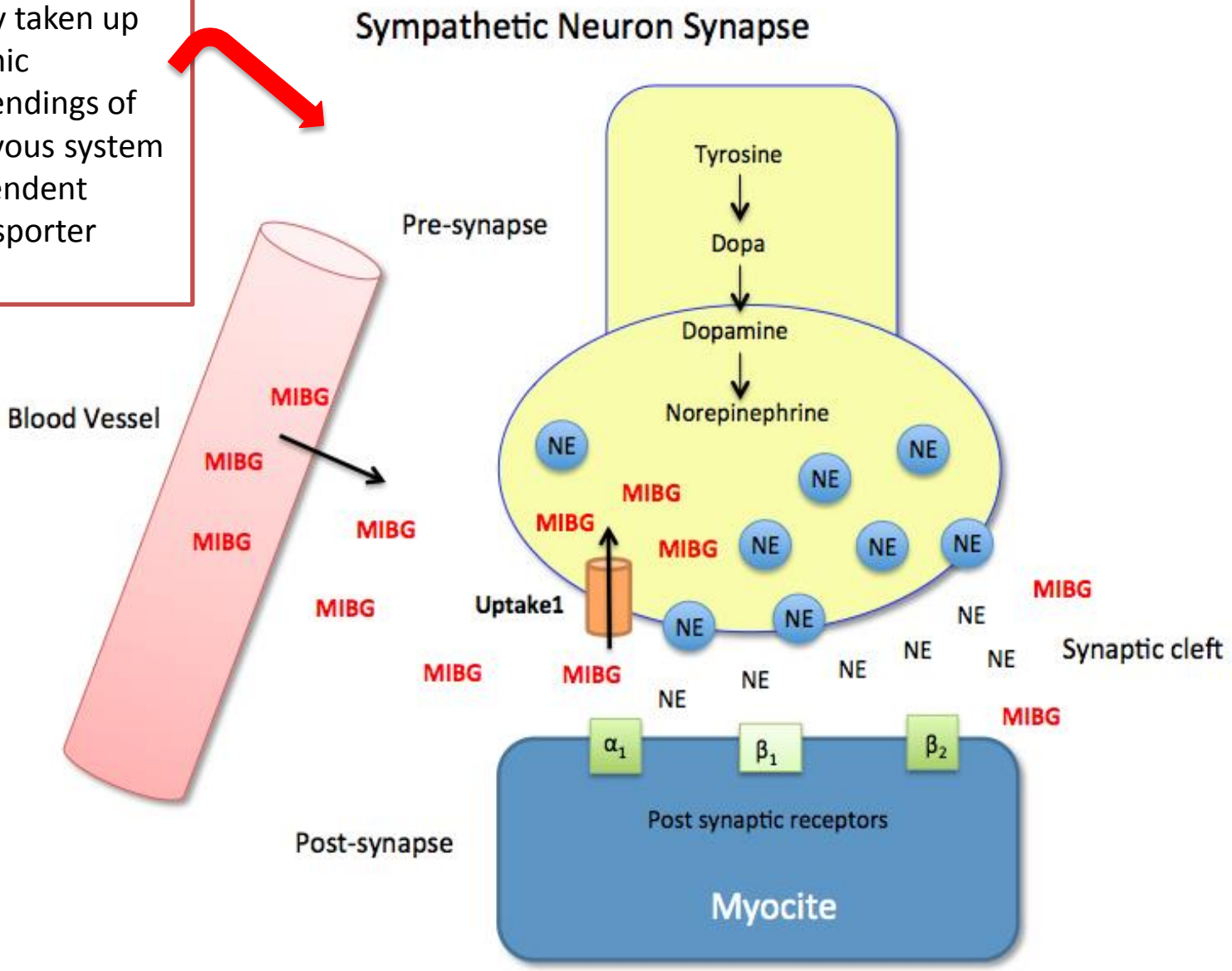
Adrenergic blocking agent



Mechanism of uptake and storage
is similar to that of Noradrenaline

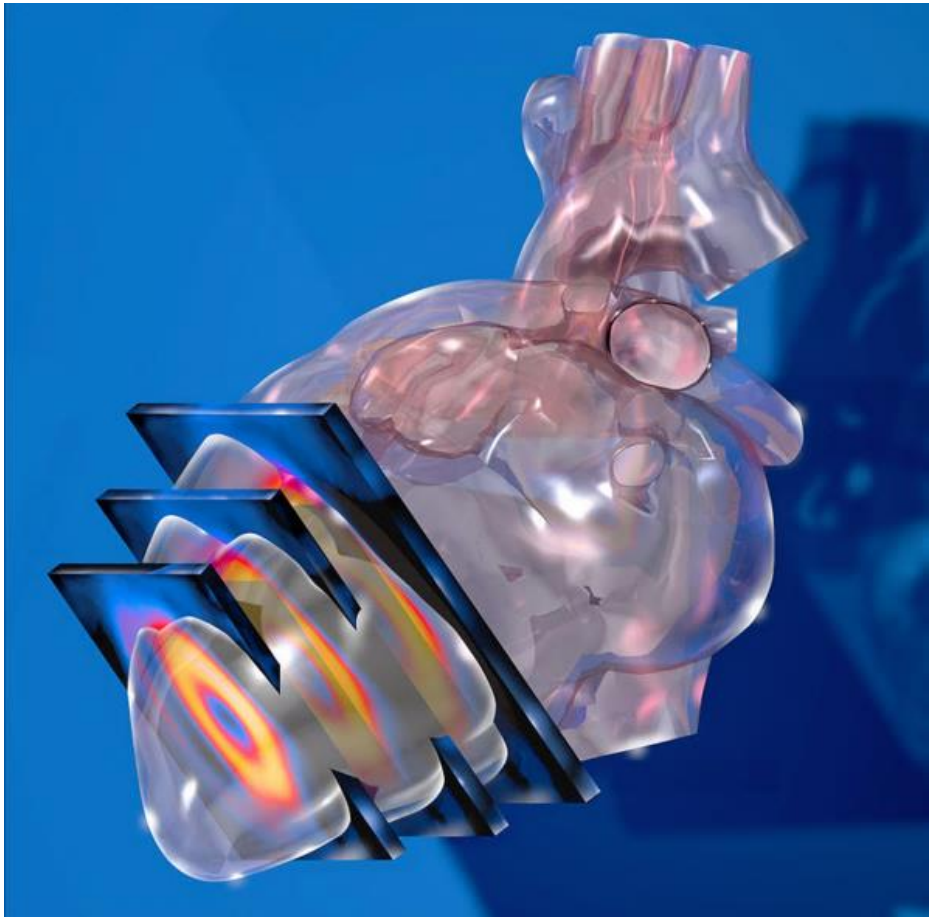
MIBG SCINTIGRAPHY

^{123}I-MIBG is actively taken up by the postganglionic presynaptic nerve endings of the adrenergic nervous system by the energy-dependent noradrenaline transporter mechanism



