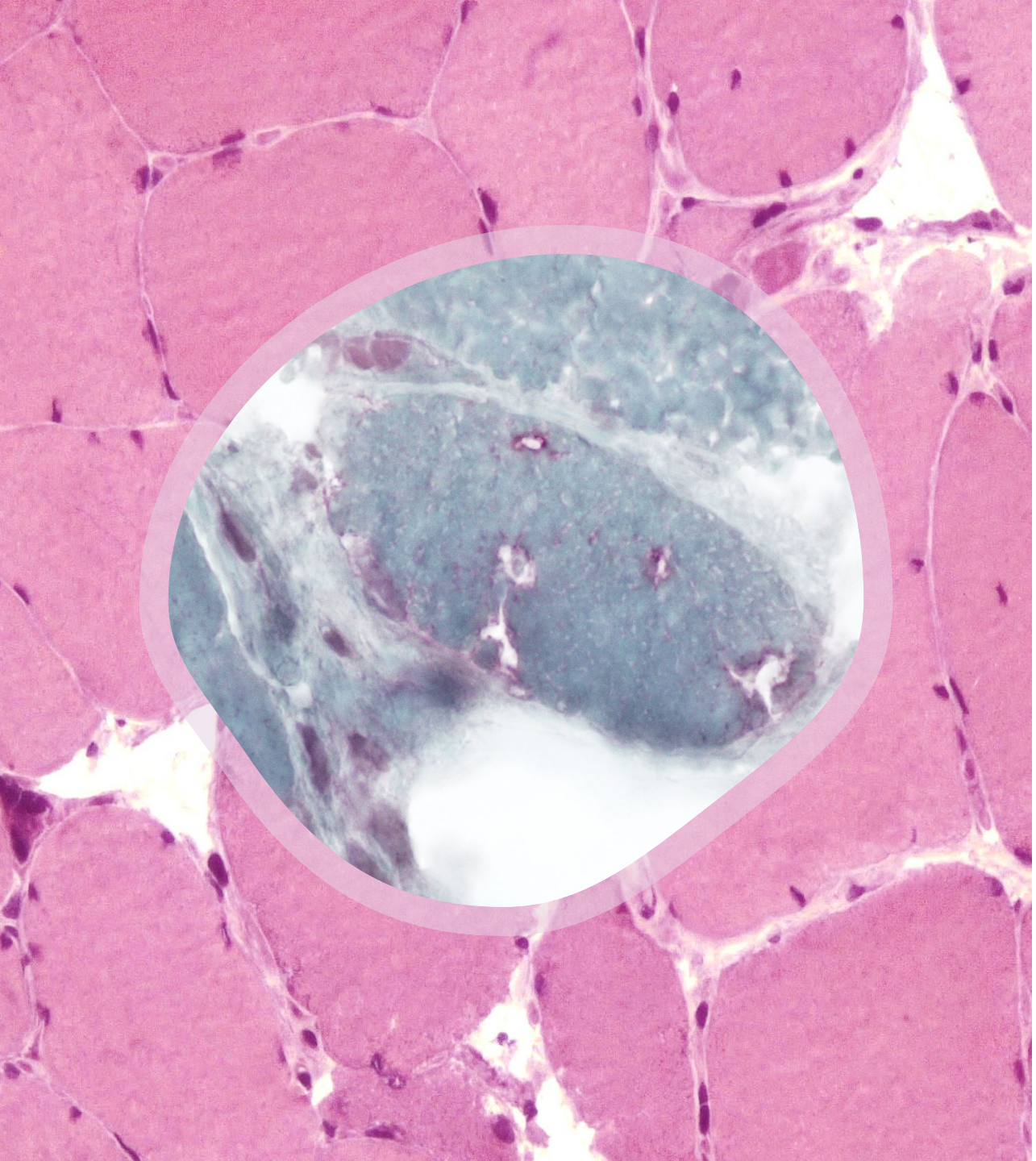


GNE myopathy, electrophysiological **pitfalls** of a challenging diagnosis: a case series

L. Bosco, C. Butera, S. Amadio, YM Falzone, M. Filippi, S.C. Previtali, U. Del Carro

Neurophysiology Unit
Institute of Experimental Neurology (INSPE)
San Raffaele Hospital (MI)

Dichiarazione sull'autonomia dei contenuti scientifici presentati

Non ho alcun coinvolgimento o interesse che possa far sorgere il problema di una distorsione nella presentazione, nel lavoro, nelle conclusioni o nelle opinioni espresse nella presentazione.

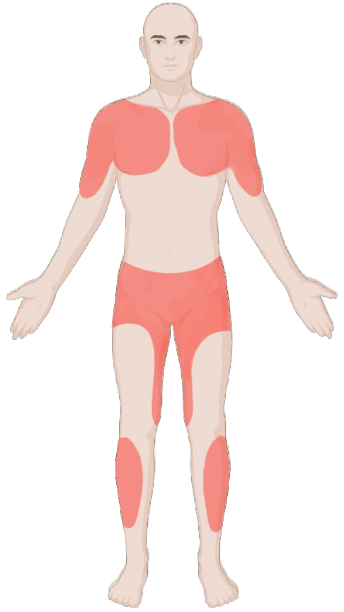
Pz. 1 ♀ 36 aa.

EMG (2009): sofferenza tronculare nervo **SPE** sinistro

EMG (2011): **neuropatia** motoria assonale cronica

NGS CMT: MPZ, MFN2, GARS, NEFL, GDAP1, RAB7, DHPLC

Pz. 2 ♂ 45 aa.

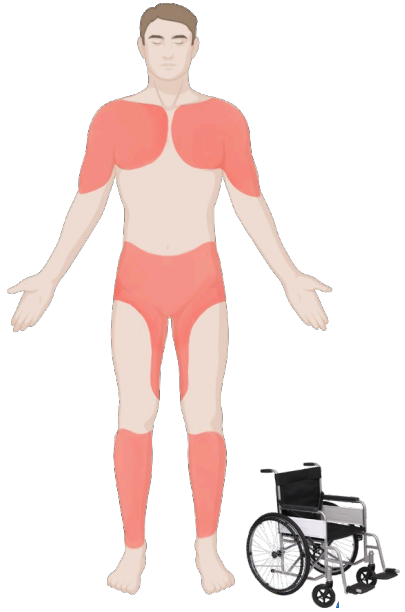


EMG (2015): **radicolopatia** assonale cronica L5 sinistra

EMG (2016): segni di sofferenza **neurogena** cronica associati a segni **miopatici**

NGS MND *(VCP, SOD1, TARDPB, FUS/TLS, C9ORF72, AR)*, **pannello distrofie, FSHD**

Pz. 3 ♂ 53 aa.

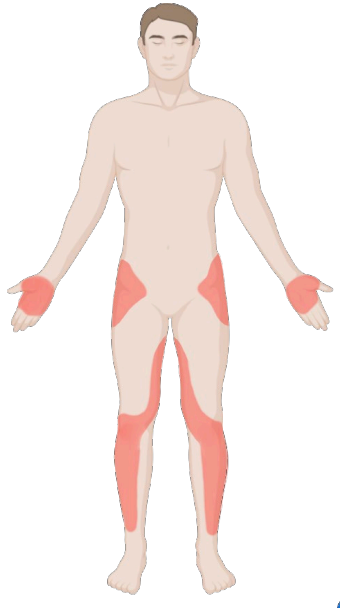


EMG (2000): **radicolopatia** assonale cronica L5 e S1 a destra

EMG (2001): neuropatia assonale/**neuronopatia** motoria con segni di denervazione in fase attiva

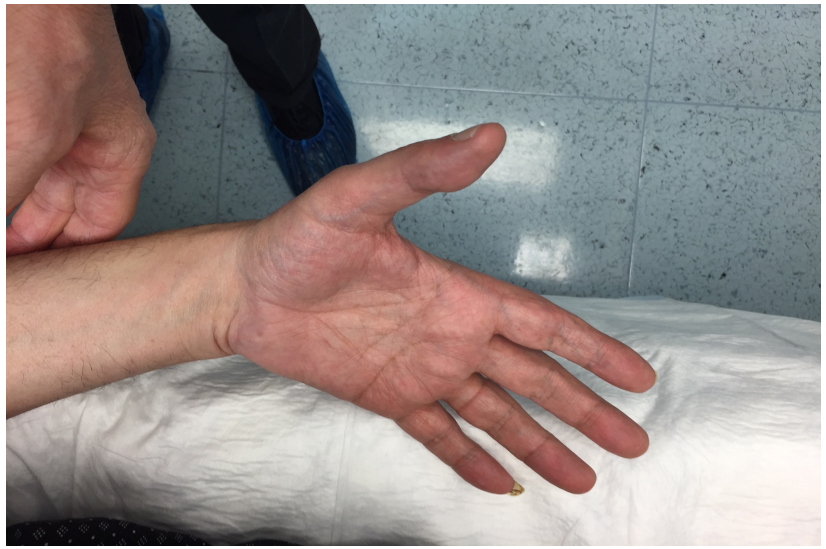
NGS CMT: MFN2, GARS, SETX, BSCL2, NEFL, GDAP1

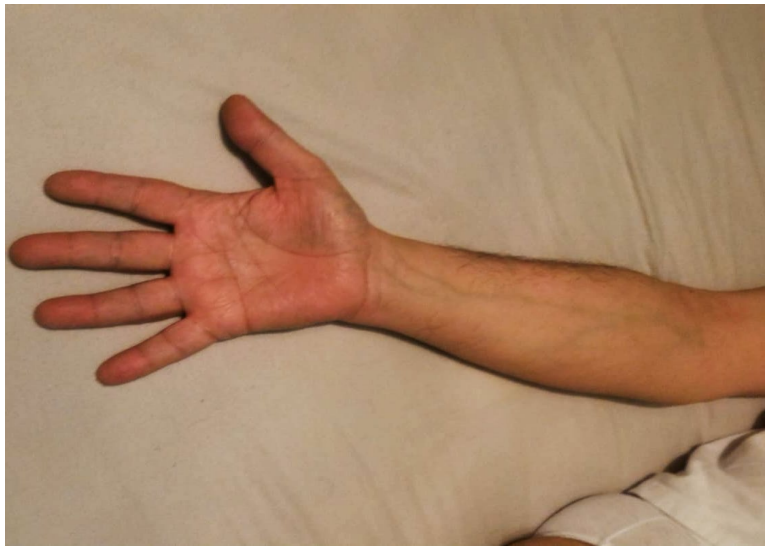
Pz. 3 ♂ 51 aa.

