ASMFA ADVANCES IN SKELETAL MUSCLE FUNCTION ASSESSMENT

VOLUNTARY CONTRACTILE RATE OF TORQUE DEVELOPMENT IN HEALTHY 50-70 YEAR OLD WOMEN: MEASUREMENT OF, ASSOCIATION WITH FUNCTIONAL TASKS AND RESPONSE TO AN INTERVENTION.

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KEY WORDS:

Speed of contraction;
Muscle function;
Torque;
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ABSTRACT

This study aimed to measure contractile rate of torque development (RTD) from maximal voluntary isometric contractions (MVC) of the knee extensors and flexors in order to determine reliability of the measure, report age-related difference in RTD, determine the association between RTD and selected functional tasks and determine the effect of progressive resistance training (PRT) on RTD in healthy 50-70y women. 136 women performed MVC's of the knee extensors and flexors. Maximal RTD was determined from the slope of the most linear phase of the torque-time trace. RTD was also determined at 0-50 ms; 0-100 ms and 0-200 ms from the onset of contraction in a subsample (n=26) of knee extensor MVC's. Functional capability was determined based on the ability to complete a 900 m gait speed test (n=128) and the number of chair rises completed in 30 seconds (n=68). 57 participants were randomised into a protein supplementation (PRO) control group or a PRO + PRT group for 12 weeks. Maximal RTD had a coefficient of variance of ≤ 17%. RTD became more dependent on maximal strength as the time from the onset of contraction increased as did its association with maximal RTD. On average, participants in the 7th decade of life had a lower (~23%; $P<0.01$) RTD than their younger counterparts in the 6th decade. RTD had a weak association with extended gait speed (r=-0.234; $P=0.008$) and was not associated with chair rise performance (r=0.076; $P=0.540$). RTD did not change in response to 12 weeks of PRT and PRO compared to a PRO only group (+9% *vs.* +13%; $P>0.05$). Maximal RTD cannot be measured reliably in healthy 50-70 year old women from the most linear slope of the torque-time trace of an isometric MVC. Age-related difference in maximal RTD appears to be greater than that of maximal strength. Maximal RTD has a weak association with functional capability and does not change in response to PRT in healthy 50-70 year old women.

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INTRODUCTION

Epidemiological studies on ageing have routinely collected data on lower extremity muscle or lean tissue mass (LTM) and maximal voluntary strength **[1-3]**. These laboratory assessed components of muscle health are thought to be central to the diagnosis of sarcopenia and associated functional disability **[4]**. However, the age-associated decline in the speed of muscle contraction has been reported to be greater than that of muscle strength **[5-8]** particularly in women **[9,10]**. Therefore, measurement of the speed of muscle contraction may provide a more sensitive measure of physiological changes in muscle prior to disability. Moreover, the ability to perform functional tasks depend on both torque production and the speed of contraction **[11]**. In fact, Sayers and colleagues **[12]** reported leg muscle contraction velocity but not muscle strength to be associated with gait speed in community dwelling older women (75 – 90y).

The challenge in reporting age-related difference in the speed of muscle contraction and its association with functional capability is the ability to measure it. To date, the ability to rapidly generate muscular force has been measured using mixed methodologies and as of yet there is no criterion method. Studies have measured rate of force development (RFD) **[13,14]**, power **[6]** or compared age-related changes in slow (0°/s - 60° /s) and fast (>60° /s) isokinetic strength measurements. As such, there is no criterion reference range from which change due to ageing or intervention can be evaluated.

Contractile rate of force development (RFD) is a term used to describe the rate at which an individual can rapidly generate muscular force. The work of Andersen and Aagaard **[13,14]** has confirmed that in vivo contractile RFD can be measured in young adults from the slope of the torque-time curve obtained during isometric conditions. The potential to measure maximal voluntary strength and simultaneously obtain a measure of the intrinsic contractile ability of muscle is attractive in research with older adults. Isometric contractions are easy to administer, require less habituation than isokinetic measures and are time efficient for generating information on large data sets across age ranges **[15]**.

The University of Limerick Healthy Ageing Study **[3,16,17]**, measured peak isometric torque from MVC's of the knee extensors and flexors in healthy older adults. The purpose of these contractions was a) to report age-related difference in maximal voluntary strength and muscle quality between the 6th and 7th decade of life; b) to determine the association between lower extremity maximal voluntary strength and selected functional tasks and c) to act as a baseline measure of maximal voluntary strength prior to dietary and/or exercise interventions. This investigation reports the contractile rate of force development based on secondary analysis of these isometric contractions.