MIBG SCINTIGRAPHY

^{123}I-MIBG

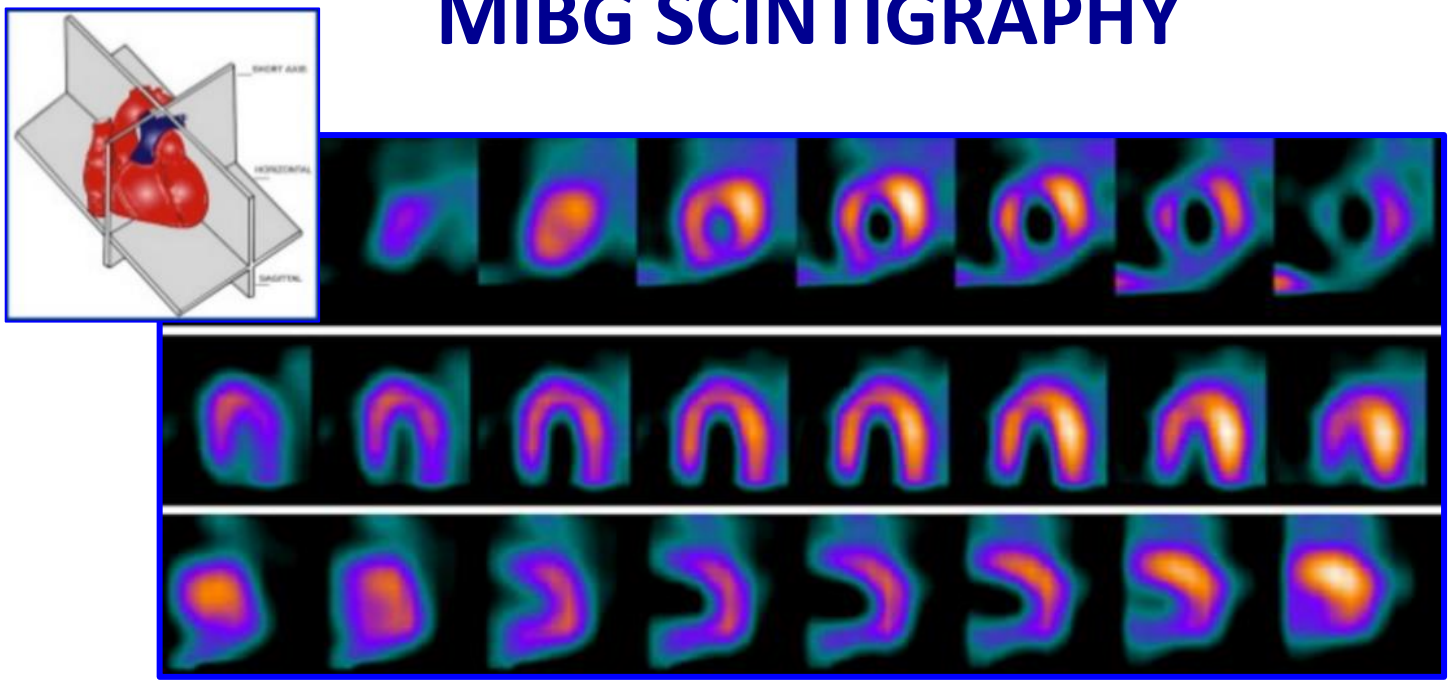


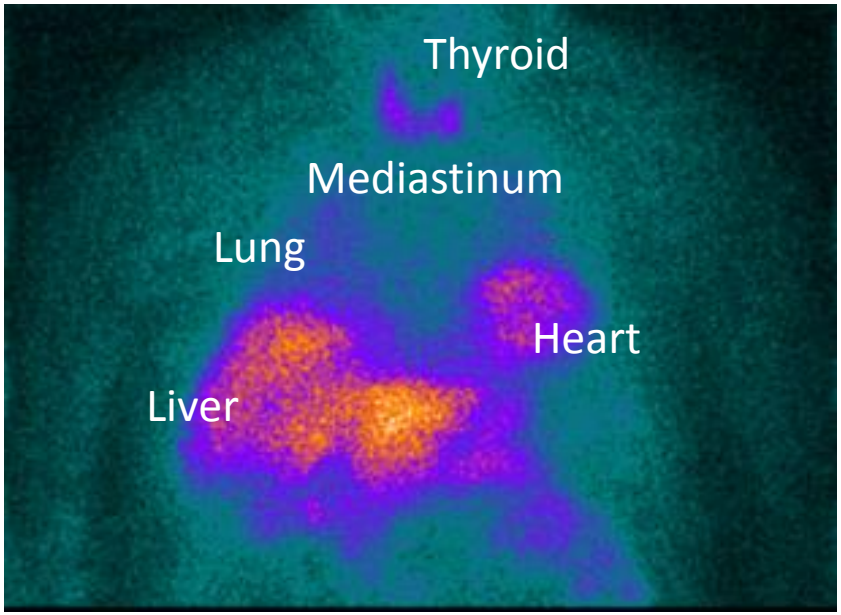
Planar and Single Photon Emission Computed Tomography (SPECT) images of the chest

15 - 30 min → EARLY PHASE

3 – 4 hours → DELAYED PHASE

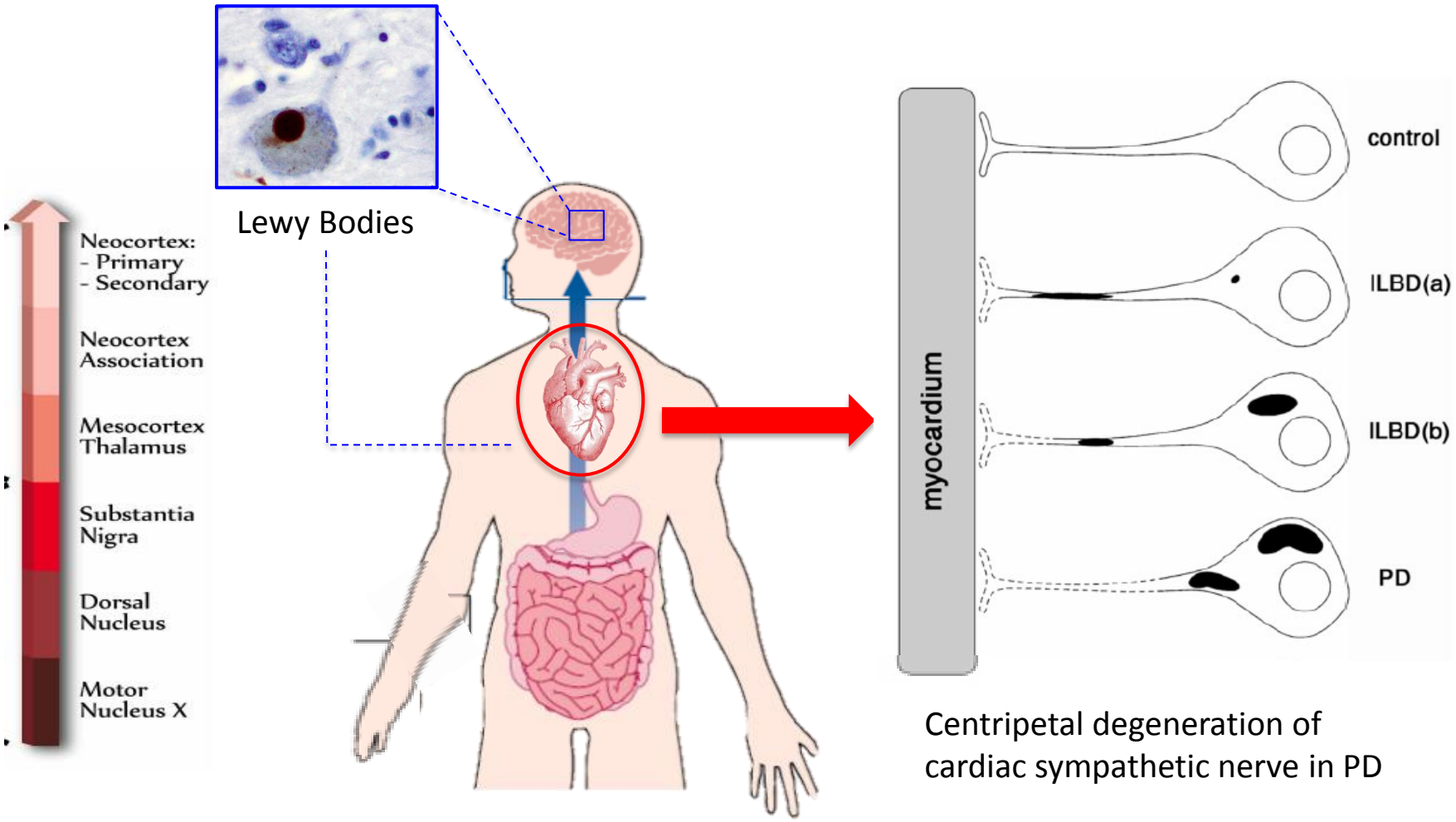
MIBG SCINTIGRAPHY





Semi-quantitative assessment
Heart to Mediastinum Ratio
(H/M ratio)
in early and late phases