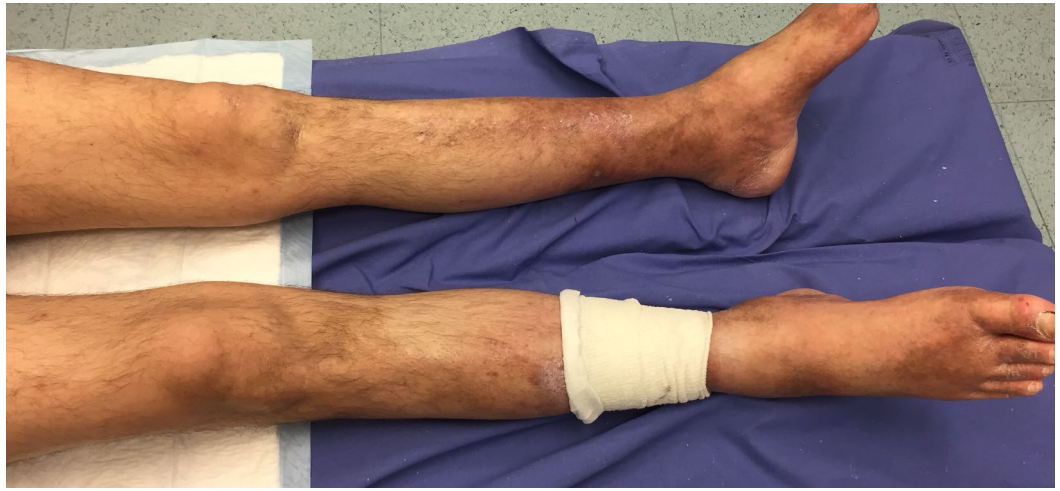


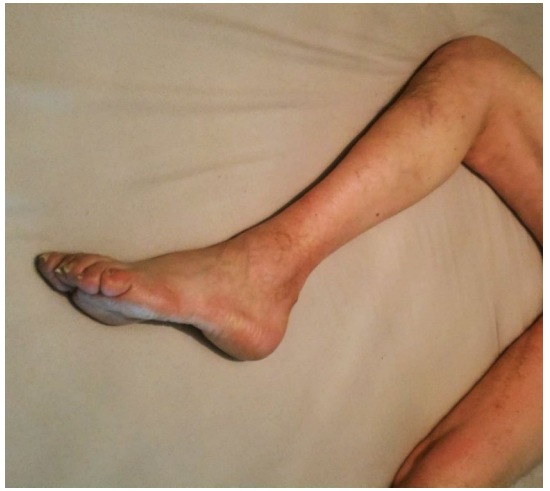
OSPEDALE SAN RAFFAELE

Pz. 3 ♂ 54aa.





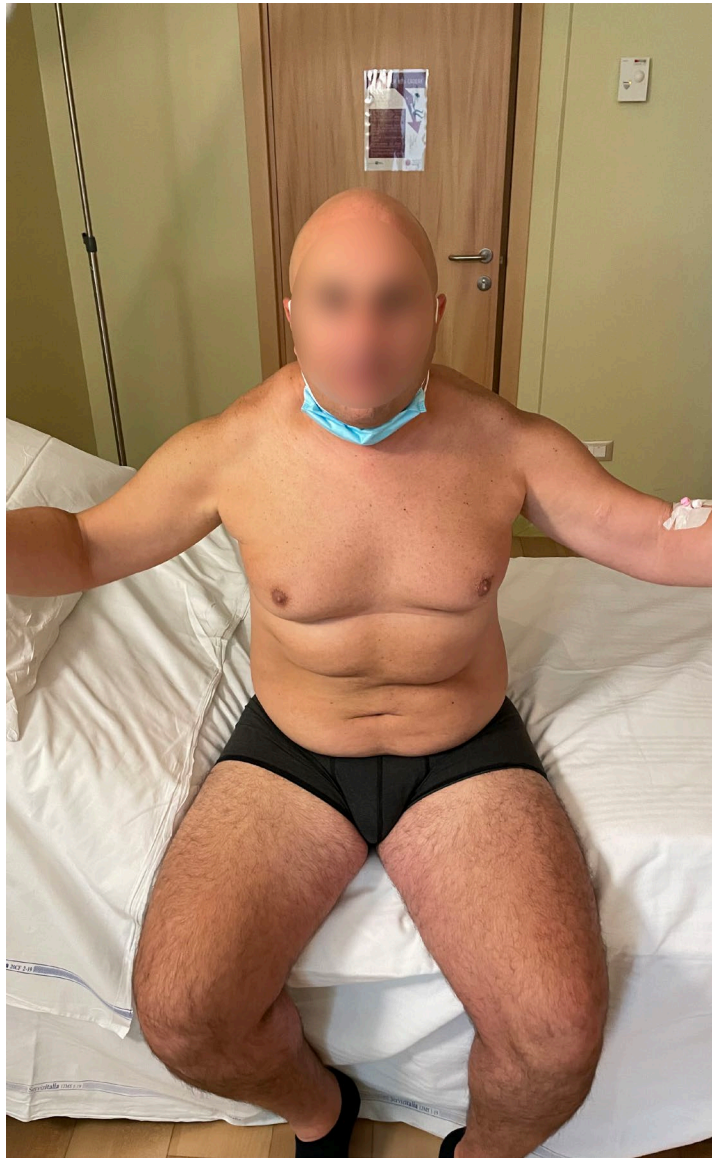


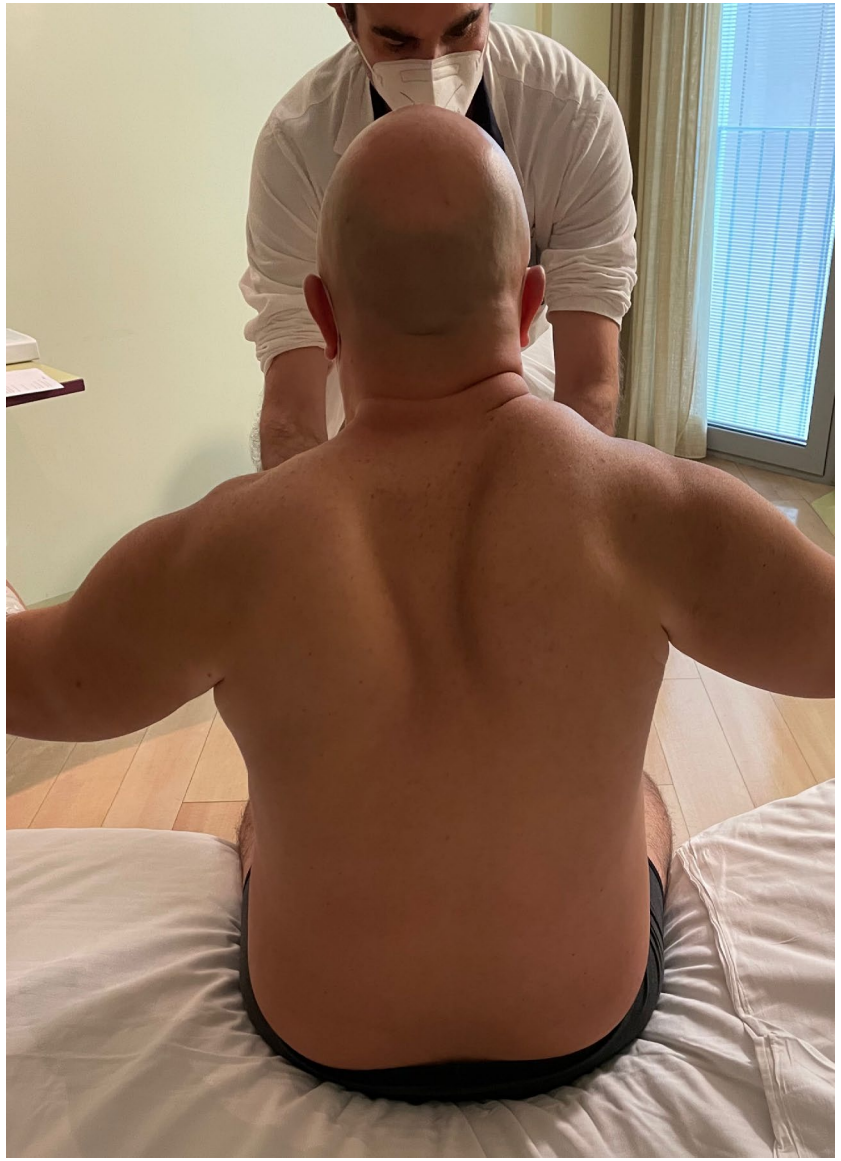


Muscoli (MRC)	DX	SN
DELTOIDE	2+	2+
BICIPITE BR	3	3
TRICIPITE BR	4	4-
ESTENSORI CARPO	4+	4+
FLESSORI DITA	4-	4+
INTEROSSEI	4	4+
OPPONENTE POL.	4	4-
ILEOPSOAS	2	2
QUADRICIPITE	**4**	**4**
TIBIALE ANTERIORE	1	1
GASTROCNEMIO	1	1

