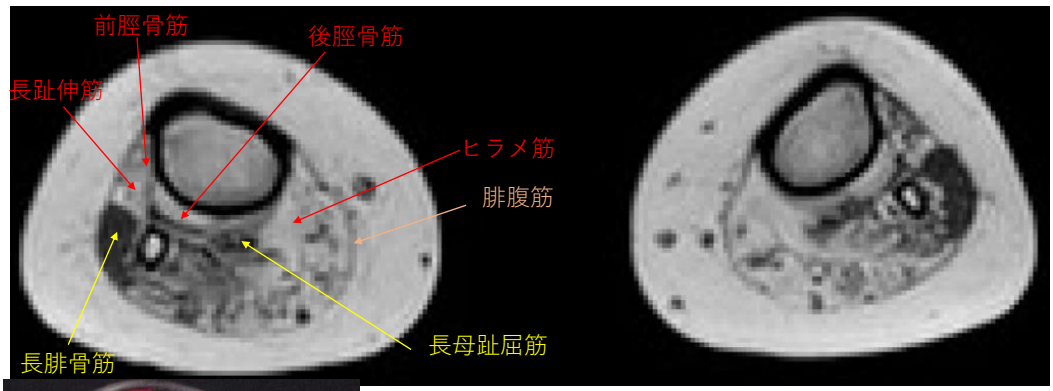
1



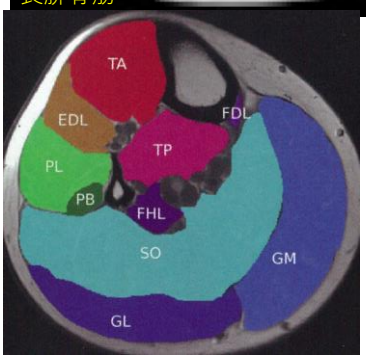


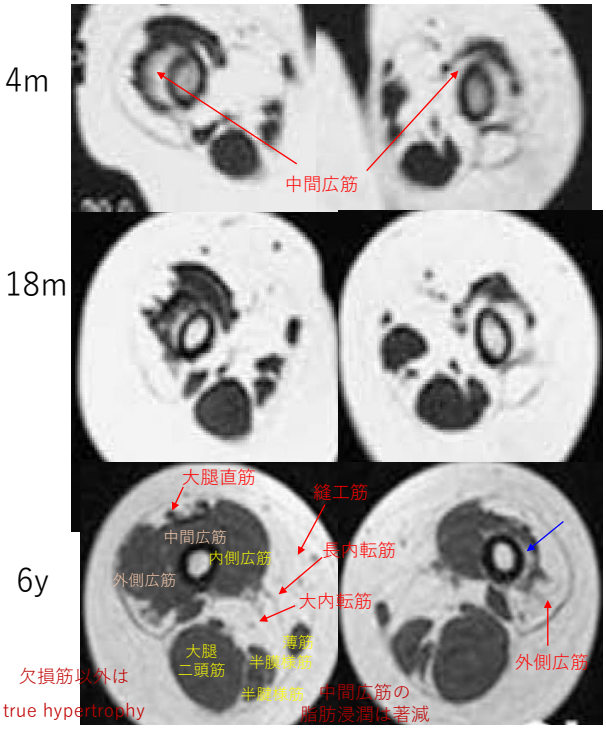
Fig 1. Lack of muscles in every compartment of the leg.　　足部変形の記載なし

Griffet J, Dieterich K, Bourg V, Bourgeois E. Amyoplasia and distal arthrogryposis. Orthop Traumatol Surg Res 2021;107(1S):102781.

Amyoplasiaは誤称

- ✓ *足背屈の常時筋収縮状態に足底屈の常時筋収縮状態が対抗していた*
- ✓ *長腓骨筋・長母趾屈筋以外は変性し、短縮強靱線維化した*

2



Mercuri E, Manzur A, Main M, Joanna Alsopp J, Muntoni F. Is there post-natal muscle growth in amyoplasia? A sequential MRI study. Neuromuscul Disord 2009;19:444-5.

- 肩内転内旋・肘伸展・前腕回内・手屈曲・屈指
- 股外旋・膝伸展・内反足

✓ *膝屈曲の常時筋収縮状態に、大腿四頭筋(膝伸筋)が対抗した*
*→力線が直行する大腿直筋・中間広筋・外側広筋は変性し、短縮強靱線維化した　*股伸展位では、大腿直筋の負荷は大きい*

✓ *股屈曲外転外旋の常時筋収縮状態に、股伸筋群・股内転筋群が対抗した*
→大内転筋・長内転筋が変性し、短縮強靱線維化した
**股屈曲外転外旋にも働く縫工筋は対抗筋に負けて変性した*

✓ 外側広筋と中間広筋は、4mでは脂肪化されていた部に、6yでは、筋が増生した

3

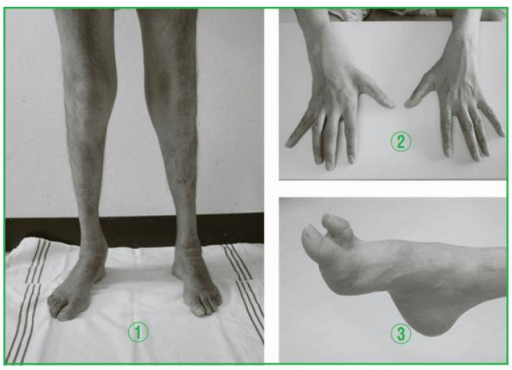


図2　大人の CMT 患者さんの足と手
子どもさんの場合はこれほどには目立たない可能性があります。①は膝の少し上から足先にかけて筋萎縮を示しています。シャンパンボトルを逆さまにしている形に似ているので「逆シャンパンボトル様萎縮」といわれます。②は手の萎縮です。特に親指と人差し指の間の筋肉が萎縮しています。③は足の変形で足の裏の筋肉が萎縮し土踏まずが高くなり，足の甲が高くなっています。「凹足」といわれます。

遺伝性ニューロパチー　橋口 昭大
日内会誌　108：1545～1551，2019

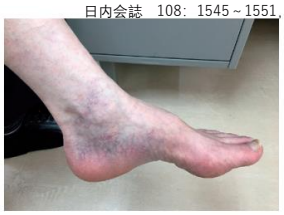
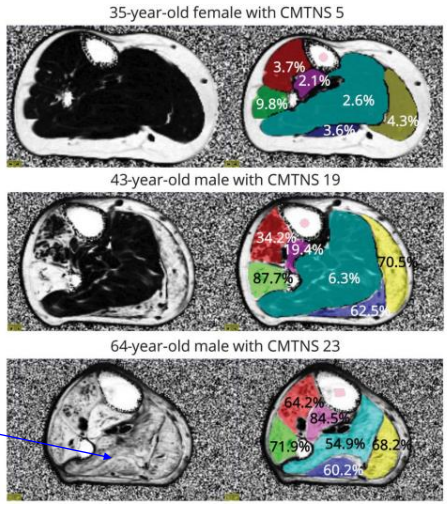


図2　凹足：pes cavus

Morrow JM, et al. Validation of MRC Centre MRI calf muscle fat fraction protocol as an outcome measure in CMT1A. Neurology 2018;91(12):e1125-e1129.