NEUROPHATHOLOGICAL HYPOTESIS



Centripetal degeneration of cardiac sympathetic nerve in PD

Satoshi Orimo, *Brain* (2008), **131**, 642–650

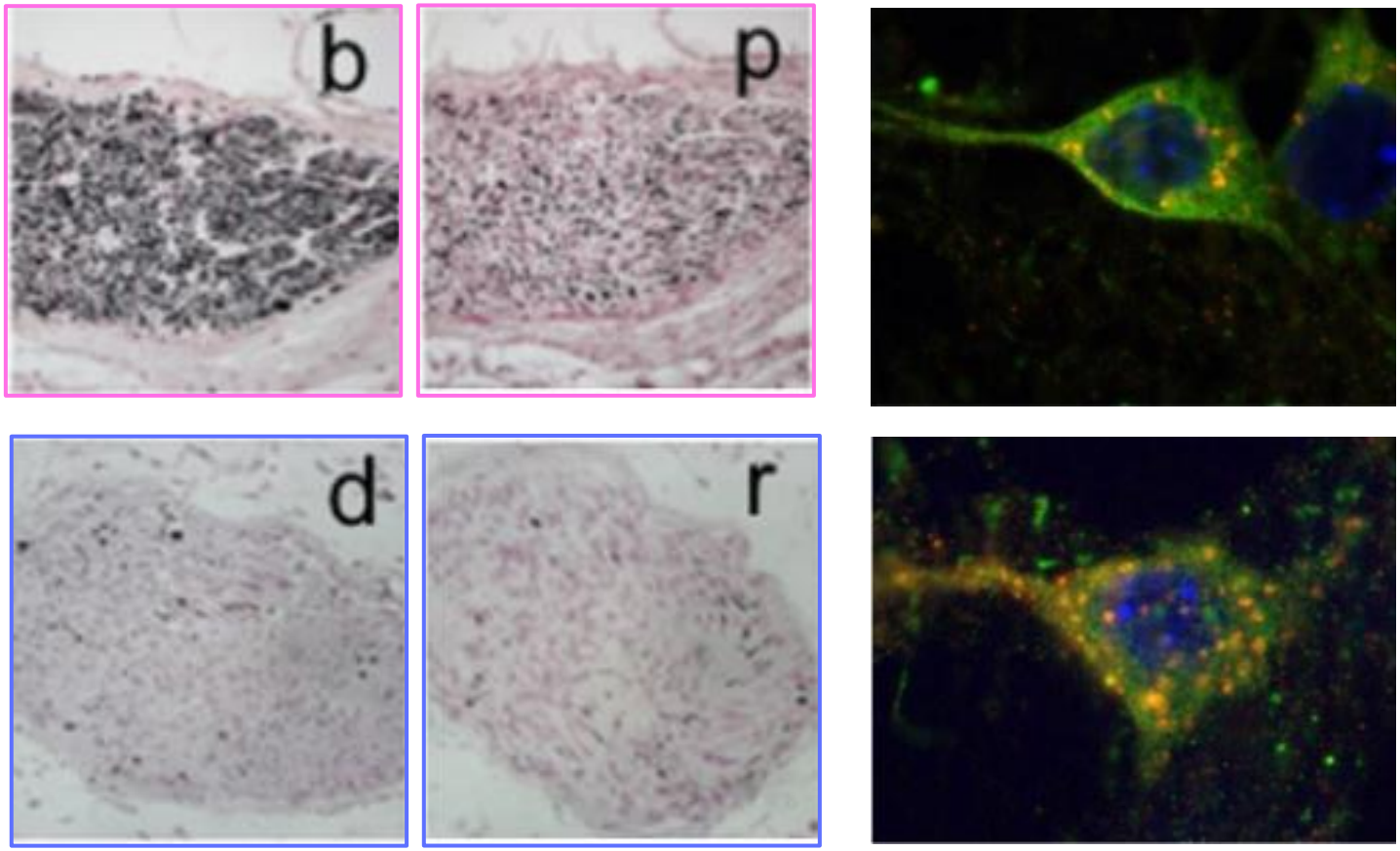
Contents lists available at ScienceDirect

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

^{123}I-*meta*-iodobenzylguanidine (MIBG) cardiac scintigraphy in α-synucleinopathies

CRTL

PD



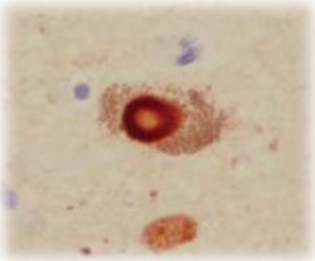
Parkinson's Disease and Parkinsonism: Neuropathology

Dennis W. Dickson

Cold Spring Harbor Perspectives in Medicine 2012;2:a009258
www.perspectivesinmedicine.org

Alfa-synucleinopathies Lewy Bodies

Parkinson Disease
Lewy Bodies Dementia
Pure Autonomic Failure



Alfa-synucleinopathies No Lewy Bodies

Multiple System Atrophy

Amyloido- and Tau-pathies

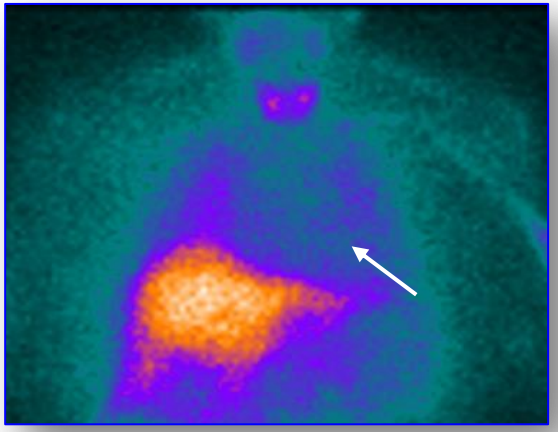
Alzheimer Disease

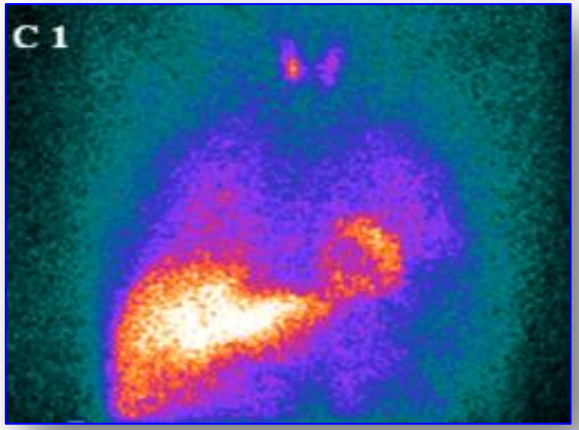
Taupathies

Progressive Supranuclear Palsy
Frontotemporal Dementia
Corticobasal Degeneration

Other forms

Genetic Parkinsonism
Vascular Parkinsonism
Iatrogenic Parkinsonism
Essential Tremor

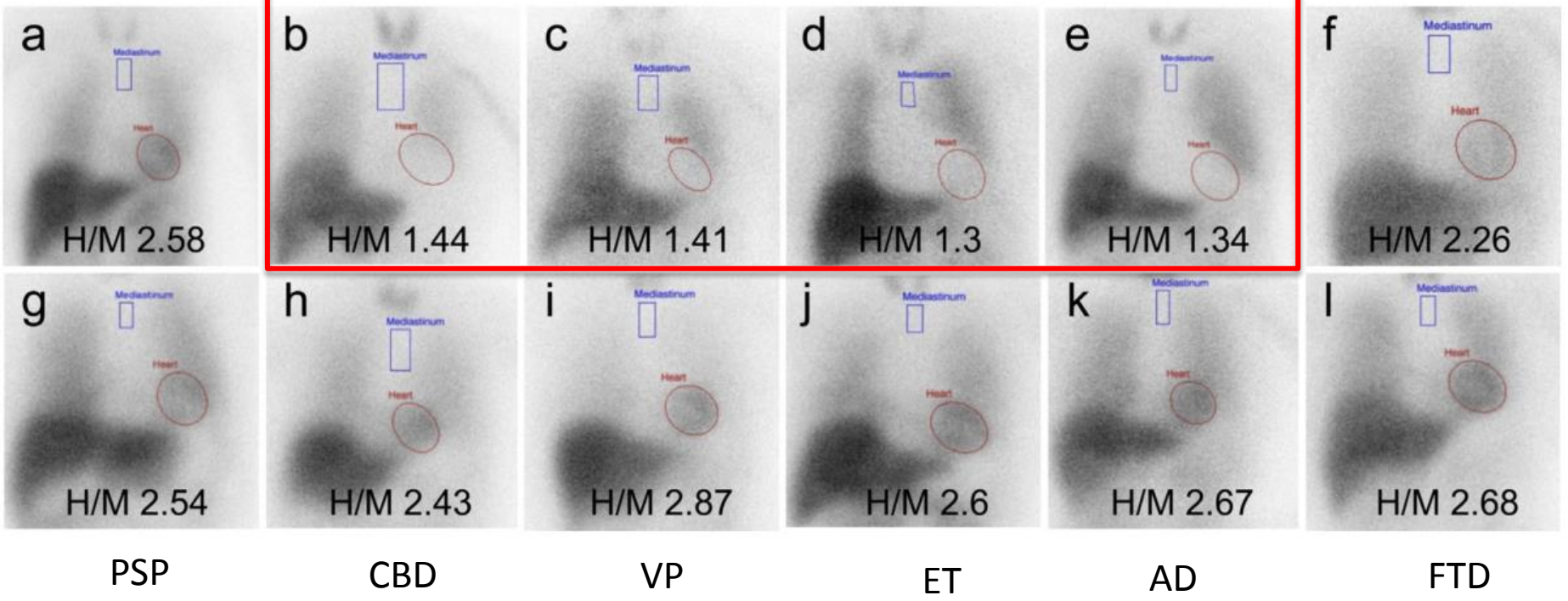




Contents lists available at ScienceDirect

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

^{123}I-*meta*-iodobenzylguanidine (MIBG) cardiac scintigraphy in α-synucleinopathies