OSPEDALE SAN RAFFAELE

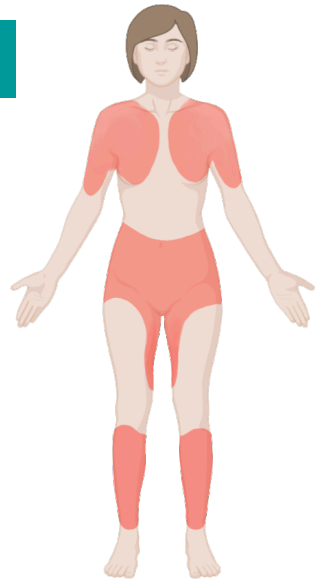
Pz. 2 ♂ 46 aa.





Muscoli (MRC)	DX	SN
ROMBOIDI	4	5
DELTOIDE	2	2
BICIPITE BR	3	3
TRICIPITE BR	4	4
FLESSORI DITA	5	5
MEDIO GLUTEO	2	2
ILEOPSOAS	2	2
QUADRICIPITE	**4+**	**4+**
ISCHIOCRURALI	2	2
TIBIALE ANTERIORE	3	2
GASTROCNEMIO	4	4

Pz. 1 ♀



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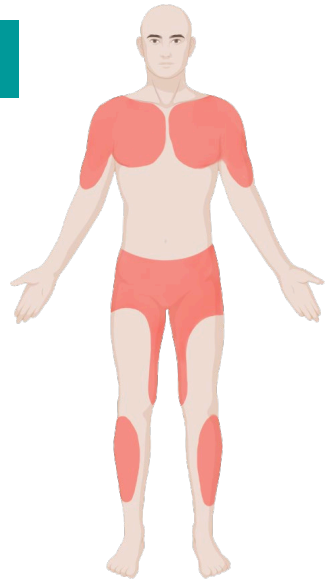
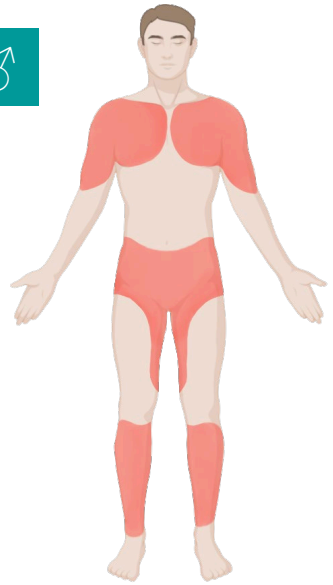
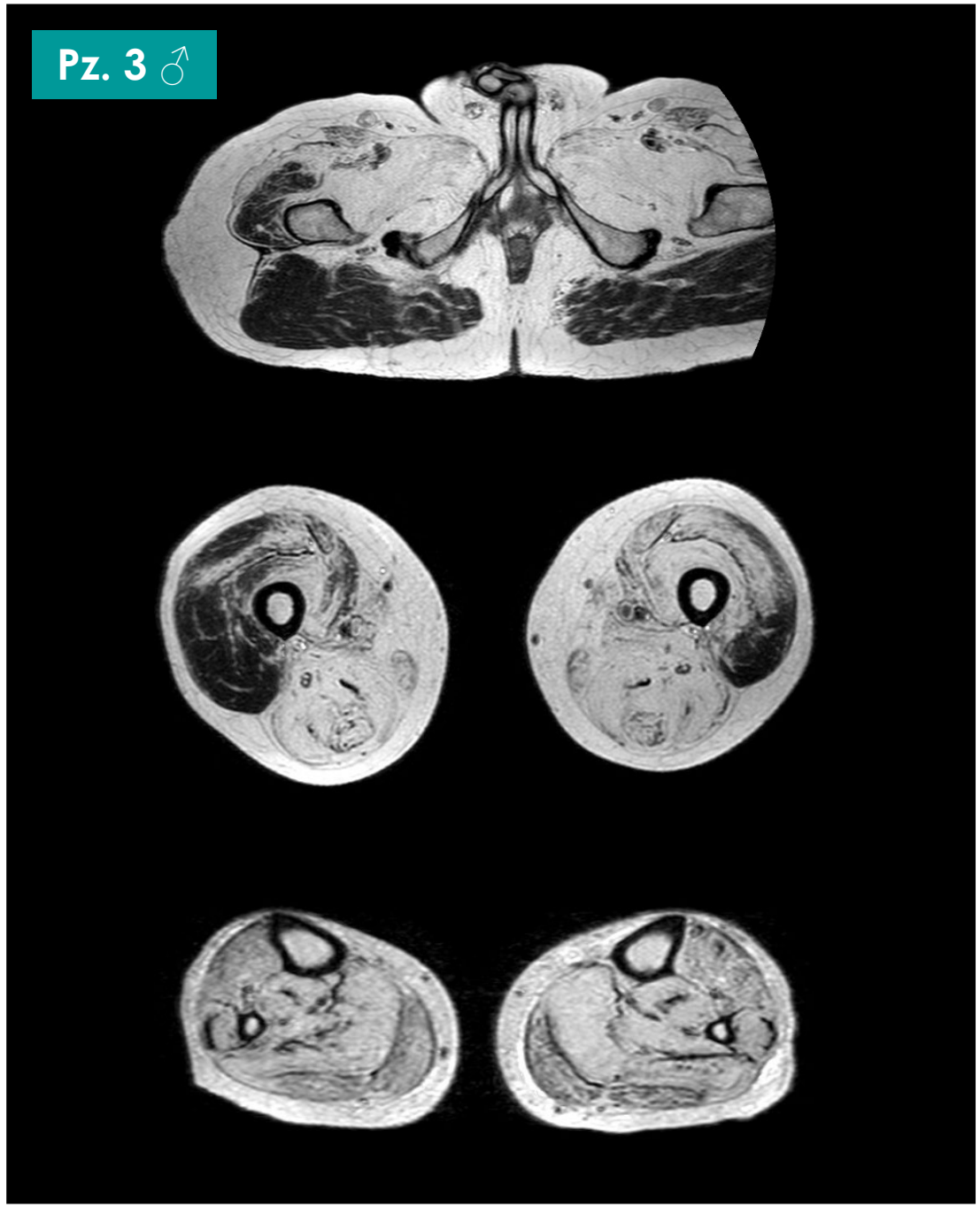


