

Quantitative skeletal muscle NMR imaging of juvenile dermatomyositis patients

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TARGET AUDIENCE: Researchers and clinicians with interest in neuromuscular diseases and biomarkers for diagnosis and therapy.

PURPOSE. In diagnostic imaging, STIR sequences (with T2-weighted reading) are routinely prescribed to detect inflammatory/lesional/oedematous anomalies in muscles, as in other organs. Caveats about the use of this qualitative approach are:

the detection of inflammation relies on a contrast between altered and unaltered muscle areas. Erroneous interpretation may arise in case of relatively homogenous involvement of all muscle groups;

due to the qualitative nature of STIR T2w sequences, a precise evaluation of disease progression or response to treatment is impossible;

the angiographic effect generated by the STIR module helps to reveal accompanying hypervascularisation but may lead to overestimation of muscle lesions.

These limitations were experienced in a small series of juvenile dermatomyositis patients, for whom qualitative muscle T1w and T2w imaging were inconclusive. For this disease, there are few reliable biomarkers if any. CK level can be strictly normal and decision to resume treatment during weaning off must rely only on clinical features, which can be difficult in the most chronic forms.

These clinical challenges prompted us to investigate whether quantitative T2 mapping performed better and might reveal muscle inflammatory/lesional/oedematous anomalies in juvenile dermatomyositis (JDM).

SUBJECTS AND METHODS. NMR imaging was performed on a 3T Magnetom Trio TIM scanner (Siemens, Erlangen) operating with arrays of surface receiver coils. The following imaging sequences were acquired: a/ whole-body coronal T1w SE; b/ whole-body axial T1w SE; c/ 4 stacks of multi TE SE centered on the limb-girdles, thighs and legs; d/ 3D AFI B1 mapping at the same levels as the multi TE SE. Total examination time was approximately 1h. Because muscle fatty infiltration were absent on T1w, STIR modules were unnecessary and T2w images were selected from the multi TE SE. The T2 maps were generated using the multi-exponential fitting and B1-based voxel sorting developed in our lab (1). Threshold for abnormality was 39ms.

Three cases of chronic or sub-chronic juvenile dermatomyositis, as confirmed by muscular pathology, were investigated before and between three and ten months after steroid treatment. Pediatric reference values were obtained in 6- and 8-yr old patients, with no muscle symptoms.

RESULTS:

CASE 1: This 7-year-old Algerian girl presented with proximal weakness, muscle wasting and weight loss. She was unable to stand from the floor and to climb stairs without help. Symptoms were present since the age of 4. The parents noticed also recurrent fevers without explanation. CK was reported slightly elevated at the age of 5 but was normal at examination. There was no skin rash. The child presented with elbows and shoulders contracture. Muscle biopsy demonstrated JDM histologically. Pre- θ T1w images were normal. No focal hyperintensity was seen on the T2w images, which appeared discretely heterogeneous. By contrast, the T2 mapping revealed that most muscles were inflamed (red ROIs, with T2s between 41 and 50ms).

CASE 2: This 12-year old Belgian boy presented with proximal and distal weakness, weight loss and fatigue. Despite he had been a good performer at sport, he became progressively unable to follow his pairs during competition and later during daily activity. He used the Gowers manoeuvre to stand from the floor. There was no skin rash, no contracture. CK were normal. Muscle pathology confirmed JDM. IV methylprednisolone followed by oral prednisolone and methotrexate allowed a complete functional recovery after 4 months.

Pre- θ T2w images showed a somewhat heterogeneous muscle texture, that might or not be rated abnormal. T2 maps revealed that most muscles were inflamed (red ROIs).