To the best of the author's knowledge it is not yet known whether contractile rate of torque development (RTD) can be measured reliably from the most linear phase of a torque-time trace generated from a MVC in healthy older women. Furthermore, it is unclear whether voluntary RTD follows the same trajectory at 0-50ms, 0-100ms and 200ms as that reported previously in young adults **[12]**. Therefore, the aims of this research were to: a) determine reliability of the measure b) report age-related difference in RTD c) determine the association between RTD and selected functional tasks and d) determine the effect of PRT on RTD in a convenience sample of healthy 50 -70 year old women.

MATERIALS AND METHODS

136 healthy women (age range: 50 -70y) were recruited as part of the University of Limerick Healthy Ageing Study **[3,16,17]**. Participants were screened by a physician and provided a full medical history. Those defined as healthy, i.e. disease free based on Greig et al. **[18]**, independent-living, fully mobile and with no indication of dairy or lactose intolerance were invited to participate and to provide written informed consent. Height was measured to the nearest 0.1cm (SECA stadiometer) and body mass (BM) was measured to the nearest 0.1kg (MC-180MA; Tanita UK Ltd.). 136 women performed MVC's of the knee extensor and flexor muscle groups. 128 and 68 participants completed a 900 m gait speed test and a 30 second chair rise test respectively. 57 of the participants were randomised into a control group (n=28; protein supplementation (PRO) only) or a progressive resistance training (PRT) + PRO group (n=29). All procedures were performed in accordance with the most recent version of the Declaration of Helsinki. The University of Limerick Healthy Ageing Study was approved by the Research Ethics Committee of the Faculty of Education and Health Sciences Research Ethics Committee (EHSREC 10/45). The trial was registered at clinicaltrials.gov as NCT02529124.

ASSESSMENT OF A MAXIMAL VOLUNTARY CONTRACTION

Procedures for the assessment of a MVC have been reported in detail in our recently published manuscript **[2]**. Briefly, participants were tested during two identical sessions held 7 days apart in order to reduce potential learning effects. Warm up consisted of 5 min on a bicycle ergometer (Monark Ergomedic; 828E, Monark Exercise AB, Vansbro, Sweden) at a workload of 40 watts. The knee extensors and flexors of the dominant limb (the limb used to kick a ball) were tested using a commercially available dynamometer (Con-Trex MJ; CMV AG, Dubendorf, Switzerland) which allows instantaneous isometric torque assessment. Participants were seated with a hip flexion angle of 110°. The back of the knee joint was on the edge of the seat with a knee angle of 60° from anatomical zero (180°), which has been demonstrated to be the angle of maximal isometric force generation **[19]**. Participants were instructed to perform two submaximal voluntary isometric contractions (50% and 75% of perceived maximum) prior to each test series similar to Maffiuletti et al. **[20]** interspersed with a 1-min rest period. The participant then performed 3 MVC's separated by 2 min of stationary rest. All measures were repeated separated by seven days in order to reduce potential learning effects.

Criteria for Acceptance of a Maximal Voluntary Contraction

A MVC produced a measure of isometric peak torque in a single effort which required >200 ms and was sustained for

~250 ms. Attempts not sustained for MVC (identified by an impact spike prior to 300 ms), containing an initial counter-movement (identified by a visible drop/rise in the torque signal) >5N·m or with a nonlinear time-torque trace (identified by a double movement) were disqualified and excluded from further analysis.

ANALYSIS OF CONTRACTILE RATE OF TORQUE DEVELOPMENT

RTD form the Linear Phase of the Torque-Time Trace

Data was exported to Microsoft Excel and the torque-time trace smoothed with a 0.1s moving average to minimise any false traces due to noise **[7]**. As the Con-Trex MJ dynamometer samples at a rate of 256 Hz, it provides data on torque every 0.003906 seconds. This allows the user to create a time column in seconds for every data point. The first MVC occurs ~150 seconds into data recording. A selection of ~100 torque-time data points are selected from just before the onset of contraction to just after MVC. Using the line function in Microsoft Excel, the most linear slope of the line was identified **(Figure 1)**. These points are then used to calculate the slope of the line i.e. the RTD.