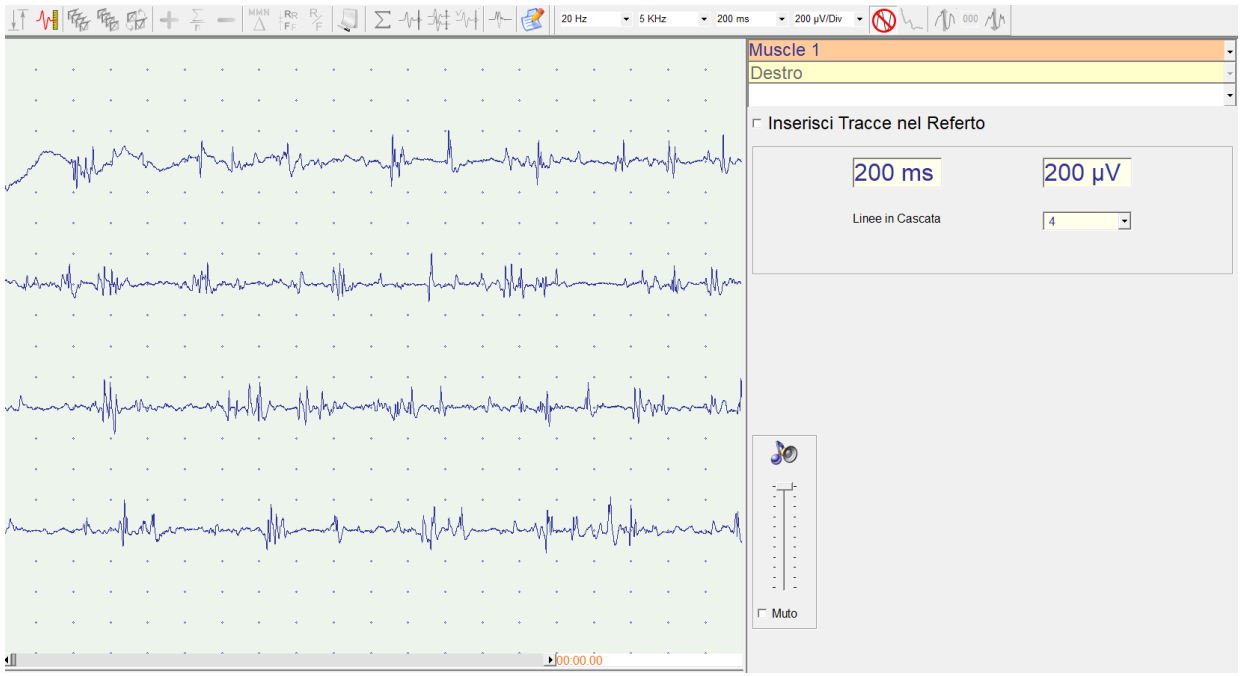
Pz. 3 ♂

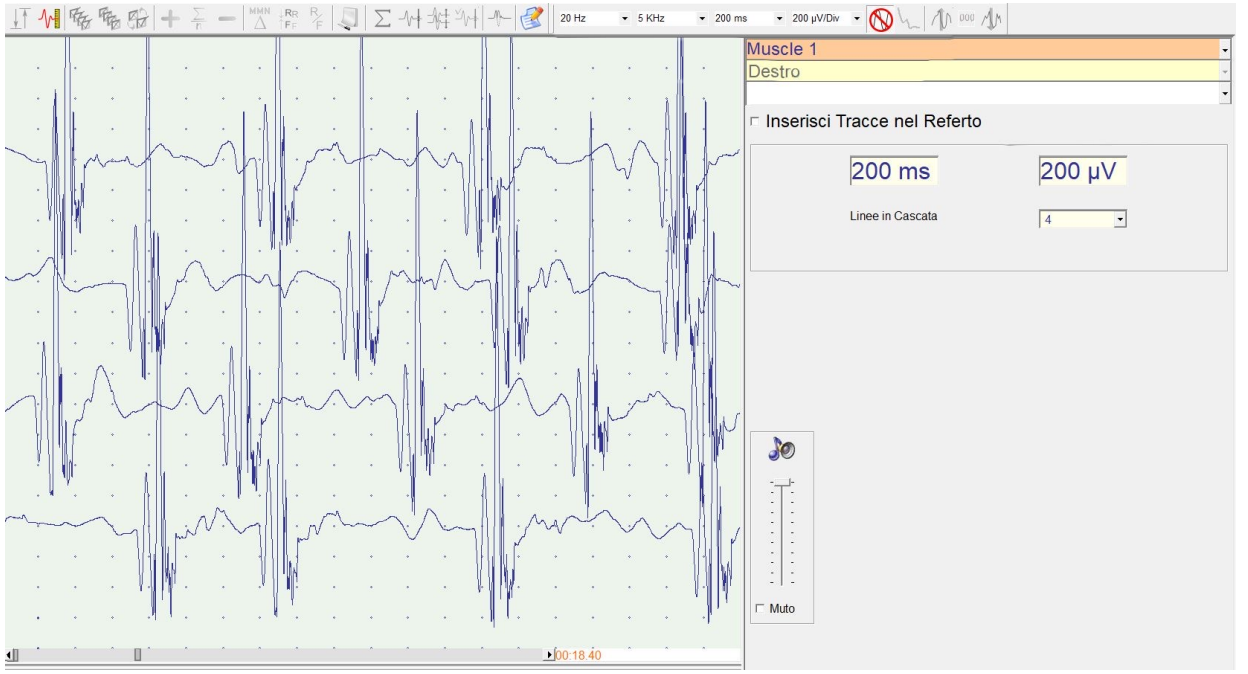


MUSCOLO	Att. spontanea	MUAP		Reclutamento	Att. spontanea	MUAP		Reclutamento	Att. spontanea	MUAP		Reclutamento
		Durata	PPP			Durata	PPP			Durata	PPP	
Deltoide	0	↓↓	↑↑	Precoce	0	↓↓	↑↑	Precoce	0	↓	↑↑	Precoce
Bicipite	0	↓↓	↑↑	Precoce	++	↓↓	↑↑	Precoce	0	↓	↑↑	Precoce
I interosseo	0	↓	↑↑	Interfer.	0	Norm.	↑↑	Interfer.	0	↓	↑	Interfer.
Vasti	0	Norm.	0	Interfer.	0	Norm.	0	Interfer.	0	Norm.	↑↑	Interfer.
M. Gluteo	0	↓	↑↑	Interfer.	0	↓	↑↑	Interfer.	0	↓↓	↑↑	Precoce
T.A.	0	Ass.	Ass.	NV	0	↑	↑↑	Transiz.	+	↑	↑↑	S.O.
G.M.	0	Ass.	Ass.	NV	+	↑	↑↑	Transiz.	+	↑	↑↑	S.O.

Pz. 3 ♂

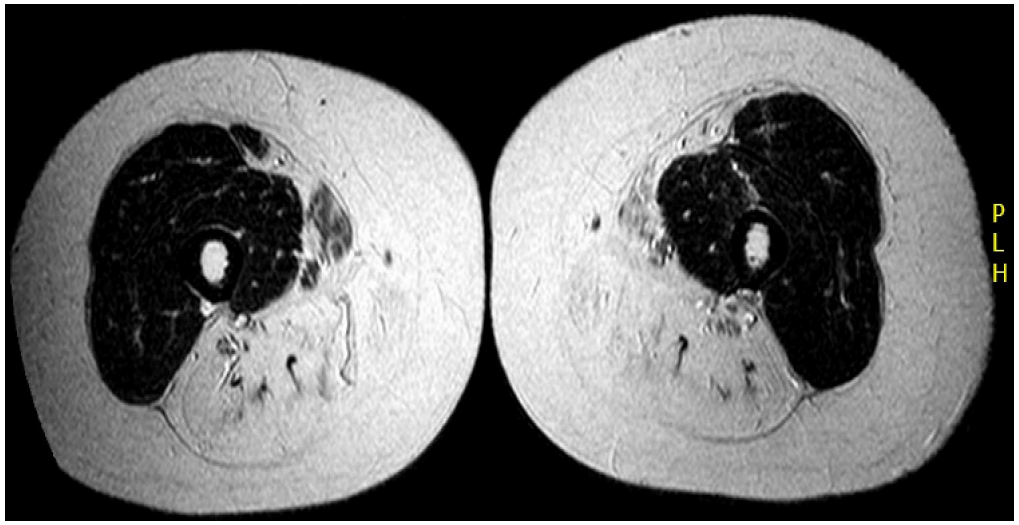


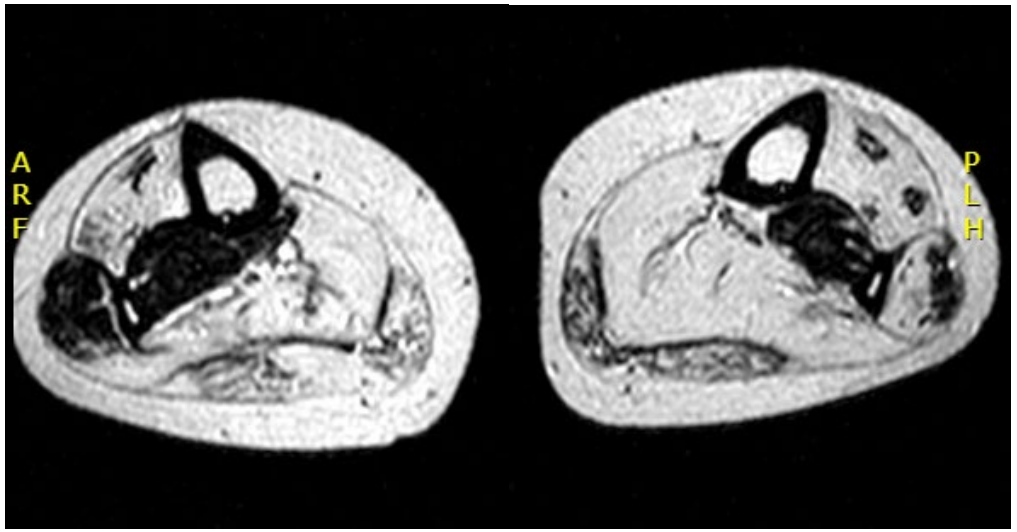

20 Hz
5 KHz
200 ms
200 µV/Div
Muscle 1
Destro
Inserisci Tracce nel Referto
200 ms
200 µV
Linee in Cascata
4
Muto
00:00.00