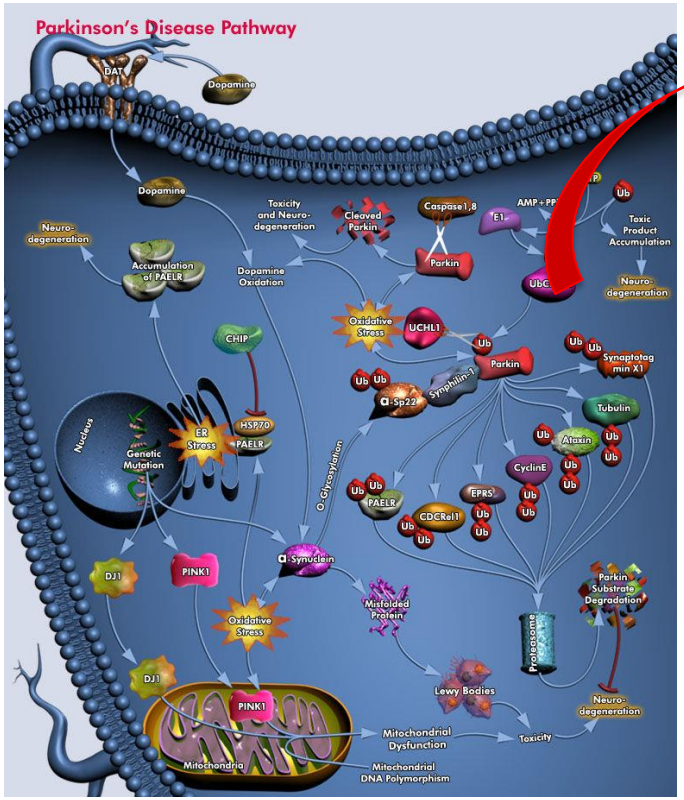


Movement Disorders
Official Journal of the International Parkinson and Movement Disorder Society

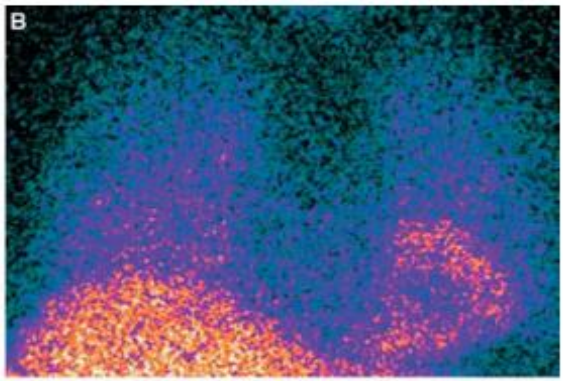
Myocardial ^{123}Metaiodobenzylguanidine Uptake in Genetic Parkinson's Disease

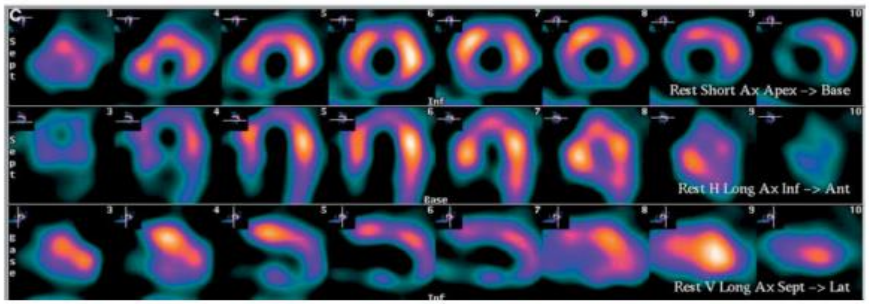
14 patients with Genetic Parkinsonism

60%



- 4 Parkin
- 2 DJ1
- 2 Pink1
- 6 LRRK2

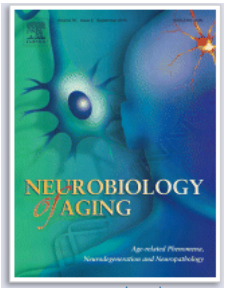




Quattrone et al, 2008; 23: 21-27

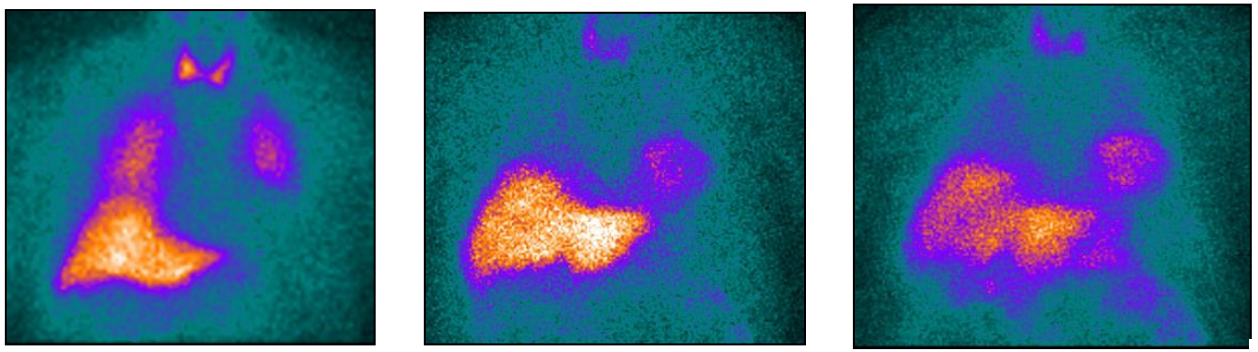
Myocardial ^{123}I-MIBG scintigraphy for differentiation of Lewy bodies disease from FTD

Fabiana Novellino [a], Antonio Bagnato [b], Maria Salsone [a], Giuseppe Lucio Cascini [c], Giuseppe Nicoletti [a,d], Gennarina Arabia [a,d], Pierfrancesco Pugliese [d], Maurizio Morelli [a], Sandra Paglionico [a], Stefania Cipullo [c], Ida Manna [d], Elvira Valeria De Marco [d], Francesca Condino [d], Carmelina Chiriaco [a], Letterio Morgante [e], Mario Zappia [f], Aldo Quattrone [a,d,*]



2010;11:1903-11

2 patients PRGR mutation



H/M ratio (mean ± SD)				
Early image	1.25 ± 0.12	1.86 ± 0.20	1.91 ± 0.17	<0.001*
Delayed image	1.14 ± 0.13	1.80 ± 0.23	1.99 ± 0.19	<0.001*

Reduction of MIBG uptake in early and delayed phases

Normal MIBG uptake in early and delayed phases

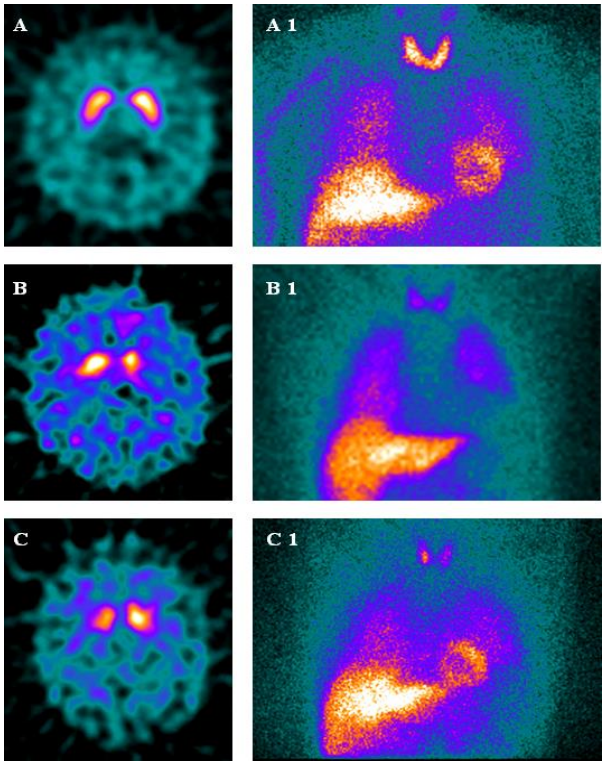
Normal MIBG uptake in early and delayed phases