In the top patient, there is a slight increase in fat fraction in peroneus longus only. In the middle row, marked involvement is seen with endstage involvement of peroneus longus and both heads of the gastrocnemius. In the bottom row, there is severe involvement of all muscle groups.

red: tibialis anterior/ extensor hallucis longus;
*論文に記載はないが、*長趾伸筋*もあり*
green: peroneus longus;
purple: tibialis posterior;
light blue: soleus;
dark blue: lateral gastrocnemius;
yellow: medial gastrocnemius

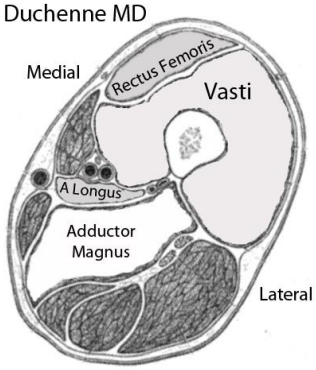
ヒラメ筋の空隙化はない

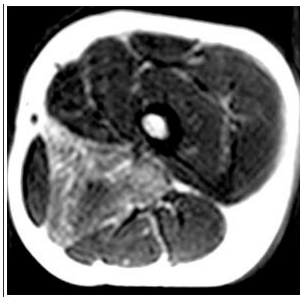
- 長腓骨筋と腓腹筋が初期に侵される
  *両筋は短縮強靱線維化して、凹足・尖足を造る
- 次に、前脛骨筋・長母趾伸筋・長趾伸筋が侵される
  *これらも短縮強靱線維化して、凹足を造る
- 後に、後脛骨筋・ヒラメ筋も侵される

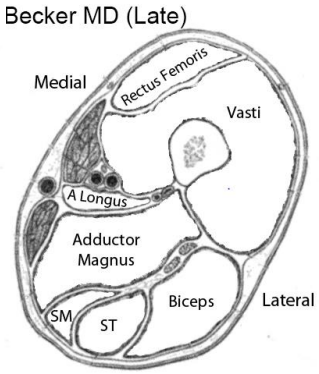
✓ 腓腹筋→ヒラメ筋の順に侵される

4

DMD







Arms [4]
- Common
  - Proximal: Periscapular (Involved early, with normal function)
  - Triceps; Biceps; Teres major
  - Distal arm: Supinator; Pronator
- Uncommon: Deltoid; Pectoralis; Hand & finger extensors

Trunk Paraspinal > Abdominal

Pelvis
- Common: Gluteus maximus & medius 大殿筋・中殿筋
- Uncommon: Obturator internus & externus

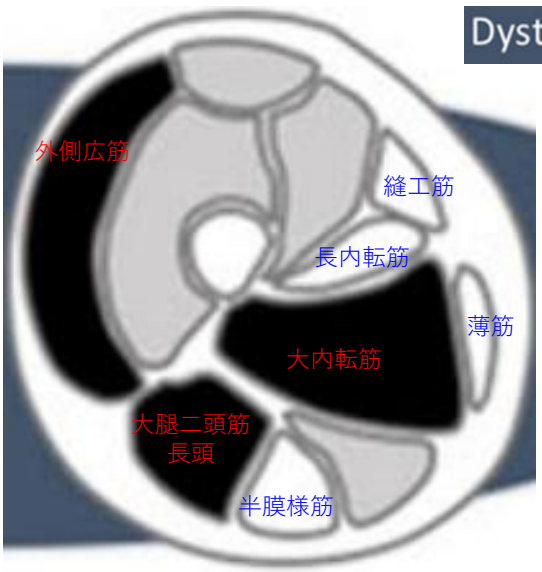
Thighs
- Common: Most anterior & Posterior compartment
- Early: Adductor magnus 大内転筋
- Uncommon: Sartorius, Gracilis, Adductor longus
  - Semimembranosus 縫工筋・薄筋・長内転筋・半膜様筋

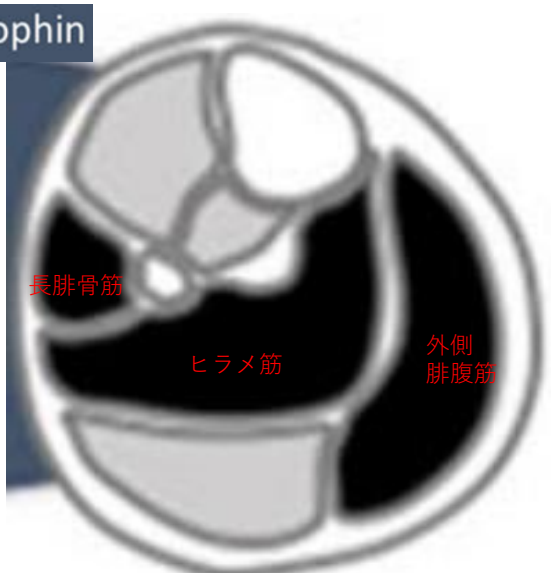
Legs 腓腹筋・ヒラメ筋・長腓骨筋
- Common: Gastrocnemius, Soleus, Peroneus
- Uncommon: Tibialis posterior 後脛骨筋

Distinguishing feature
- Soleus & Obturator externus:
  - Less involved than in Dysferlinopathy

荷重駆動筋が侵されやすい
*大内転筋は股伸展筋
*長内転筋は股屈曲筋

5





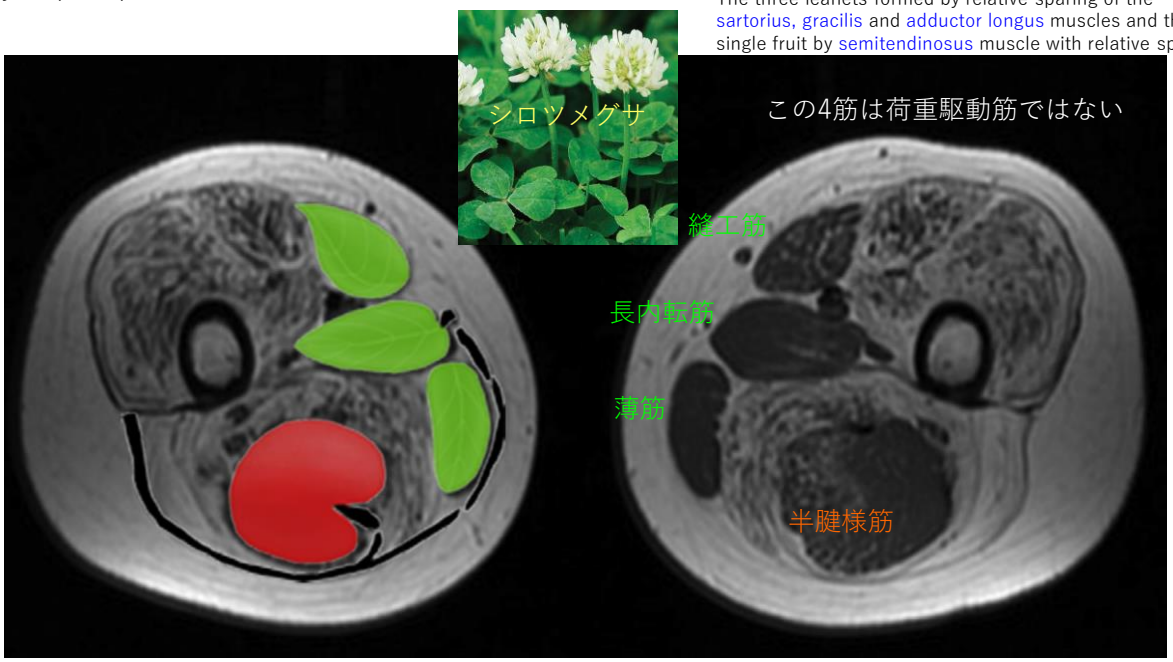
✓ 大内転筋・大腿二頭筋長頭は股関節の伸展筋
✓ 外側広筋が膝伸展負荷が大
✓ 腓腹筋は外側の方が荷重負荷が大
✓ 長腓骨筋は荷重駆動筋

➢ DMDの仮性肥大は、下腿三頭筋・三角筋・棘下筋・前脛骨筋にあり

6

Zheng Y, et al. The trefoil with single fruit sign in muscle magnetic resonance imaging is highly specific for dystrophinopathies. Eur J Radiol 2015;84:1992-8.

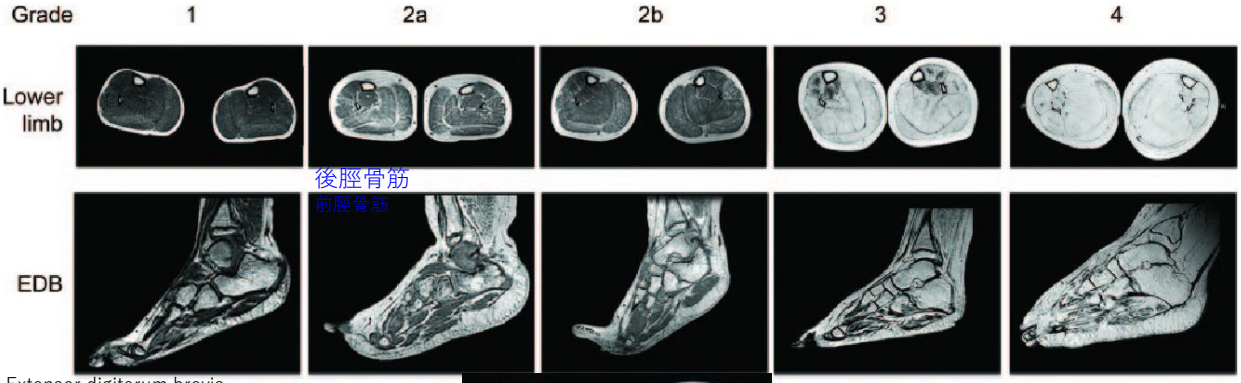
The three leaflets formed by relative sparing of the sartorius, gracilis and adductor longus muscles and the single fruit by semitendinosus muscle with relative sparing.