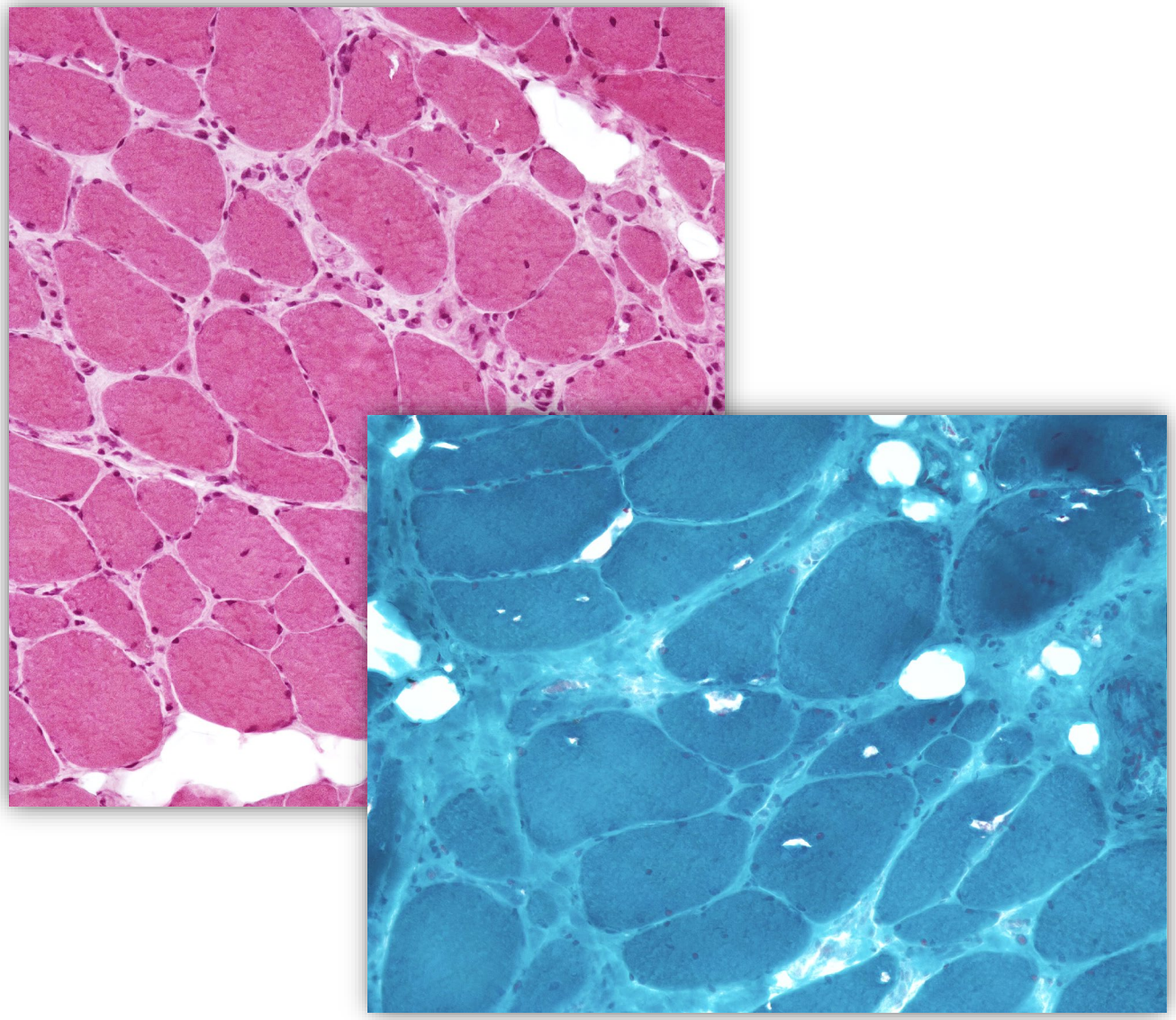

20 Hz
5 KHz
200 ms
200 µV/Div
Muscle 1
Destro
Inserisci Tracce nel Referto
200 ms
200 µV
Linee in Cascata
4
Muto
00:18.40