Combined Use of DAT-SPECT and Cardiac MIBG Scintigraphy in Mixed Tremors

Fabiana Novellino, MD,[1] Gennarina Arabia, MD, MSc,[1] Antonio Bagnato, MD,[2] Giuseppe Lucio Cascini, MD,[3] Maria Salsone, MD,[1] Giuseppe Nicoletti, MD,[4] Demetrio Messina, MD,[4] Maurizio Morelli, MD,[1] Sandra Paglionico, MD,[1] Laura Giofrè, MD,[1] Antonino Restuccia, MD,[3] Giusi Torchia, PhD,[1] Francesca Condino, PhD,[4] and Aldo Quattrone, MD[1,4*]

Movement Disorders
Vol. 24, No. 15, 2009, pp. 2242–2248

FONDAZIONE neureca ONLUS



→ Gruppo 1:
DAT-SPECT normale
MIBG normale
30%
TE

→ Gruppo 2:
DAT-SPECT patologico
MIBG patologica
40%
MP

→ Gruppo 3:
DAT-SPECT patologico
MIBG normale
30%
Parkinsonismo

Movement Disorders
Vol. 24, No. 11, 2009, pp. 1650–1655

MIBG Scintigraphy for Differentiating Parkinson's Disease Autonomic Dysfunction from Parkinsonism-Predomina Multiple System Atrophy

Eun Joo Chung, MD, PhD,[1] Won Yong Lee, MD, PhD,[2]* Won Tae Yoon, MD,[2]
Byeong Joon Kim, MD, PhD,[2] and Gyeong Han Lee, MD, PhD[3]

RESEARCH ARTICLE

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

Hiroaki Fujita[1], Keisuke Suzuki[1]*, Ayaka Numao[1], Yuji Watanabe[1], Tomoyuki Uchiyama[1,2], Tomoyuki Miyamoto[3], Masayuki Miyamoto[4], Koichi Hirata[1]

Cardiac sympathetic denervation is cor Parkinsonian midline motor symptoms

Joong-Seok Kim [a,*], Kwang-Soo Lee [a], In-Uk Song [a], Yeong-In Kim [a], Sung-Hoon Kim [b], I-Ryung You [b], Hee-Tae Kim [c]

Different patterns of cardiac sympathetic denervation in tremor-type compared to akinetic-rigid-type Parkinson's disease: Molecular imaging with ^{123}I-MIBG

A. CHIARAVALLOTI[1], A. STEFANI[2,3], M. TAVOLOZZA[1], M. PIERANTOZZI[2,3], D. DI BIAGIO[1], E. OLIVOLA[2,3], B. DI PIETRO[1], M. STAMPANONI[2,3], R. DANIELI[1], G. SIMONETTI[1], P. STANZIONE[2,3] and O. SCHILLACI[1,4]

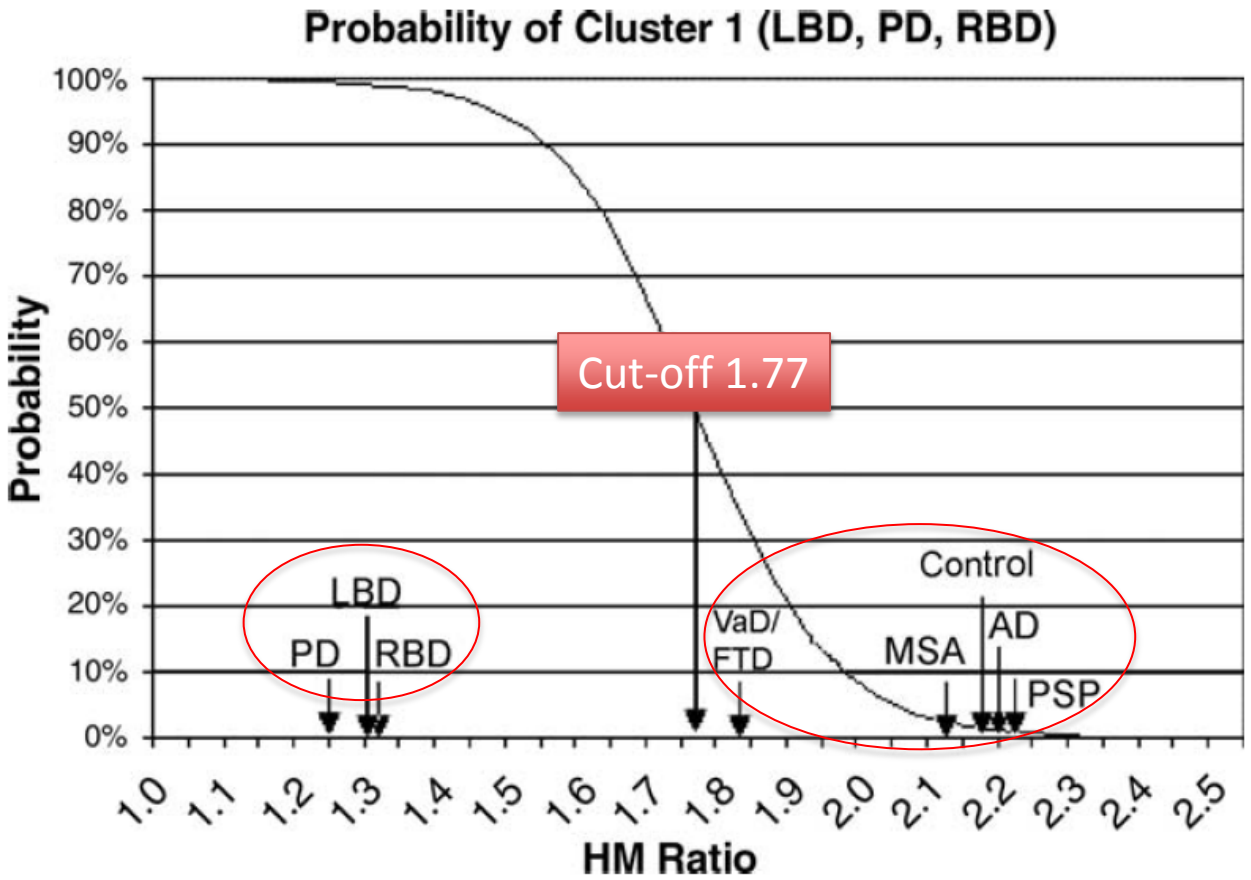
MIBG myocardial scintigraphy in pre-motor Parkinson's disease: A review

Ryuji Sakakibara [a,*], Fuyuki Tateno [a], Masahiko Kishi [a], Yohei Tsuyusaki [a], Hitoshi Terada [b], Tsutomu Inaoka [b]

RESEARCH ARTICLE

Meta-Analysis of ^{123}I-MIBG Cardiac Scintigraphy for the Diagnosis of Lewy Body–Related Disorders