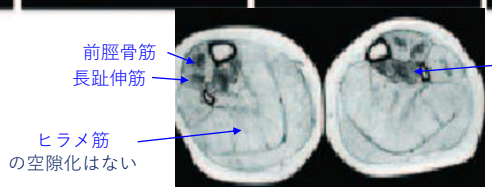


7

Kinali M, et al. Muscle histology vs MRI in Duchenne muscular dystrophy. Neurology 2011;76:346-53.

Stage 0: Normal appearance
Stage 1: Scattered small areas of increased density
Stage 2a: Numerous discrete areas of increased density less than 30% of the volume of the muscle
Stage 2b: Numerous discrete areas of increased density with early confluence, 30%– 60% of the volume of the muscle
Stage 3: Washed-out appearance due to confluent areas in-creased density with muscle still present at the periphery
Stage 4: End-stage appearance, muscle entirely replaced by areas of increased density





✓ 末期の足内反は、後脛骨筋と前脛骨筋による

8

Aivazoglou LU, Guimarães JB, Link TM, Costa MAF, Cardoso FN, de Mattos Lombardi Badia B, Farias IB, de Rezende Pinto WBV, de Souza PVS, Oliveira ASB, de Siqueira Carvalho AA, Aihara AY, da Rocha Corrêa Fernandes A. MR imaging of inherited myopathies: a review and proposal of imaging algorithms. Eur Radiol 2021;31(11):8498-8512.

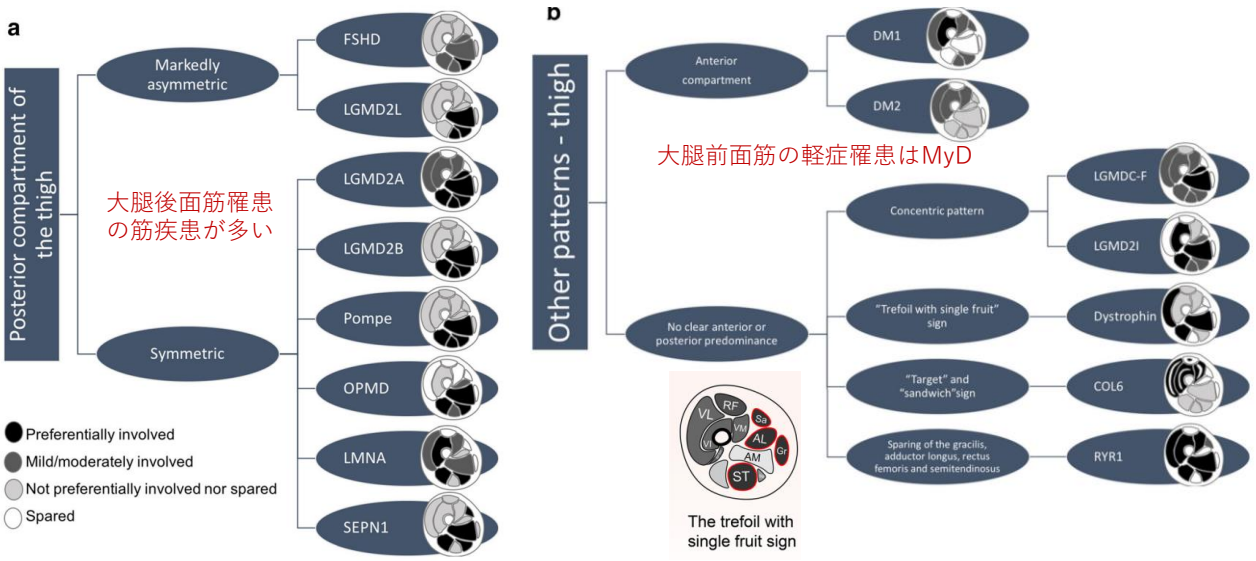


Fig. 3 MRI algorithm for the thighs, with predominant fatty infiltration of the posterior compartment (a) and other patterns (b). Abbreviations: FSHD: facioscapulohumeral dystrophy; LGMD: limb-girdle muscular dystrophy; OPMD: oculopharyngeal muscular dystrophy; LMNA: laminopathies; SEPN1: selenoprotein-related myopathies; DM: myotonic dystrophy; COL6: collagen VI– related disorders; RYR1: ryanodine receptor–related myopathies

9

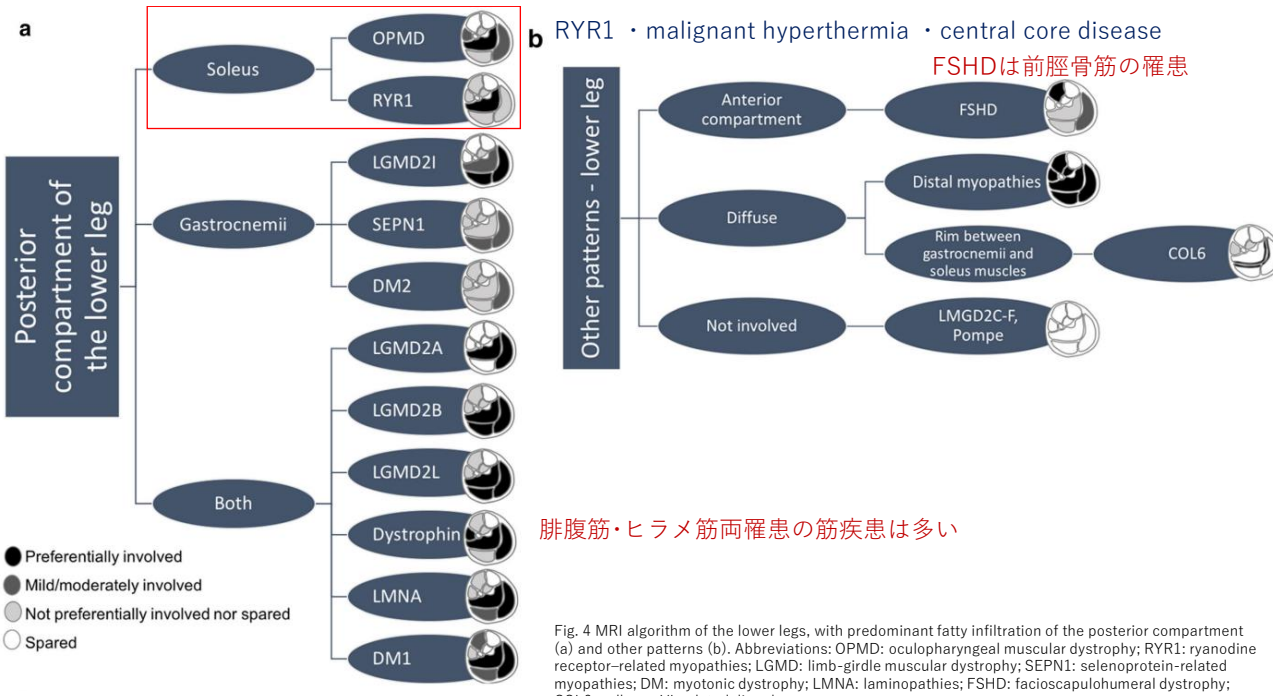


Fig. 4 MRI algorithm of the lower legs, with predominant fatty infiltration of the posterior compartment (a) and other patterns (b). Abbreviations: OPMD: oculopharyngeal muscular dystrophy; RYR1: ryanodine receptor–related myopathies; LGMD: limb-girdle muscular dystrophy; SEPN1: selenoprotein-related myopathies; DM: myotonic dystrophy; LMNA: laminopathies; FSHD: facioscapulohumeral dystrophy; COL6: collagen VI–related disorders