OSPEDALE SAN RAFFAELE

Pz. 1 ♀ 43aa

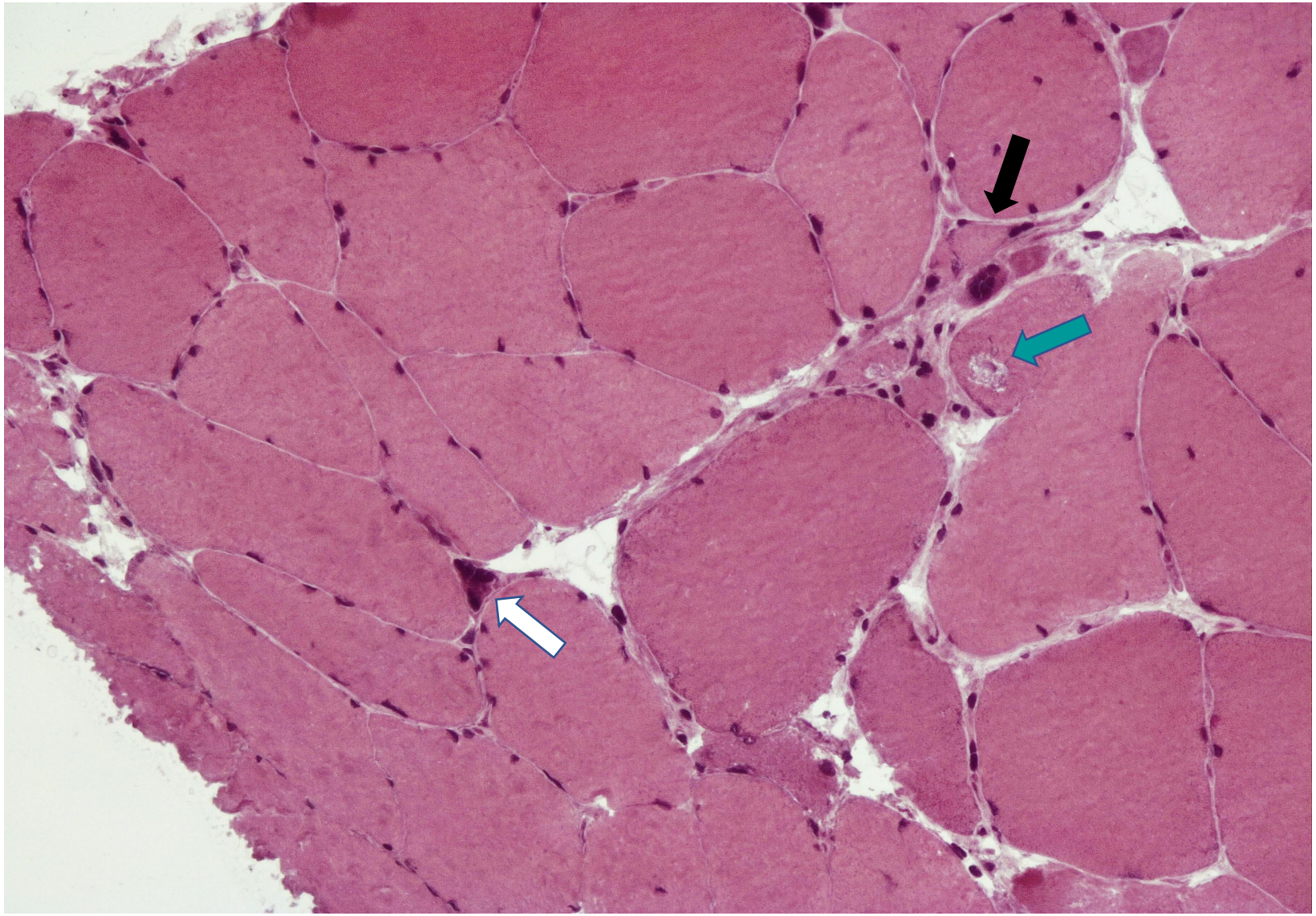


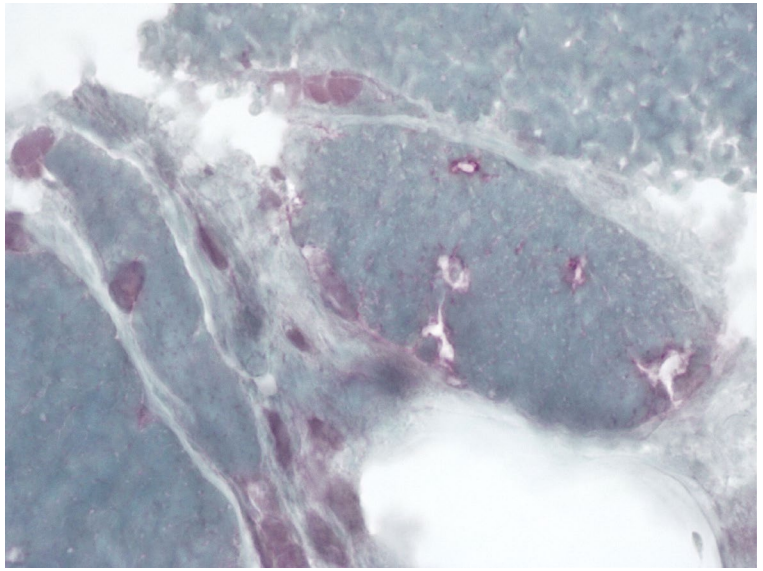


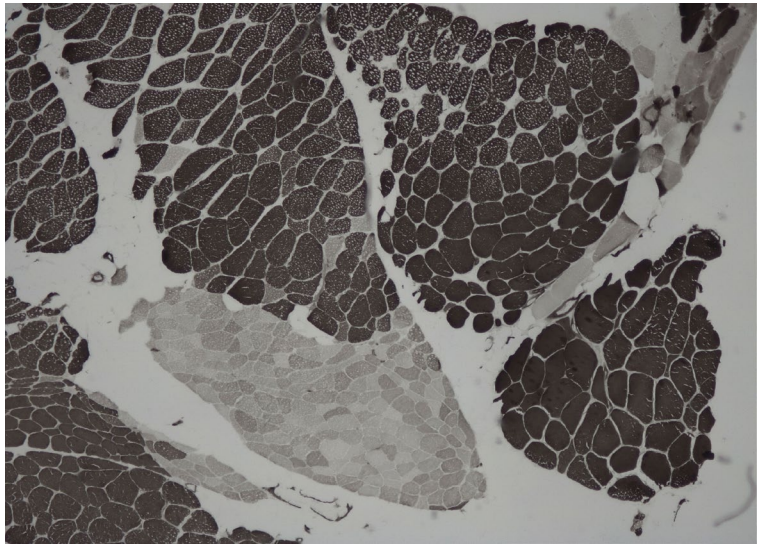


OSPEDALE SAN RAFFAELE

Pz. 3 ♂ 53aa



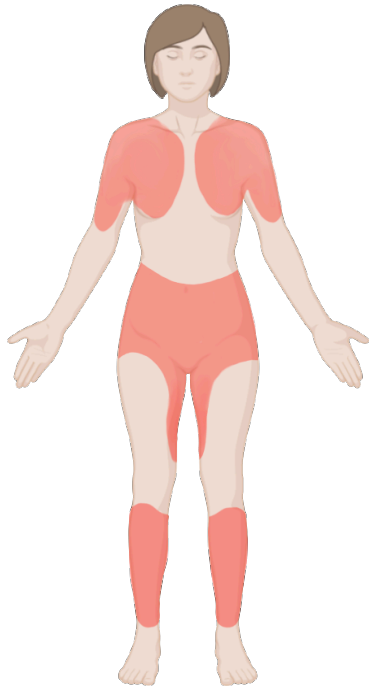




GNE myopathy *(aka: Nonaka myopathy; HIBM2)*

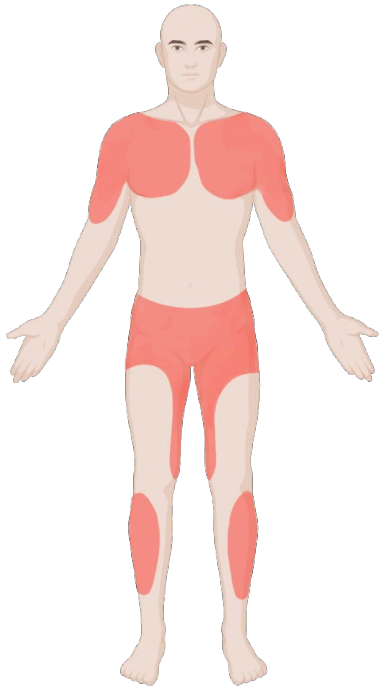
Ritardo alla diagnosi

5 anni



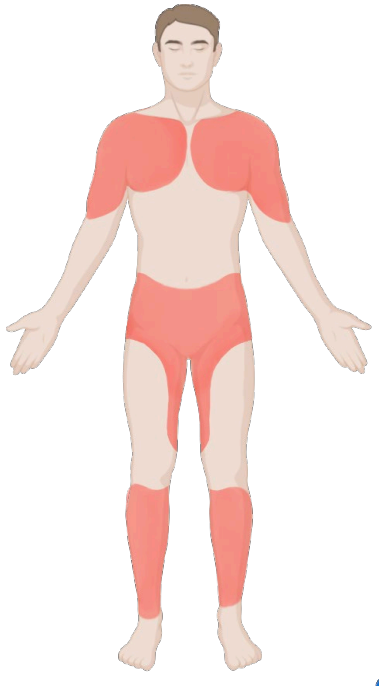
GNE c.1504+5G>C
p.Ala662Val

4 anni

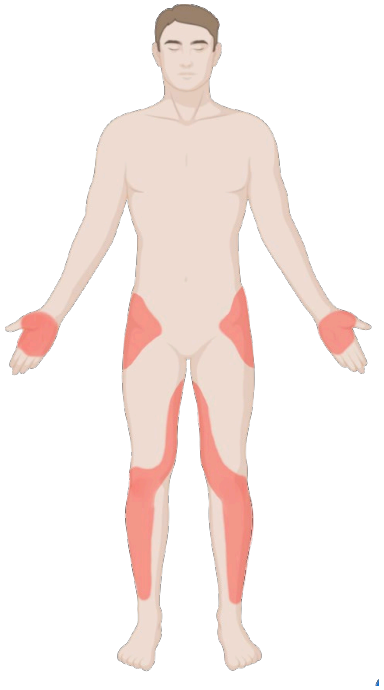


GNE p.Leu570Pro &
p.Cys581Phe

17 anni



17 anni



GNE p.Glu33Gly
& p.Tyr706His

GNE myopathy

(aka: Nonaka myopathy; HIBM2)

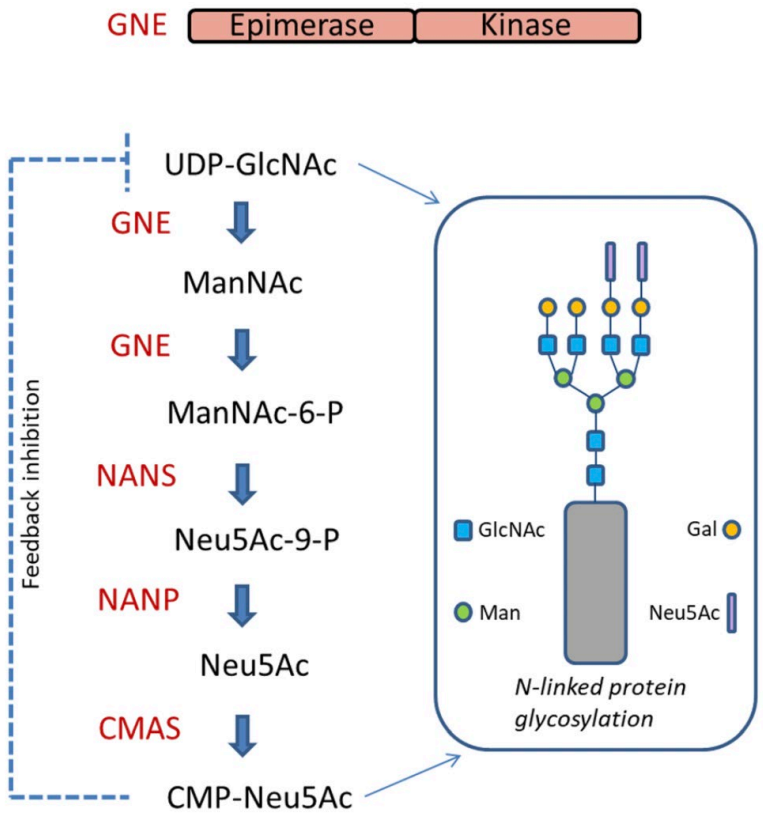


Table 1 GNE myopathy at a glance

GNE myopathy at a glance	
Onset	20s
Prevalence	1/ 1.000.000
Genetic	Autosomal-recessive
First symptom	Foot drop
Additional symptoms	Hand weakness
Unusual mimicking of other myopathic diseases	Scapuloperoneal syndrome, LGMD, CMT, MTM, LGMD2B
Quadriceps sparing	Good strength in 95% of the patients
Progression	Slowly from distal to proximal
Beevor's sign	Positive in 90% of an Indian cohort
Cardiac involvement	Risk of cardiomyopathy is not increased
Respiratory involvement	Mild to moderate decrease in FVC in non-ambulatory patients

Type	Inheritance Pattern	Gene or Locus	Early Weakness	CK	Muscle
HIBM1	Dominant	Desmin	25 to 40 years Legs: Distal; Quadriceps	Normal, or Slight ↑	Myopathic Vacuoles
Oculopharyngodistal	Dominant	Autosomal	40 years Extraocular	3x ↑	Myopathic Vacuoles
Vocal cord & Pharyngeal (MPD2)	Dominant	Matrin 3	35 to 57 years Legs, Hands or Vocal cord	Normal to ↑ 8x	Myopathic Vacuoles
Myopathy + Paget's & Dementia	Dominant	VCP	20 to 40 years Legs Proximal & Distal	Normal or Slight ↑	Myopathic Vacuoles
Myopathy + Paget's	Dominant	HNRNPA2B1	35 to 42 years Legs: Distal Scapular	Normal or High	Myopathic
MPD3	Dominant	HNRNPA1	32 to 45 years Distal Legs & Hands	Normal or Slight ↑	Myopathic Vacuoles
Cytoplasmic body	Dominant	Autosomal	40 to 50 years Hands	Normal or Slight ↑	Myofibrillary inclusions
Myopathy with Anterior leg sparing (MPD4)	Dominant	Filamin C	0 to 30 years Distal Legs & Hands	Normal or Slight ↑	Varied fiber size No vacuoles
Nonaka-HIBMR (HIBM2)	Recessive, or Sporadic	GNE	20 to 40 years Legs: Anterior	↑ up to 5x	Myopathic Vacuoles
Miyoshi ± LGMD 2B	Recessive, or Sporadic	Dysferlin	20 to 50 years Legs: Posterior	10x to 150x ↑	Myopathic No vacuoles
LGMD 2G	Recessive	Telethonin	12 years Legs: Proximal & Anterior distal	3x to 17x ↑	Myopathic Vacuoles