Alisha E. King, MD,[1] Jim Mintz, PhD,[1] and Donald R. Royall, MD[1,2,3,4,5]*



46 studies
2680 subjects

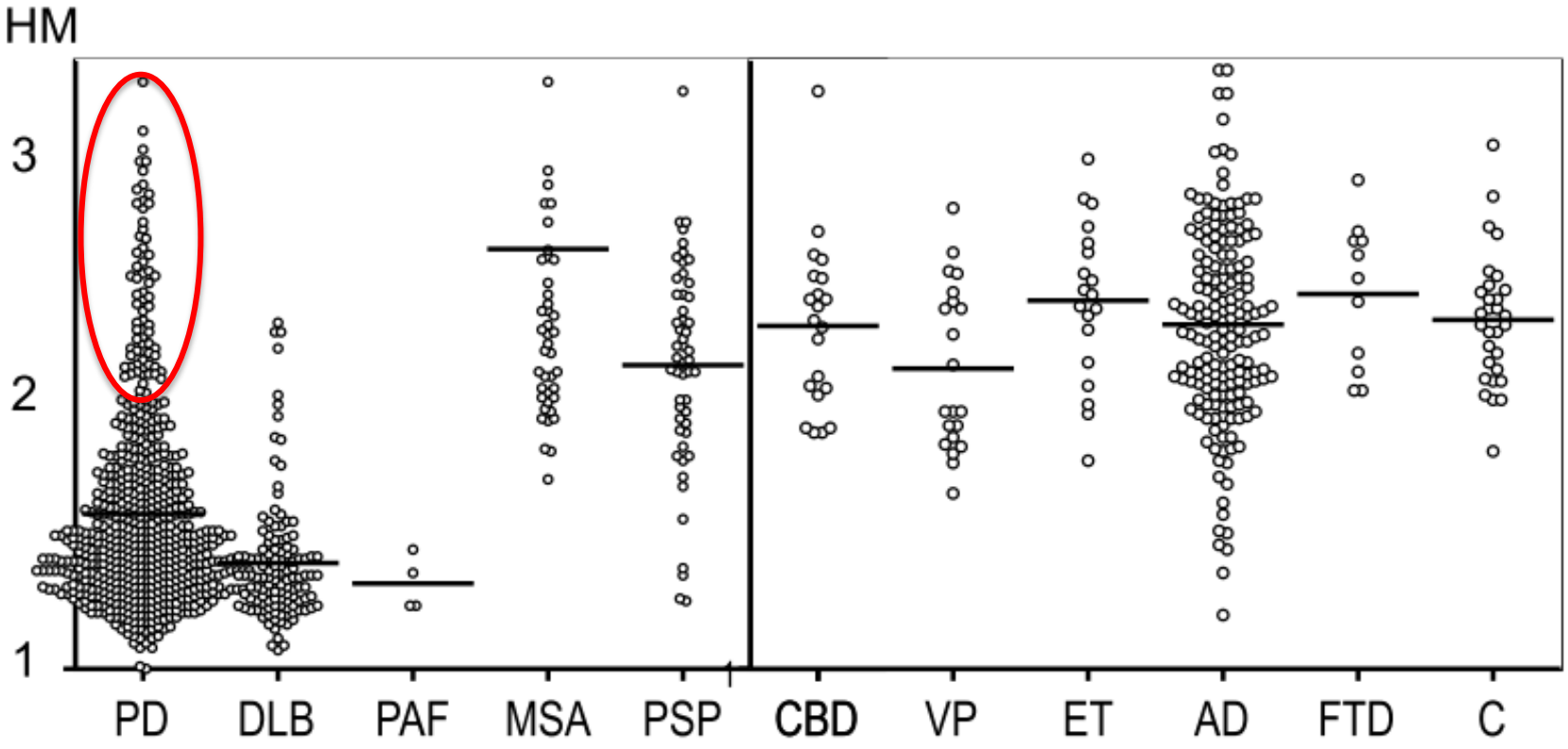
Sensitivity 94%
Specificity 91%

Movement Disorders, Vol. 26, No. 7, 2011

Contents lists available at ScienceDirect

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

^{123}I-*meta*-iodobenzylguanidine (MIBG) cardiac scintigraphy in α-synucleinopathies



ELSEVIER

Cardiac ^{123}I-MIBG scintigraphy can assess the disease severity and phenotype of PD

Shinji Saiki[a,*], Genjiro Hirose[a], Koichiro Sakai[a], Satoshi Kataoka[a], Ariyuki Hori[a], Misuzu Saiki[a], Muichi Kaito[a], Kotaro Higashi[b], Suzuka Taki[b], Kazuo Kakeshita[b], Susumu Fujino[c], Miho Miaki[a]

Journal of the Neurological Sciences
220 (2004) 105–111

Relationship and factor structure in multisystem neurodegeneration in Parkinson disease

Takaaki Hattori, M.D., Ph.D.[1,2,3,*], Satoshi Orimo, M.D., Ph.D.[2], Mark Hallett, M.D.[3], Tianxia Wu, Ph.D.[4], Akira Inaba, M.D., Ph.D.[2], Reo Azuma, M.D.[2], and Hidehiro Mizusawa, M.D., Ph.D.[1]

Acta Neurol Scand. 2014 130(6): 347–353

Reliability of MIBG myocardial scintigraphy in the diagnosis of Parkinson's disease

H Nagayama, M Hamamoto, M Ueda, J Nagashima, Y Katayama

J Neurol Neurosurg Psychiatry 2005;**76**:249–251. doi: 10.1136/jnnp.2004.037028

Correlation between ^{123}I-MIBG uptake and disease severity evaluated by H-Y stage and UPDRS III

Research Article

Myocardial ^{123}I-MIBG Uptake and Cardiovascular Autonomic Function in Parkinson's Disease

Akira Katagiri,[1] Masato Asahina,[1,2] Nobuyuki Araki,[1] Anupama Poudel,[1] Yoshikatsu Fujinuma,[1] Yoshitaka Yamanaka,[1] and Satoshi Kuwabara[1]

Table 2: Correlation between MIBG scintigraphy and autonomic function tests.

	Early H/M ratio (P value)	Delayed H/M ratio (P value)	Washout rate (P value)
HRV			
LF component	0.02 (0.89)	−0.02 (0.90)	0.00 (0.99)
HF component	0.18 (0.21)	0.13 (0.35)	−0.20 (0.17)
LF/HF ratio	−0.16 (0.28)	−0.16 (0.27)	0.26 (0.07)
$CV_{R\text{-}R}$	0.21 (0.15)	0.19 (0.19)	−0.27 (0.06)
HUT test			
SBP change	0.17 (0.23)	0.24 (0.09)	**−0.34 (0.02)**
DBP change	0.07 (0.63)	0.14 (0.32)	**−0.29 (0.04)**
HR change	0.20 (0.16)	0.15 (0.30)	0.12 (0.43)

Parkinson's Disease
Volume 2015, Article ID 805351, 5 pages
http://dx.doi.org/10.1155/2015/805351

Cardiac sympathetic denervation in bradykinesia-dominant Parkinson's disease

Masahiko Suzuki[a], Mitsuyoshi Urashima[b], Hisayoshi Oka[a], Masaya Hashimoto[a] and Kenichiro Taira[a]

Table 2 Single and multiple linear regression models of early and delayed H/M ratios

	Single linear regression model		Multiple linear regression model	
	H/M ratio			
	Early	Delayed	Early[a]	Delayed[b]
Age at onset	−1.53 (0.127)	−1.80 (0.074)	−2.63 (0.009)	−2.84 (0.005)
Disease duration	−2.43 (0.016)	−3.48 (0.001)	−2.47 (0.015)	−2.75 (0.001)
Male	−1.26 (0.211)	0.31 (0.754)	−1.36 (0.175)	0.38 (0.704)
HY stage	−1.79 (0.075)	−3.64 (0.001)	0.19 (0.851)	−0.93 (0.356)
Tremor	3.27 (0.001)	3.78 (<0.001)	0.05 (0.959)	−0.13 (0.896)
Bradykinesia	−8.24 (<0.001)	−9.67 (<0.001)	−6.62 (<0.001)	−7.78 (<0.001)
Rigidity	−0.33 (0.738)	−0.19 (0.846)	−0.68 (0.499)	−0.44 (0.659)
Postural instability	−1.08 (0.283)	−2.43 (0.017)	0.76 (0.446)	1.15 (0.254)

H/M, heart to mediastinum; HY, Hoehn and Yahr.
Data are t (*P* value) of the correlation.
[a]R^2=0.3759.
[b]R^2=0.4649.