10

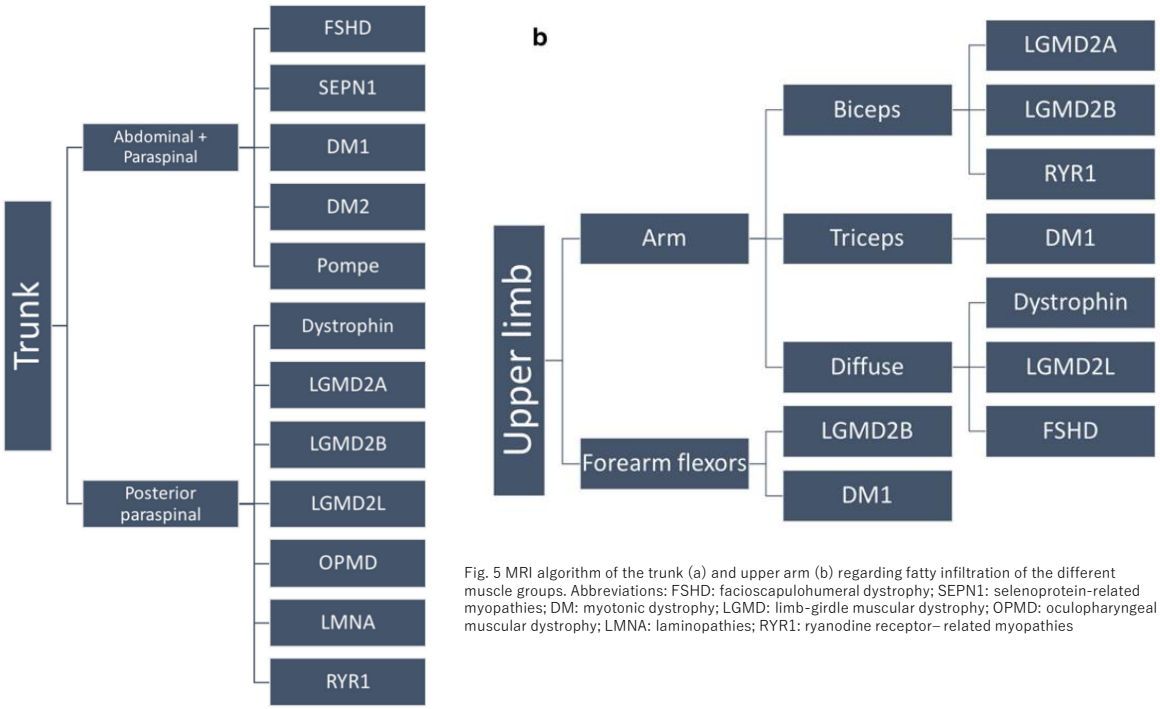


Fig. 5 MRI algorithm of the trunk (a) and upper arm (b) regarding fatty infiltration of the different muscle groups. Abbreviations: FSHD: facioscapulohumeral dystrophy; SEPN1: selenoprotein-related myopathies; DM: myotonic dystrophy; LGMD: limb-girdle muscular dystrophy; OPMD: oculopharyngeal muscular dystrophy; LMNA: laminopathies; RYR1: ryanodine receptor– related myopathies

11

Neuromuscular HP

Sartorius involvement
縫工筋
- ACTA1: NEM3
- BICD2: SMALED2
- CRYAB: MFM2
- Desmin: MFM1
- DYNC1H1: SMA-LED
- FHL1: Reducing Body Myopathy
- LMOD3: NEM10
- MATR3: MPD2
- MYPN: Rod myopathy
- POLG: Distal myopathy
- RYR1: Central core
- SECISBP2: Multisystem Selenoprotein Deficiency
- SEPN1: CMD + Spine rigidity
- TMEM8C: Carey-Fineman-Ziter
- TNPO3: LGMD 1F

Gracilis muscle involvement
薄筋
- Desmin: MFM1
- CRYAB: MFM2
- FHL1: Reducing Body Myopathy
- MYH2: Myopathy, Early-onset with Ophthalmoplegia
- MYPN: Rod myopathy
- POLG: Distal myopathy

Semitendinosus involvement
半腱様筋
- Myopathy involvement
  - ANO5: LGMD 2L
  - BAG3: MFM6
  - CASQ1: VMCQA
  - CRYAB: MFM2
  - Desmin: MFM1
  - DNM2: Centronuclear myopathy
  - ETFDH: Myopathy
  - Titin: HMERF

Aivazoglouらのアルゴリズム

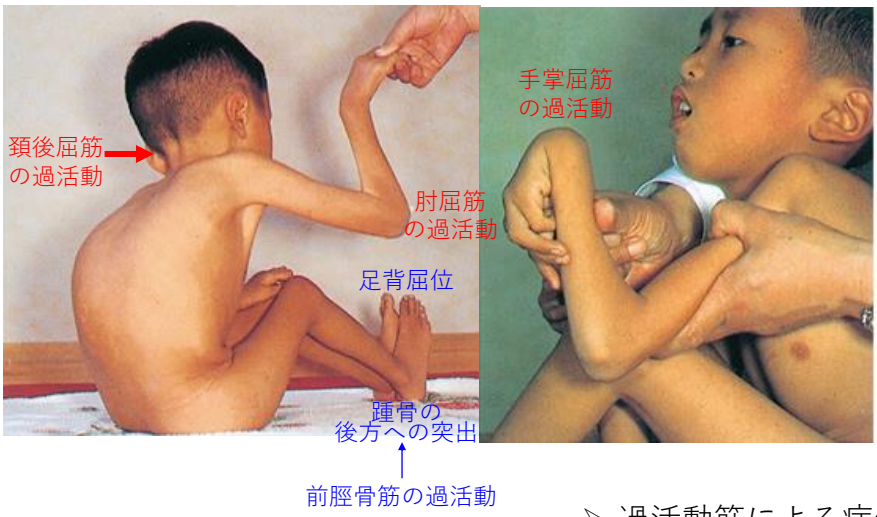
後脛骨筋は侵されにくい筋

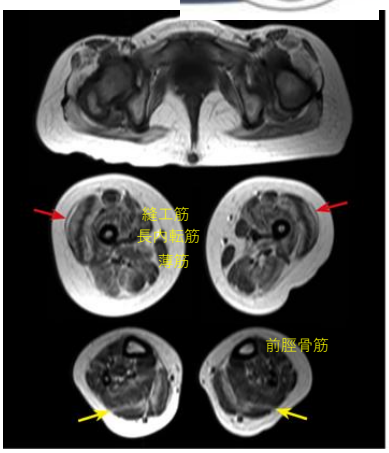
後脛骨筋の罹患
- 強度　distal myopathy　*diffuseに包含*
- 軽度~中等度　なし
- 非優先的か無侵襲　OPMD; RYR1; LGMD21; SEPN1; DM2; LGMD2; Dystrophin; LMNA
- 無侵襲　DM1; LGMD2A; FSHD

12

Ullrich congenital muscular dystrophy (Collagen VI-Related Dystrophies)

生下時より躯幹近位に近い関節拘縮と遠位関節の過伸展



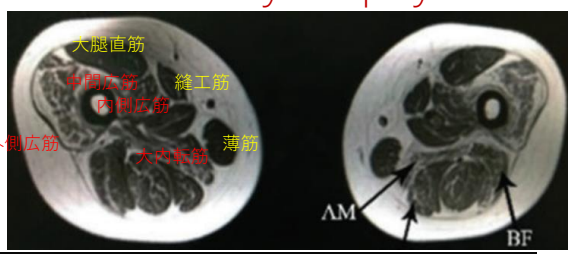


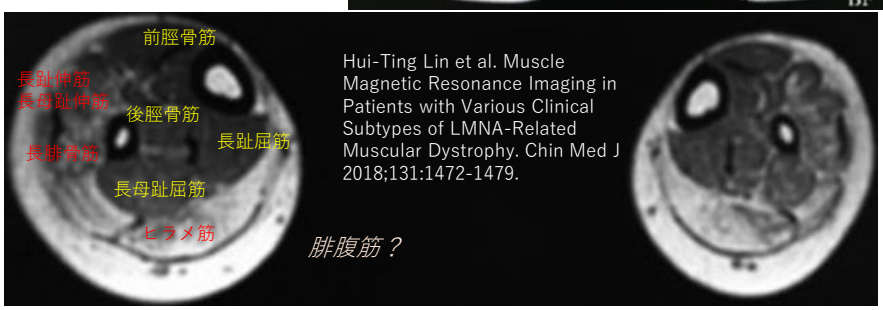
➢ 過活動筋による症候あり

13

Emery-Dreifuss muscular dystrophy

早期発症の足関節拘縮





Hui-Ting Lin et al. Muscle Magnetic Resonance Imaging in Patients with Various Clinical Subtypes of LMNA-Related Muscular Dystrophy. Chin Med J 2018;131:1472-1479.