Welander	Dominant	TIA1	> 40 years Hands: Extensor	Normal, or Slight ↑	Myopathic ± Vacuoles
Finnish (Tibial;. Udd)	Dominant	Titin	40 to 50 years Legs: Anterior	Normal, or Slight ↑	Myopathic Vacuoles
HMERF	Dominant	Titin	12 to 75 years Distal anterior legs Respiratory	Normal or Slight ↑	Myopathic Eosin inclusions Cytoplasmic body Vacuoles
Gowers-Laing (MPD1)	Dominant	MYH7	1.5 to 25 years Dorsiflex: Ankle; Toe	↑ up to 3x	Myopathic: Mild Vacuoles: Few
Distal dystrophy + Rimmed vacuoles	Dominant	DNAJB6	10 to 50 years Legs: Distal	Normal, or Slight ↑	Myopathic Vacuoles
Miyoshi-like 3 (MMD3)	Recessive	Anoctamin 5	11 to 50 years Legs: Posterior	3x to 100x ↑	Myopathic Sarcolemmal lesions
Nebulin	Recessive	Nebulin	Child or Adult Toe & finger extensor	Normal	Myopathic Rods, Small
Adolescent	Recessive	ADSSL1	Adolescent Posterior legs; Face	Mildly high	Myopathic Vacuoles, Few

Myofibrillar myopathies

Desmin	Dominant or Recessive	2q35	20 to 40 years Legs	Mild ↑	Myopathic Desmin ↑
aB-crystallin	Dominant	11q22	Adult Distal	Mild ↑	Myopathic Desmin ↑
Scapuloperoneal	Dominant	FHL1	20 to 58 years Distal; Legs	1.5x to 10x ↑	Myopathic, Focal Desmin inclusions
ZASP, Markesbery	Dominant	ZASP	Child to 73 years Distal in 9%	Normal to 6x ↑	Myopathic Desmin inclusions Vacuoles: Small

Clinical and Electrophysiological Findings in Hereditary Inclusion Body Myopathy Compared With Sporadic Inclusion Body Myositis

Mohamed Kazamel, MD, Eric J. Sorenson, MD, and Margherita Milone, MD, PhD

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Journal of
CLINICAL
NEUROMUSCULAR
DISEASE

Volume 17, Number 4
June 2016

TABLE 2. Electrophysiological Findings in hIBM and sIBM

Electrophysiological Finding	hIBM, n	sIBM, n	*P*
Myopathic MUPs	8	40	0.33
Neuropathic MUPs			
Upper extremity	6	29	1
Lower extremity	9	32	0.18
Axial muscles	3	7	0.32
Proximal muscles	8	27	0.25
Distal muscles	6	30	0.70
Myotonic discharges	4	12	0.45
CRDs	1	6	1
Neuropathic NCS	1	13	0.67
Frequency of Fibs			
Overall	7	41	0.03
Upper extremity	5	40	0.003
Lower extremity	7	40	0.08
Axial muscles	3	19	0.65
Proximal muscles	5	39	0.003
Distal muscles	7	39	0.14
Fibs severity grade	Mean	Mean	
Upper extremity	0.8	1.7	0.0004
Lower extremity	1.3	1.7	0.17
Axial muscles	1	0.9	0.72
Proximal muscles	0.9	1.8	0.002
Distal muscles	1	1.6	0.01

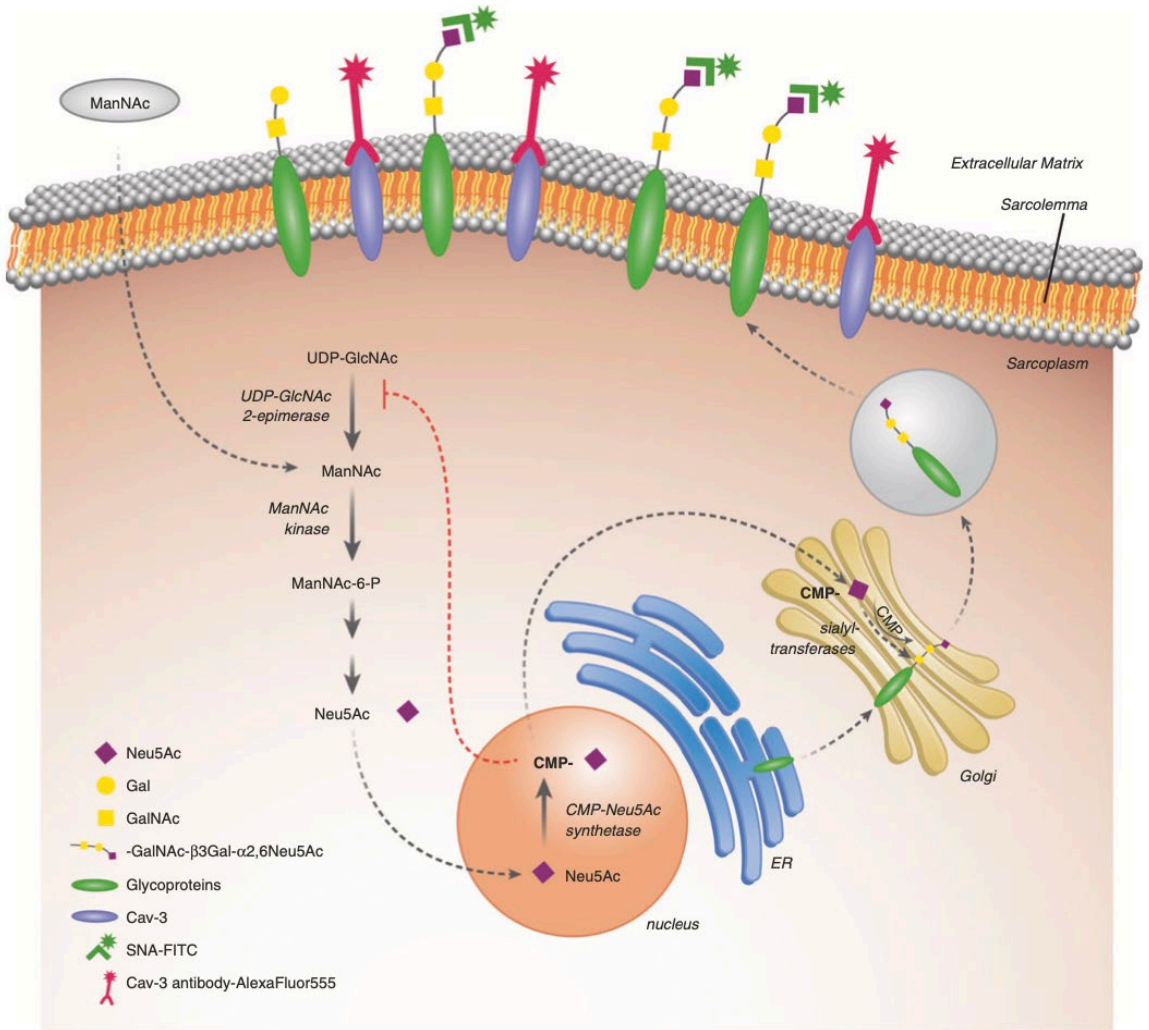
Genetics in Medicine

ARTICLE

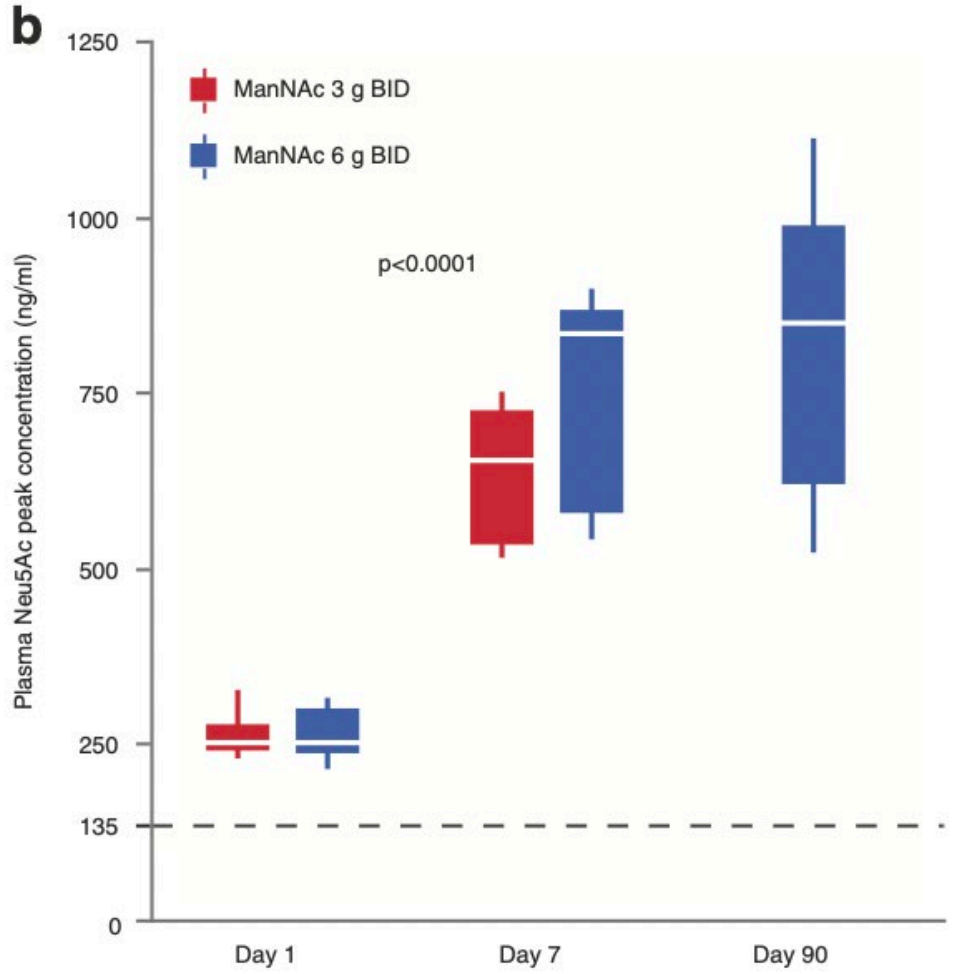
Safety and efficacy of *N*-acetylmannosamine (ManNAc) in patients with GNE myopathy: an open-label phase 2 study