143 PD patients → The results suggest a close link between myocardial sympathetic MIBG uptake and bradykinesia, age at onset and disease duration

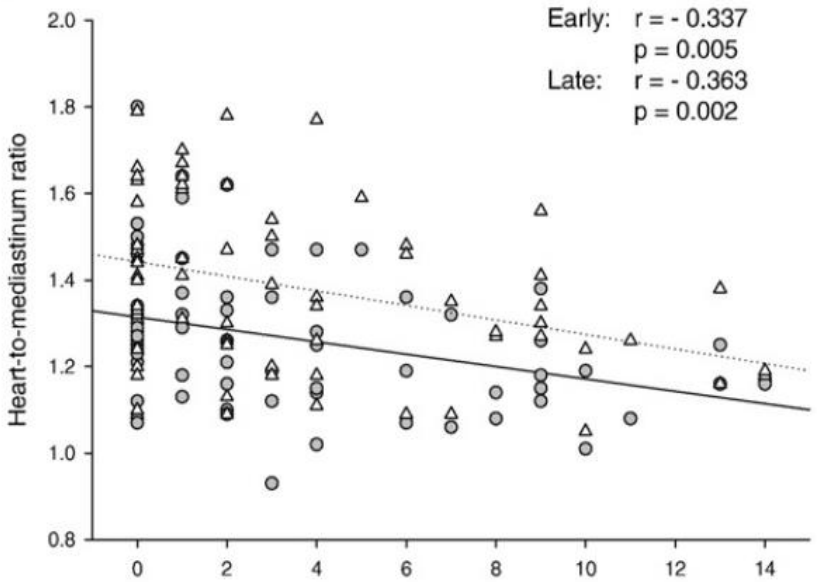
NEUROREPORT Vol 18 No 17 19 November 2007

Journal of the Neurological Sciences

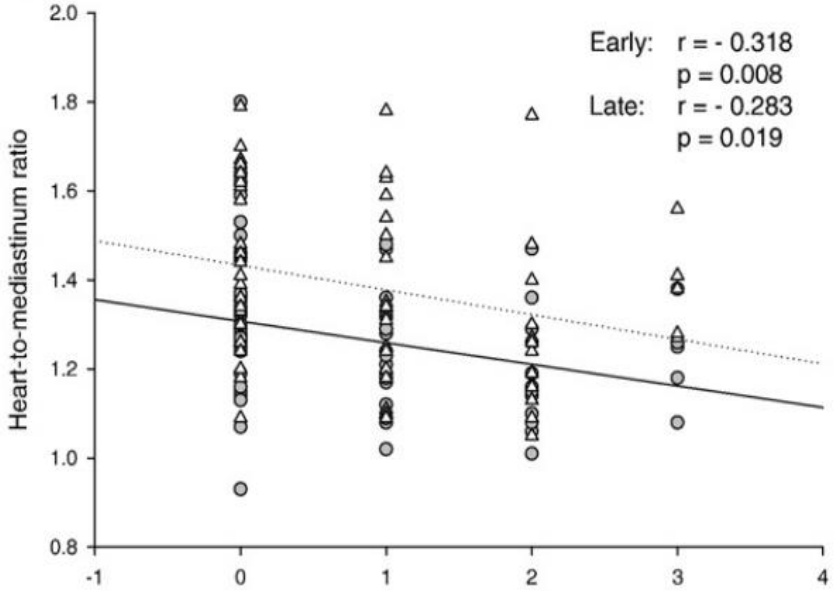
Cardiac sympathetic denervation is correlated with Parkinsonian midline motor symptoms

Joong-Seok Kim [a,*], Kwang-Soo Lee [a], In-Uk Song [a], Yeong-In Kim [a], Sung-Hoon Kim [b], I-Ryung You [b], Hee-Tae Kim [c]

Posture and gait



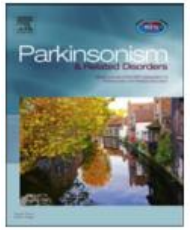
Speech



Journal of the Neurological Sciences 270 (2008) 122–126

Myocardial MIBG scintigraphy may predict the course of motor symptoms in Parkinson's disease☆

Julia Dorschner[a], Georgios Farmakis[b], Stefanie Behnke[a], Dirk Hellwig[b], Susanne Schneider[a], Klaus Fassbender[a], Carl-Martin Kirsch[b], Ulrich Dillmann[a], Jörg Spiegel[a,*]



: 17 (2011) 372–375

40 PD patients

Baseline
MIBG scintigraphy
Clinical evaluation
- Rigidity
- Bradykinesia
- Resting tremor
- Postural tremor
- Axial Symptoms

Follow-up 3-8 years
Clinical evaluation
- Rigidity
- Bradykinesia
- Resting tremor
- Postural tremor
- Axial Symptoms

Correlation between MIBG uptake and rate of disease progression

$$\frac{\text{motor symptom (follow-up) - motor symptom (baseline visit)}}{\text{time (in years) between follow- up visit and baseline visit}}$$

Table 1
Correlations of motor symptoms with myocardial MIBG uptake.

Correlation	At the baseline visit	At the follow-up visit	Annual progress between baseline and follow-up visit
	p-value; correlation coeff.	*p*-value; correlation coeff.	*p*-value; correlation coeff.
Resting tremor versus MIBG	$p = 0.52$; $r = +0.12$	$p = 0.55$; $r = +0.11$	$p = 0.86$; $r = +0.03$
Postural/action tremor versus MIBG	$p = 0.35$; $r = +0.17$	$p = 0.37$; $r = +0.16$	$p = 0.71$; $r = +0.07$
Rigidity versus MIBG	$p = 0.056$; $r = -0.34$	**$p < 0.01$; $r = -0.46$**	**$p < 0.05$; $r = -0.41$**
Bradykinesia versus MIBG	**$p < 0.01$; $r = -0.49$**	$p = 0.052$; $r = -0.35$	$p = 0.26$; $r = -0.20$
Axial symptoms versus MIBG	**$p < 0.01$; $r = -0.55$**	**$p < 0.0001$; $r = -0.64$**	**$p < 0.01$; $r = -0.49$**

Differences in myocardial sympathetic degeneration and the clinical features of the subtypes of Parkinson's disease

Eun Joo Chung [a], Eung Gyu Kim [a], Moo Seong Kim [b], Sang Kyun Bae [c], Dae Hyun Seog [d], S. June Oh [e], Minkyung Oh [f], Sang Jin Kim [a,*]

Table 1
Clinical characteristics (mean ± standard deviation) of patients with subtypes of Parkinson's disease

Characteristics	ART	MT	TDT	HC	*p*-value
Sex (M/F)	3/7	5/3	5/4	5/7	0.74
Age (years)	62.9 ± 7.52	62.8 ± 5.52	57.22 ± 7.17	61.3 ± 3.37	0.76
Onset age (years)	60.3 ± 7.20	61.63 ± 5.95	33 ± 7.35		0.194
Disease duration (months)	28.3 ± 35.19	13.75 ± 12.22	20.89 ± 10.22		0.347
MIBG uptake	1.35 ± 0.22	1.35 ± 0.32	1.69 ± 0.39	2.17 ± 0.18	0.049§, 0.02†
UPDRS motor	34.6 ± 18.28	24.63 ± 7.78	16.22 ± 4.15		0.002¶, 0.022†, 0.019‡
H–Y stage	2.8 ± 0.48	2.38 ± 0.69	2.0 ± 0.43		0.006¶, 0.001†
Hypokinesia	8.3 ± 4.72	8.13 ± 3.18	4.5 ± 1.85		0.07, 0.037†, 0.017‡
Rigidity	14.2 ± 7.19	5.0 ± 2.67	2.78 ± 0.44		0.004¶,††, 0.0001†,0.026‡
Tremor	1.6 ± 2.84	5.38 ± 1.92	6.22 ± 0.83		0.0001¶

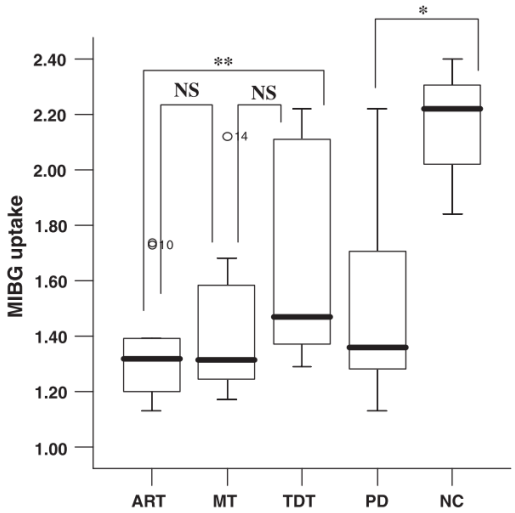


Table 2
Correlation between MIBG uptake and clinical characteristics in the three subgroups of patients with Parkinson's disease