✓ ヒラメ筋の短縮強靱線維化により、抗重力張力を持つ
✓ バネのようなelastic recoil機能を持つ

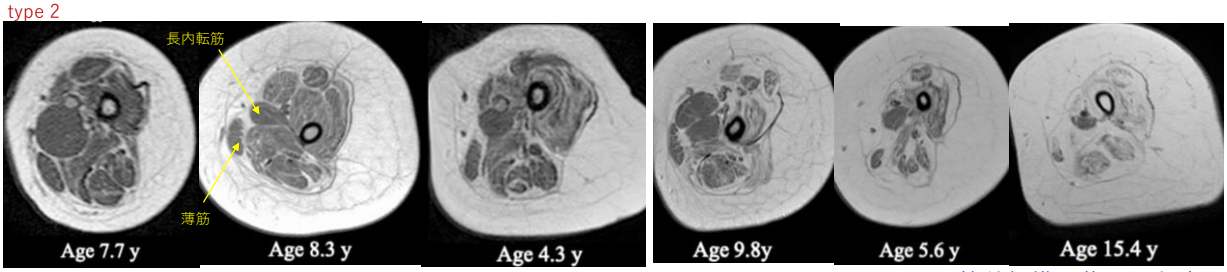
14

Brogna C, et al. MRI patterns of muscle involvement in type 2 and 3 spinal muscular atrophy patients. J Neurol 2020;267:898-912.

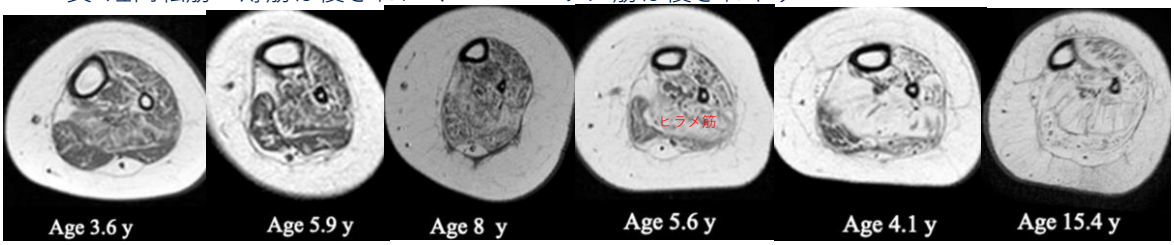
Mercuri classification of fatty infiltration
Stage 0 Normal appearance
Stage 1 Scattered small areas of or increased density by MRI
Stage 2a (2.0) Numerous discrete areas of increased density less than 30% of the volume of the muscle
Stage 2b (2.5) Numerous discrete areas of increased density with beginning confluence, 30–60% of the volume of the muscle
Stage 3 Washed-out appearance due to confluent areas increased density with muscle still present at the periphery
Stage 4 End-stage appearance, muscle replaced by increased density connective tissue and fat

Muscle Groups: atrophy scores
Grade 0: normal muscle
Grade 1: peripheral muscle volume loss
Grade 2: < 50% of muscle volume loss
Grade 3: > 50% of muscle volume loss