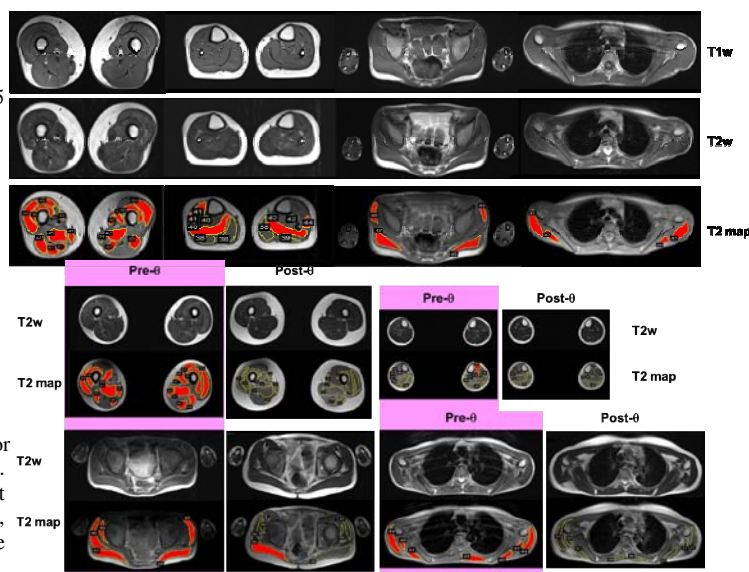
Legs															
	PER_D	ED_D	TA_D	TP_D	SOL_D	IS_MED_D	G_LAT_D	PER_G	ED_G	TA_G	TP_G	SOL_G	IS_MED_G	G_LAT_G	
Pre- θ	36	33	33	34	35	35	34	38	33	-	37	36	34	35	
3months θ	36	34	35	35	35	33	32	37	37	37	34	35			

Right Thigh															
	VL_D	RF_D	VM_D	VI_D	SAR_D	GRA_D	SM_D	ST_D	RF_G	AL_G	AM_G				
Pre- θ	50	45	47	50	40	42	47	48	50	43	45				
3months θ	36	34	35	35	33	32	37	37	37	34	35				

Left Thigh															
	VL_G	RF_G	VM_G	VI_G	SAR_G	GRA_G	SM_G	ST_G	RF_D	AL_D	AM_D				
Pre- θ	50	45	47	50	40	42	47	48	50	43	45				
3months θ	36	34	35	35	33	32	37	37	37	34	35				

Pelvic Girdle															
	ER_D	GM_D	GMX_D	PS_D	ER_G	GMX_G	GMX_G	PS_G							
Pre- θ	-	46	48	50	45	47	39	47							
3months θ	36	36	39	37	37	36	36	37							

Scapular Girdle															
	BB_D	BR_D	DLT_D	ER_D	ISP_D	SBSC_D	TR_D	BB_G	BR_G	DLT_G	ER_G	ISP_G	SBSC_G	TR_G	
Pre- θ	32	37	34	37	36	36	37	-	38	37	35	34	35	38	
3months θ	32	37	34	37	36	36	37	-	38	37	35	34	35	38	



Steroid treatment normalized T2s, as evident on the quantitative evaluation.

CASE 3: This 7-year-old Belgian girl presented with muscle pain for 6 months, associated with fatigue during long walk. There was no weight loss. CK level was 1.5 normal range. A mild eruption appeared after 7 months of evolution on the dorsal face of the fingers. Examination revealed mild proximal weakness and hips contracture. Muscle biopsy demonstrated JDM. Corticoids and methotrexate allowed a complete functional recovery after 6 months.

The table with T2 values to the left show the regression of the inflammatory lesions, as evaluated quantitatively muscle by muscle, after steroid therapy was initiated. T2s are in ms; abnormal values are highlighted in red.

DISCUSSION AND CONCLUSION.

- Routine diagnostic imaging approaches may fail to detect muscle inflammatory changes, as illustrated here in 3 juvenile dermatomyositis patients.
- While qualitative imaging was negative, quantitative T2 mapping unambiguously revealed the existence of inflammatory/lesional changes in these patients.
- Quantitative T2 mapping allowed a precise monitoring of muscle response to steroid therapy. Similarly, it may help in making the decision of initiating or resuming treatment.
- This is our first report of successful implementation of T2 mapping to limb-girdle investigation. This will considerably expand the field of application of quantitative imaging.
- Quantitative NMR imaging has a major role to play not only in clinical trials but also for diagnostic purposes and for individual therapeutic adjustments.

REFERENCE.

1. Carlier PG et al, Neuromuscul Disord 2012, 22, 807.