Comparison	ART	MT	TDT
MIBG uptake vs. age at onset	$r = 0.11$, $p = 0.76$	$r = 0.001$, $p = 0.98$	$r = -0.5$, $p = 0.18$
MIBG uptake vs. disease duration	$r = -0.06$, $p = 0.86$	$r = -0.28$, $p = 0.51$	$r = 0.21$, $p = 0.59$
MIBG uptake vs. UPDRS motor	$r = -0.23$, $p = 0.53$	$r = -0.57$, $p = 0.14$	$r = -0.48$, $p = 0.19$
MIBG uptake vs. hypokinesia	$r = -0.75$, $p = 0.01$	$r = -0.8$, $p = 0.02$	$r = -0.33$, $p = 0.39$
MIBG uptake vs. rigidity	$r = -0.16$, $p = 0.67$	$r = -0.14$, $p = 0.75$	$r = -0.07$, $p = 0.85$
MIBG uptake vs. tremor	$r = -0.3$, $p = 0.37$	$r = -0.56$, $p = 0.15$	$r = -0.2$, $p = 0.6$

ELSEVIER

Cardiac ^{123}I-MIBG scintigraphy can assess the disease severity and phenotype of PD

Shinji Saiki[a,*], Genjiro Hirose[a], Koichiro Sakai[a], Satoshi Kataoka[a], Ariyuki Hori[a], Misuzu Saiki[a], Muichi Kaito[a], Kotaro Higashi[b], Suzuka Taki[b], Kazuo Kakeshita[b], Susumu Fujino[c], Miho Miaki[a]

Journal of the Neurological Sciences
220 (2004) 105–111

Table 4
Characteristics of the Parkinson's disease phenotypes

		PIGD-dominant (N=12)	Tremor-dominant (N=15)	Significance
Age at MIBG test		69.7 (10.3)	65.3 (11.1)	NS[a]
Age at onset		63.5 (12.5)	60.1 (10.9)	NS[a]
MIBG	Early H/M ratio	1.30 (0.0978)	1.58 (0.210)	$p < 0.01$*
	Delayed H/M ratio	1.20 (0.148)	1.46 (0.353)	$p < 0.05$*
	Washout rate	31.0 (11.1)	29.8 (9.76)	NS*
UPDRS		53.1 (22.3)	34.4 (16.0)	$p < 0.05$*

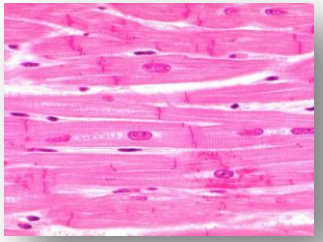
PIGD=postural instability gait difficulty; MIBG=^{123}I-metaiodobenzylguanidine; H/M=heart to mediastinum; UPDRS=Unified Parkinson's Disease Rating Scale.

JNNP

Quantitative correlation between cardiac MIBG uptake and remaining axons in the MIBG uptake and remaining axons in the cardiac sympathetic nerve in Lewy body cardiac sympathetic nerve in Lewy body disease

Makoto Takahashi, Masako Ikemura, Teruaki Oka, Toshiki Uchihara, Koichi Wakabayashi, Akiyoshi Kakita, Hitoshi Takahashi, Mari Yoshida, Shuta Toru, Takayoshi Kobayashi and Satoshi Orimo

Cardiac tissue samples



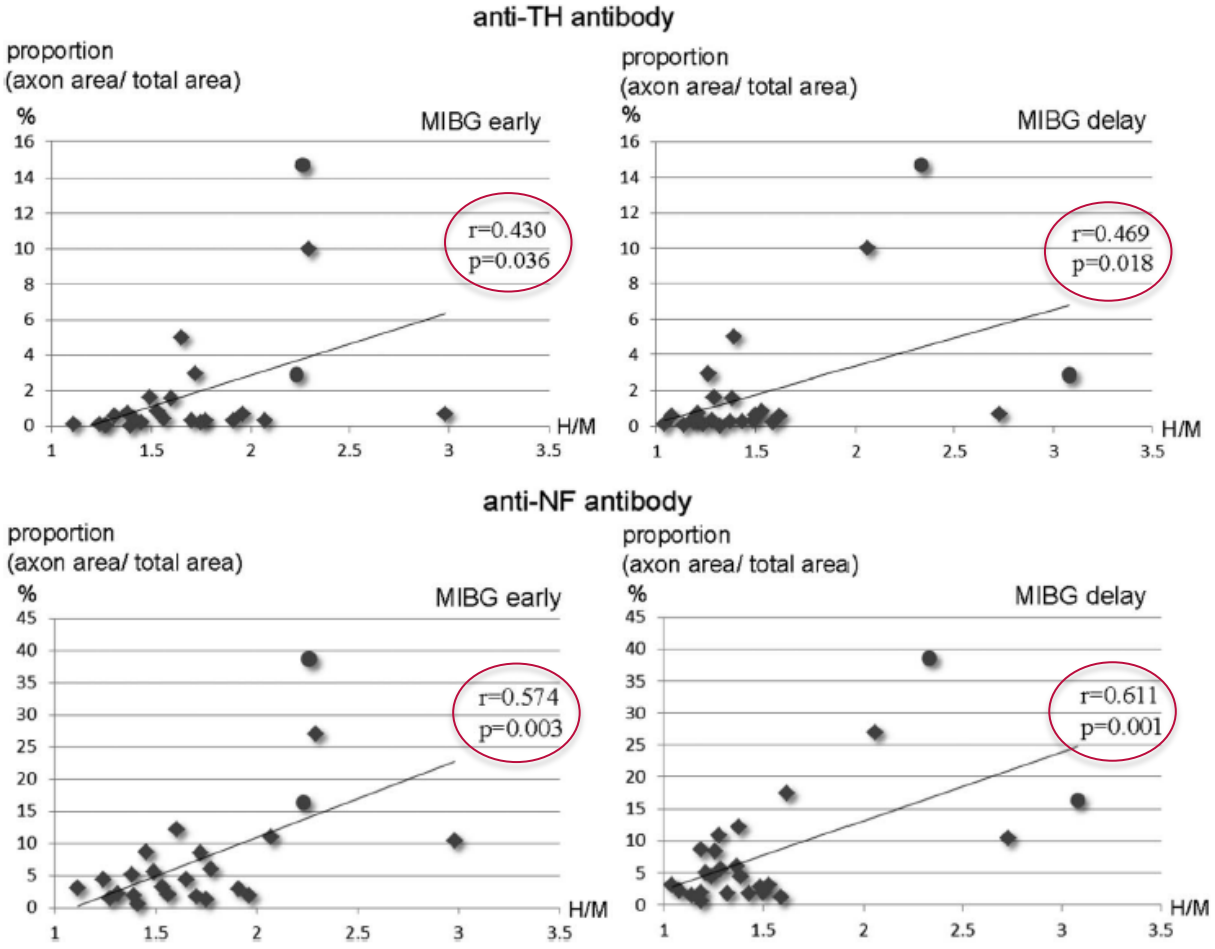
8 PD patients
15 LBD patients
2 non Lewy bodies disease -> CTRL

↓

Autopsy-confirmed diagnosis

↓

^{123}I-MIBG cardiac scintigraphy in life



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Sensitivity and specificity of metaiodobenzylguanidine (MIBG) myocardial accumulation in the diagnosis of Lewy body diseases in a movement disorder clinic☆

Fuyuki Tateno 17 (2011) 395–397

182 new patients

Low H/M ratio in 91.3% of Lewy Bodies Diseases (116/127 patients; 90% PD, 94.1% DLB)

Normal H/M ratio in 89.1% of diseases control (49/55 patients; 100% in AD, 88.9% in PSP)

In order to diagnose Lewy body diseases sensitivity and specificity of myocardial MIBG were high, also in a movement disorder clinic

Take Home Messages

The ^{123}I-MIBG cardiac scintigraphy is a useful marker of function of sympathetic endings in the heart. Reduced MIBG uptake indicates post-ganglionic sympathetic dysfunction, which reflect the Lewy Bodies accumulation in paravertebral sympathetic ganglia.

MIBG scintigraphy is a sensitive tool that allows to distinguish Lewy Bodies pathologies (PD, PDD, DLB, PAF) from other no-Lewy parkinsonism (MSA, PSP; CBD, VP, FTD, AD, ET)

MIBG scintigraphy is differently affected in different PD phenotypes (ART > TD; late > early stages)

Although careful interpretation of the result of MIBG cardiac scintigraphy is required (possibility of false positive and false negative; medications, peripheral autonomic neuropathies, and congestive heart failure can affect cardiac MIBG uptake) and despite it remains a not-routinely executable examination, it represent a useful technique in specialized movement disorders clinic to refine the diagnosis of parkinsonian disorders


Thank You