type 2

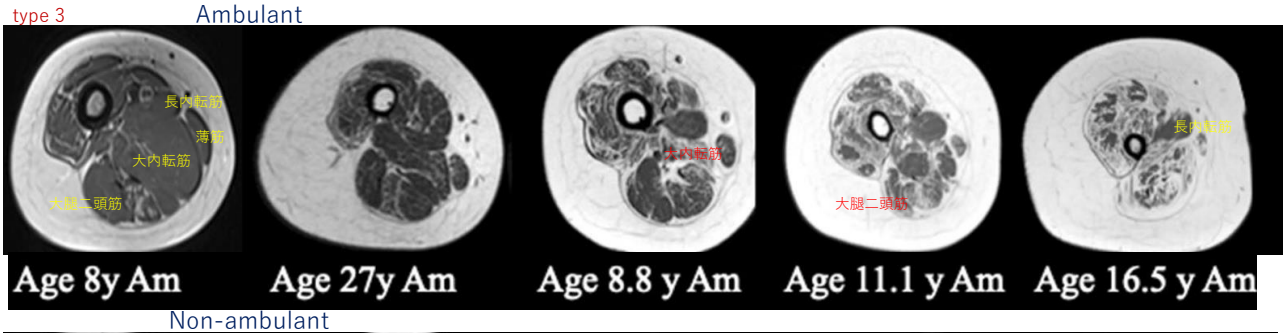


・長･短内転筋・薄筋は侵されにくい ・ヒラメ筋は侵されやすい *筋外組織の著明な脂肪化*

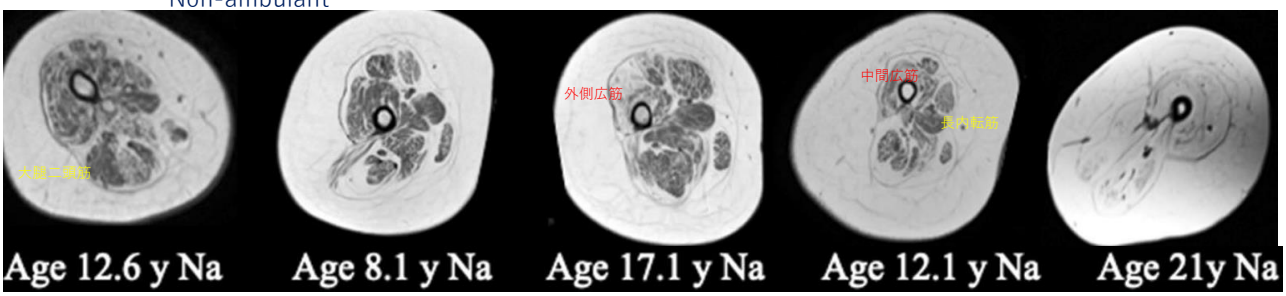


15

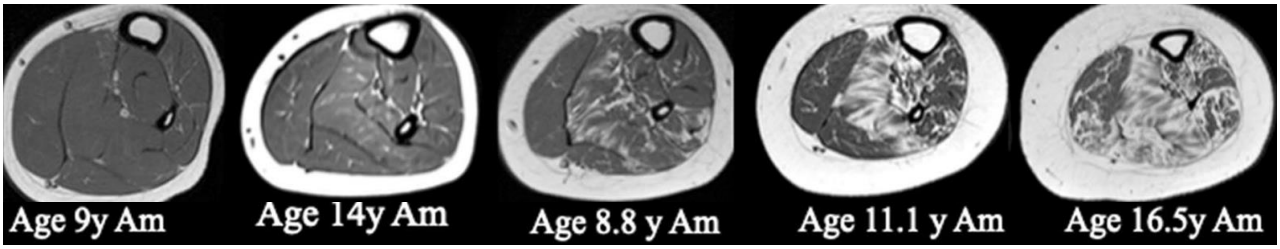
type 3 Ambulant

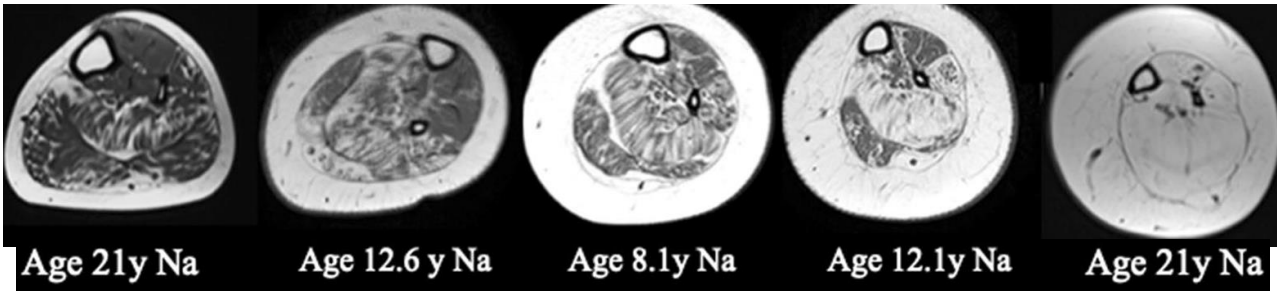


Non-ambulant



16

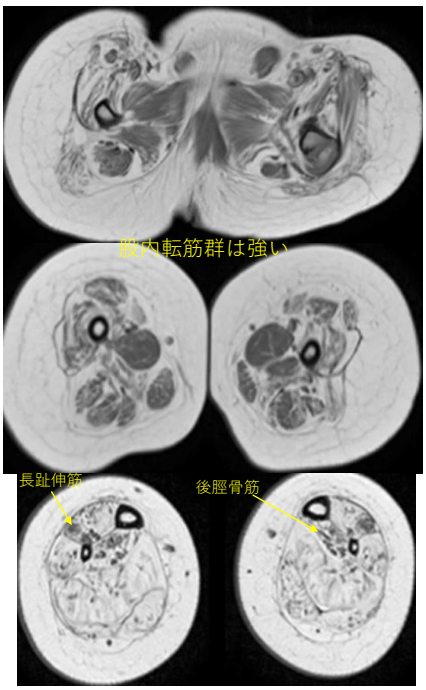




・ヒラメ筋は侵されやすい

✓ ヒラメ筋は筋外と筋内で筋外で空隙化する

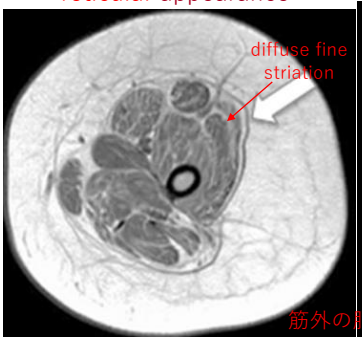
17



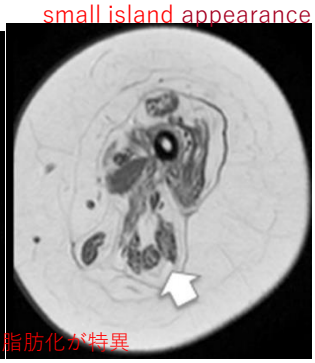
type 2では、近位より遠位の方が脂肪浸潤が強い

18

SMAの
reticular appearance

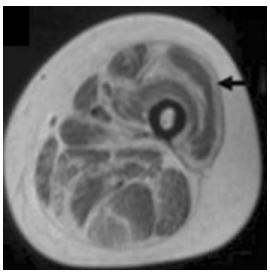


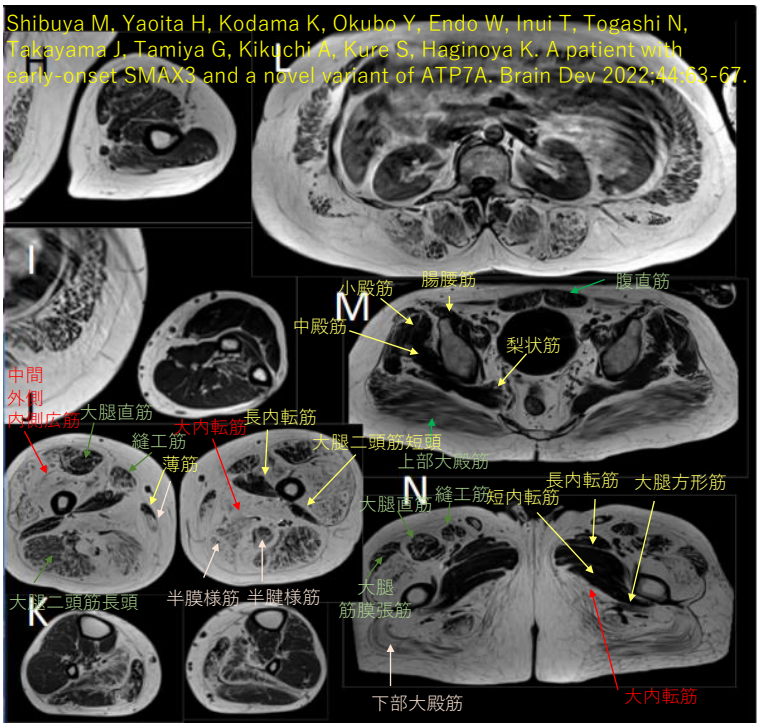
SMAの
small island appearance



DMDの
moth eaten appearance

Bethlem myopathyの
sandwich appearance





侵襲筋と無侵襲筋の二極化

- 非脂肪化筋→*真性肥大*
  - 腸腰筋
  - 中殿筋 ・小殿筋
  - 梨状筋
  - 短内転筋 ・長内転筋
  - 大腿方形筋
  - 大腿二頭筋短頭
  - 薄筋（前部）
  - 下腿前面筋（前脛骨筋・長腓骨筋・後脛骨筋・長趾伸筋）
- 弱脂肪化筋
  - 腹直筋
  - 上部大殿筋
  - 大腿筋膜張筋
  - 大腿直筋
  - 縫工筋
  - 大腿二頭筋長頭
  - 外側腓腹筋
- 中脂肪化筋
  - 下部大殿筋
  - 薄筋（後部）
  - 半膜様筋
  - 半腱様筋
  - 内側腓腹筋
  - ヒラメ筋

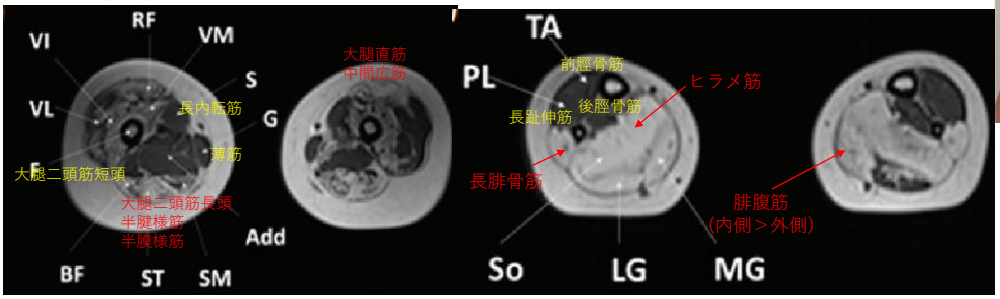
荷重駆動筋が侵されやすい

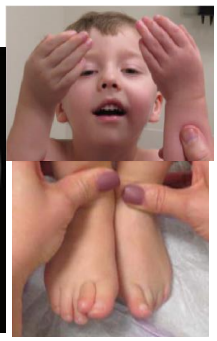
- 強脂肪化筋
  - 大内転筋
  - 内側広筋 ・外側広筋 ・中間広筋

19

Averdunk L, et al. Recognizable Pattern of Arthrogryposis and Congenital Myopathy Caused by the Recurrent TTN Metatranscript-only c.39974-11T > G Splice Variant. Neuropediatrics 2022;53:309-320.