Nuria Carrillo[1,2], May C. Malicdan[1,9], Petcharat Leoyklang[1], Joseph A. Shrader[3], Galen Joe[3], Christina Slota[2], John Perreault[2], John D. Heiss[4], Bradley Class[2], Chia-Ying Liu[5], Kennan Bradley[1], Colleen Jodarski[1], Carla Ciccone[1], Claire Driscoll[1], Rebecca Parks[3], Scott Van Wart[6], Levent Bayman[7], Christopher S. Coffey[7], Melanie Quintana[8], Scott M. Berry[8], Marjan Huizing[1,9] and William A. Gahl[1] ✉

a



b



Genetics inMedicine

ARTICLE

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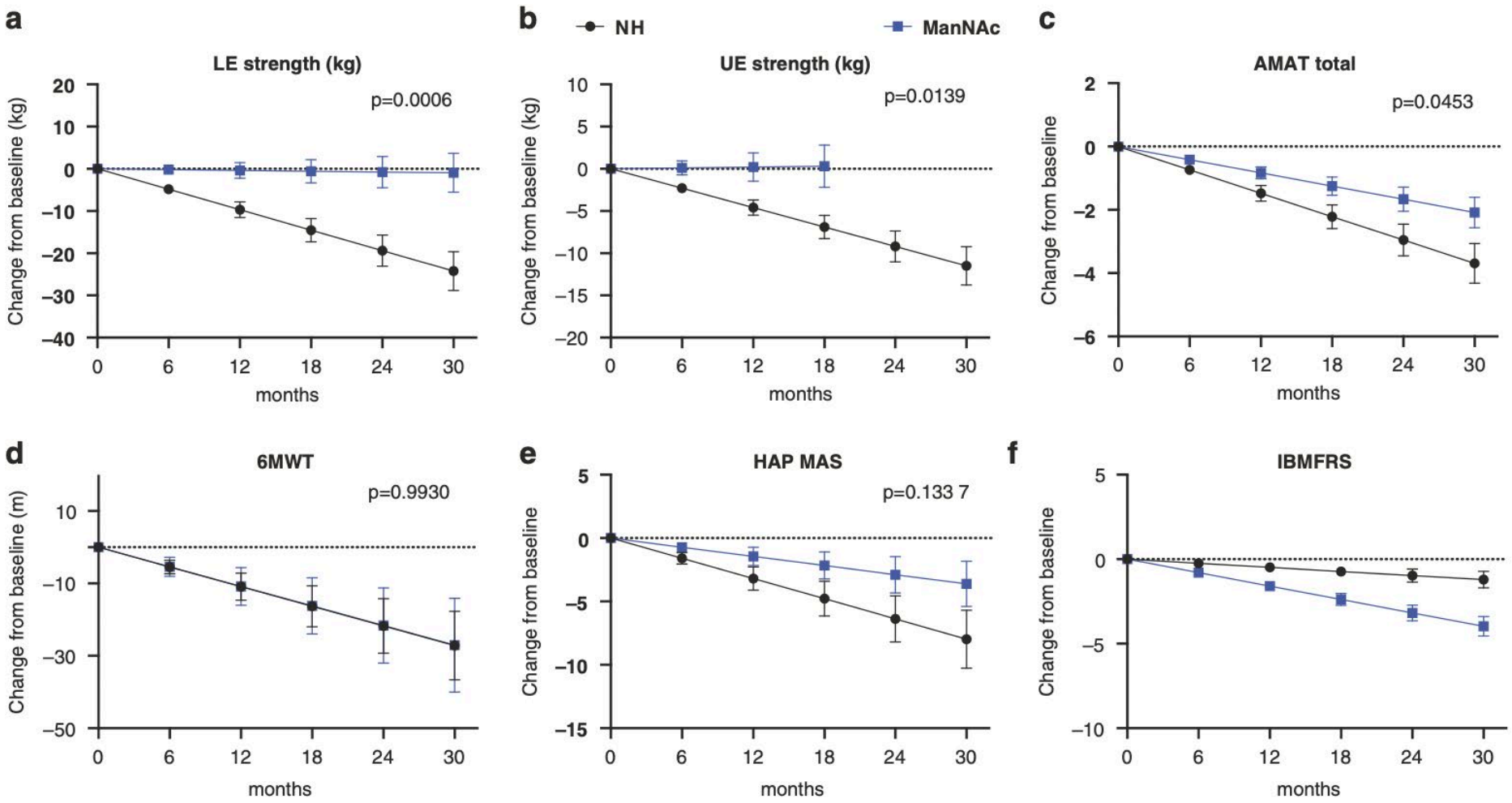
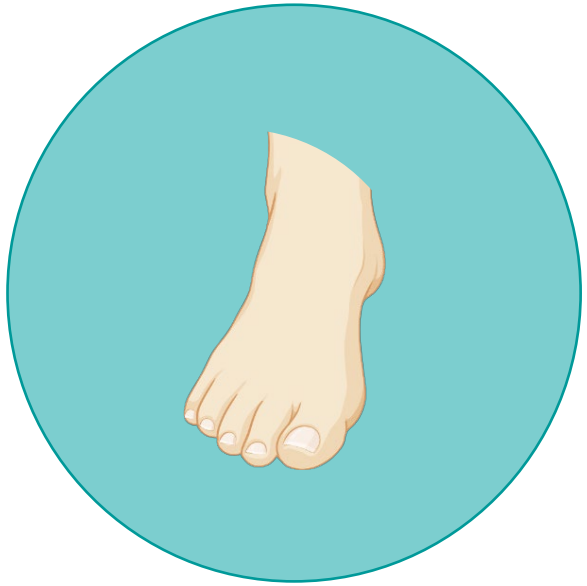
Nuria Carrillo[1,2], May C. Malicdan[1,9], Petcharat Leoyklang[1], Joseph A. Shrader[3], Galen Joe[3], Christina Slota[2], John Perreault[2], John D. Heiss[4], Bradley Class[2], Chia-Ying Liu[5], Kennan Bradley[1], Colleen Jodarski[1], Carla Ciccone[1], Claire Driscoll[1], Rebecca Parks[3], Scott Van Wart[6], Levent Bayman[7], Christopher S. Coffey[7], Melanie Quintana[8], Scott M. Berry[8], Marjan Huizing[1,9] and William A. Gahl[1] ✉

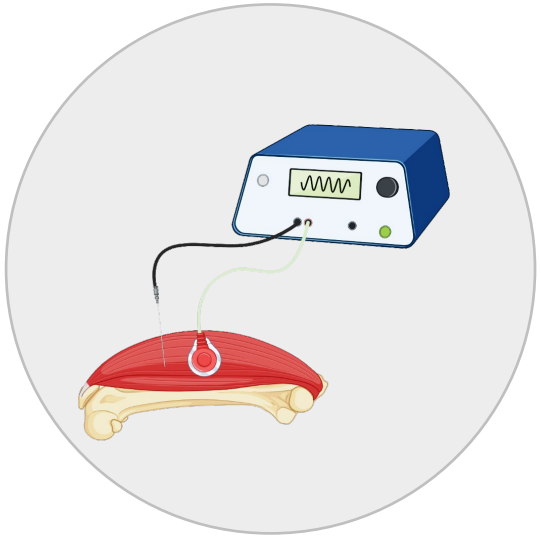


OSPEDALE SAN RAFFAELE

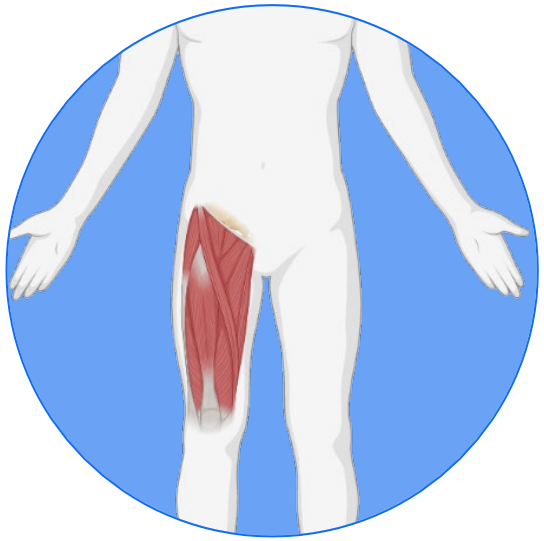
Punti salienti



Piede cadente =/= neuropatia



In quadri atipici estendere lo studio



Quadricipite risparmiato → **GNE**

The Hereditary Inclusion Body Myopathy Enigma and its Future Therapy

Zohar Argov* and Stella Mitrani-Rosenbaum†