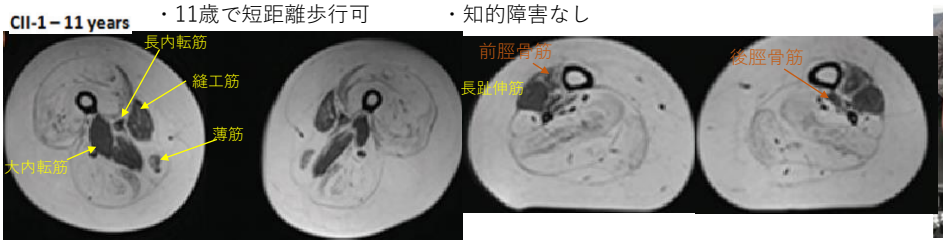
CII-2 – 4 years　・4歳で座位不可　・知的障害なし

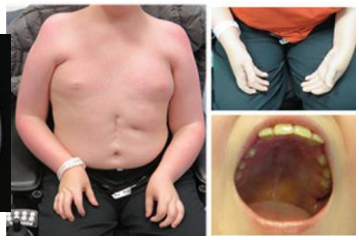




ulnar deviation of wrist, flexion contracture of fingers, elbows, shoulder, knee, abduction of hips, talipes

CII-1 – 11 years　・11歳で短距離歩行可　・知的障害なし

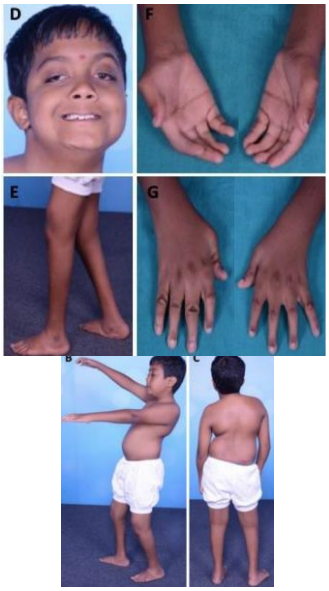




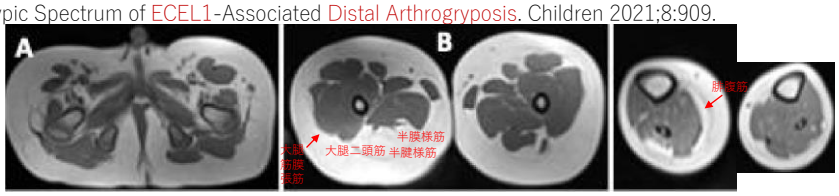
✓股膝屈曲の常時筋収縮状態に対し、股膝伸展の常時筋収縮状態が対抗し、膝屈筋伸筋ともに変性する
✓足背屈の常時筋収縮状態に対し、足底屈の常時筋収縮状態が対抗し、足底屈筋優位に変性する

20

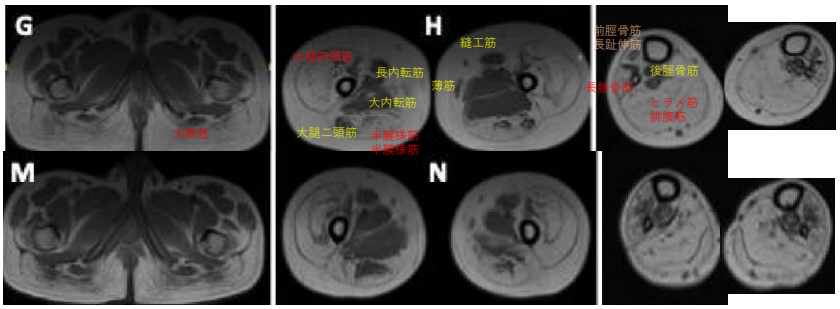
Huddar A, et al. Expanding the Phenotypic Spectrum of ECEL1-Associated Distal Arthrogryposis. Children 2021;8:909.



Patient 1. (B,C) kyphoscoliosis with bilateral hip and knee contracture; (D) asymmetric ptosis; (E) calf atrophy, contracture at the knee, pes planus, prominent calcaneum; (F,G) contractures of fingers with absent abductor pollicis brevis.



Patient 1. midleg reveal volume loss with fatty replacement, most pronounced in bilateral tensor fascia lata (Mercuri Grade 3), right semimembranosus (Grade 3), semitendinosus (Grade 3), bilateral biceps femoris (Grade 2b). Grade 2a fatty replacement is seen in the lateral compartment of the right leg and gastrocnemius.

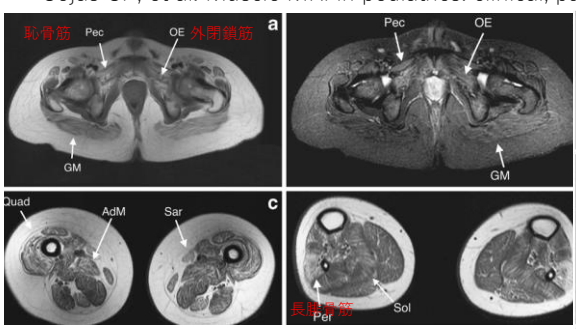


Patient 2 and 3. midleg reveal volume loss with fatty replacement, most pronounced in bilateral gluteus maximus (Mercuri Grade 3), vasti (Grade3), rectus femoris (Grade 2a), semimembranosus (Grade 2b), semitendinosus (Grade 2b), biceps femoris (Grade 2b). Grade 2b fatty replacement is seen in the anterior, lateral, and deep posterior compartments of the legs. The superficial posterior compartment of both legs reveals Grade 4 atrophy with fatty replacement.

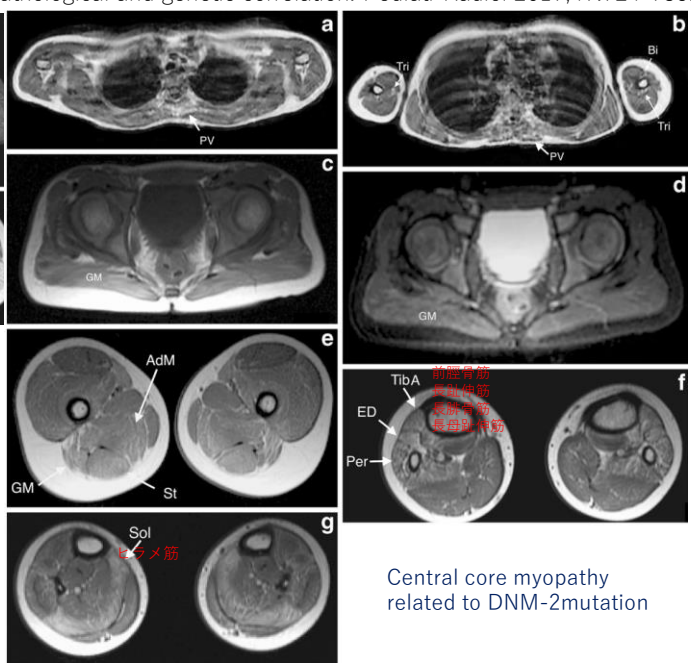
✓ 股膝屈曲の常時筋収縮状態に対し、股膝伸展の常時筋収縮状態が対抗し、膝屈筋伸筋ともに変性する
✓ 足背屈の常時筋収縮状態に対し、足底屈の常時筋収縮状態が対抗し、足底屈筋優位に変性する

21

Cejas CP, et al. Muscle MRI in pediatrics: clinical, pathological and genetic correlation. Pediatr Radiol 2017;47:724-735.



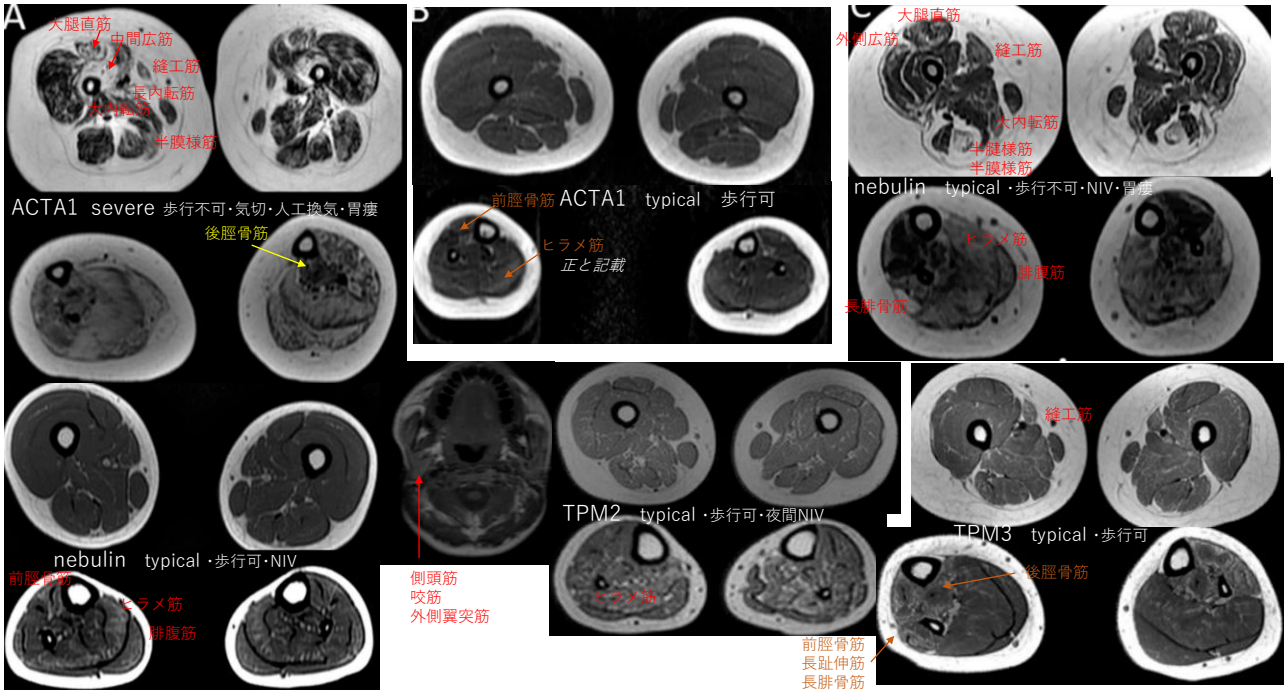
Central core myopathy due to RYR-1 mutation



Central core myopathy related to DNM-2mutation

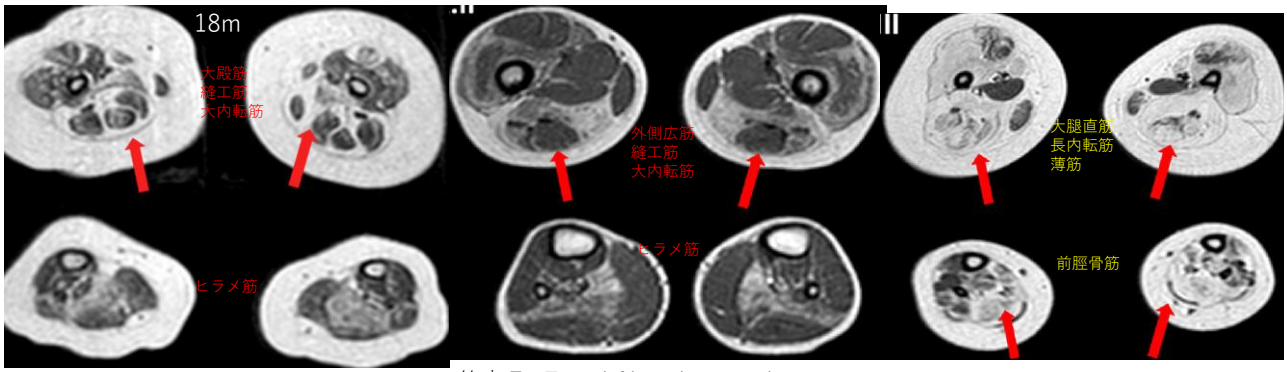
22

Gurgel-Giannetti J1, et al. Nemaline Myopathy in Brazilian Patients: Molecular and Clinical Characterization. Int J Mol Sci 2022;23:11995.



23

Mauri E, et al. Early Findings in Neonatal Cases of RYR1-Related Congenital Myopathies. Front Neurol 2021;12:664618.



筋病理：fiber size variability
3歳で座位
胃瘻・NIV

筋病理：Type 1 fibers hypotrophy,
fiber splitting
7歳で独歩可、発語可、呼吸管理不要

筋病理：Z-line streaming
8歳で独歩不可、胃瘻、呼吸管理不要

24

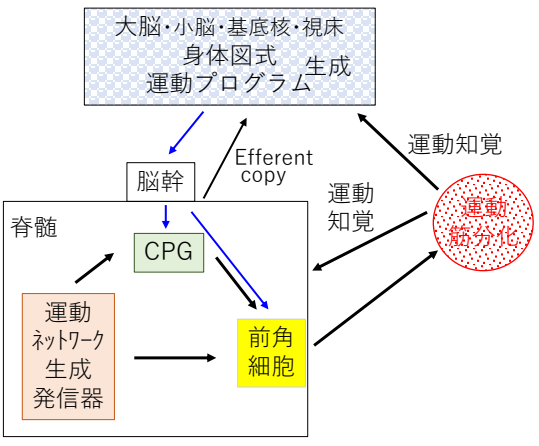
神経筋疾患の罹患筋の分布

- 後天性発症の神経筋疾患では、個別遺伝子変異により侵されやすい特定の筋群が、荷重負荷により変性し、脂肪化・短縮強靱線維化する
  - ✓ *筋力不全線維に興奮性入力が持続し変性する*
- 先天性発症の神経筋疾患(先天性ミオパチー・先天性多発性拘縮症)では、個別遺伝子変異により侵されやすい特定の筋群が、胎児期運動負荷により変性し、短縮強靱線維化する
  - ✓ *胎生期自動運動の発信器は脊髄にある。これと生成途上の大脳性運動ネットワークの運動負荷が加わる*
  - ✓ *胎生期のwrithingでは屈筋優勢である。対抗する伸筋負荷が大であり、伸筋が変性しやすい*
  - ✓ *筋力不全線維に興奮性入力が持続し変性する*

25

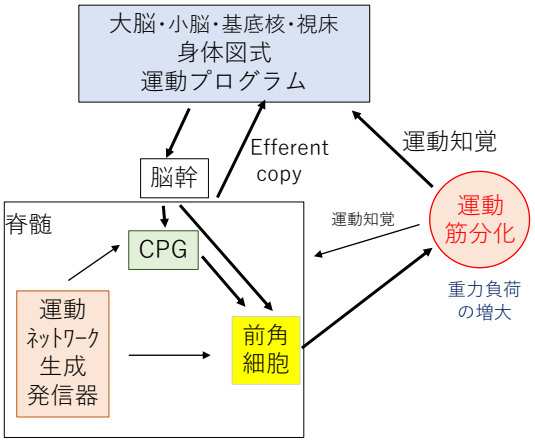
定型発達

胎児運動



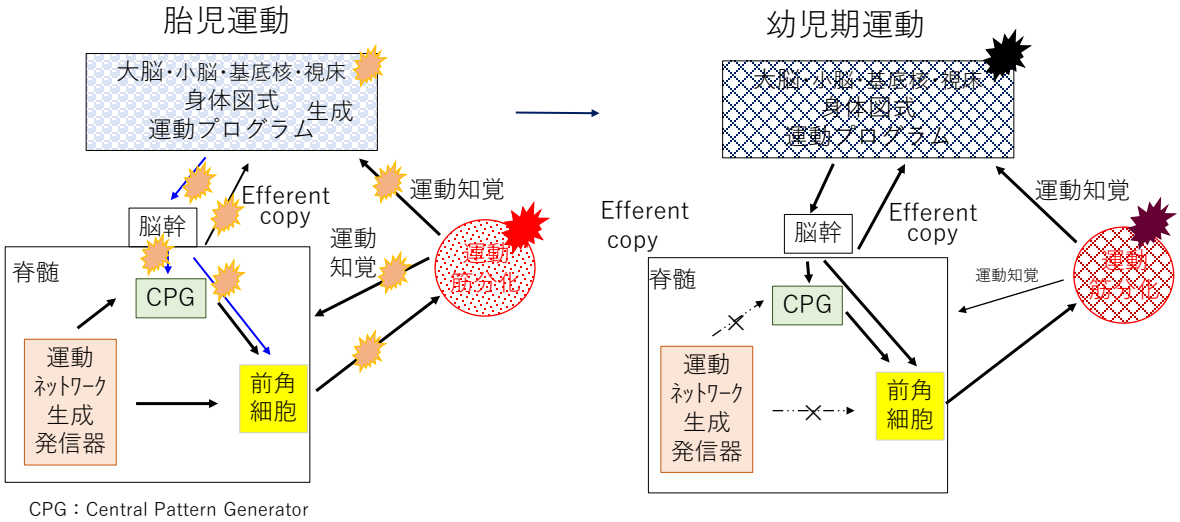
CPG：Central Pattern Generator

新生児~乳児期運動



26

筋機能発現機構に遺伝子変異があると



CPG：Central Pattern Generator

✓ 企図した運動効果を出せない筋線維には興奮入力が持続し、変性に至る
→先天性ミオパチー・多発性関節拘縮症(AMC)

27