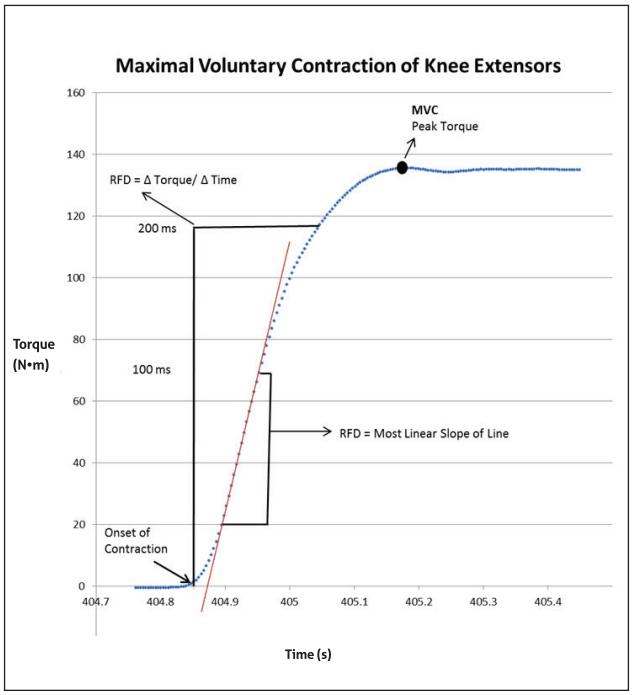

Figure 1: Analysis of RTD from a maximum voluntary contraction of the knee extensors

RTD at Different Time Points

26 contractions of the knee extensors underwent analysis of RTD at 3 different time points after the onset of contraction (0-50 ms; 0 – 100 ms; 0 – 200 ms). Five seconds prior to the onset of muscle contraction was identified. The difference between adjacent data points in the lead up to the onset of contraction were identified in a separate column. The average of the difference between adjacent points was calculated and multiplied by 5 to obtain the point at which torque rises 5 times above baseline. From the identified baseline the slope of the torque-time curve (i.e. Δtorque/Δtime) was calculated from the first 13 data points (i.e. 0-50ms), 26 data points (0-100 ms) and 52 data points (0-200 ms).

Functional Tasks

The ability to rise from a chair was assessed by counting the number of chair rises completed in 30 seconds **[21]**. Maximal extended gait speed (n=128), using a one or a combination of walking, jogging or running, was assessed by the time taken to complete 900 m (4 laps of a 225 m indoor track) **[16,17]**. All measures were repeated separated by 7 days in order to reduce the potential for a learning effect. All measurements were conducted by the same exercise scientist to exclude issues with inter-tester reliability.

Dietary Protein Supplementation and Progressive Resistance Training

Assessment of habitual dietary protein intake and dietary protein supplementation has been described in detail in our recently published manuscript **[22]**. Briefly, dietary analysis and regulation of supplement intake was undertaken by a registered dietician. Participants had habitual dietary intake assessed using a 4-day food diary encompassing two week days and two weekend days. Food intake data were coded and subsequently analysed using WISP© (Tinuviel Software, Anglesey, UK). Participants were instructed to take a supplement at their two smaller protein containing meals of the day i.e. typically breakfast and lunch. Sachets were provided in powder format and could be mixed with water to make-up a powdered beverage or incorporated into meals. Supplements were prescribed relative to the median 4 levels of participants' body mass (BM) i.e. 45-59.9 kg, median of 52.5 kg; 60-74.9 kg, median of 67.5 kg; 75-89.9 kg, median of 82.5 kg and 90-105 kg, median of 97.5 kg). Each supplement dose provided 0.165 g protein ·kg-1 BW·d-1 of median BM.

Supervised (qualified sport and exercise scientist or chartered physiotherapist) PRT was performed on three non-consecutive days of week at a University sports hall. Each session lasted 45-60 minutes and consisted of a warm up, PRT and a cool down. Participants were provided with equipment (aerobics step and therabands) and while they had the option of performing a maximum of two of the sessions at home, most preferred to attend. The first three weeks of the programme had an emphasis on ensuring the correct exercise technique and monitoring the appropriate amount of exercise and rest intervals for each individual. Between weeks 3 and 12, the programme was designed to promote muscle hypertrophy (4-6 sets, 8-15 repetitions) as recommended by Bird et al. **[23]**. The PRT programme consisted of a number of upper and lower body exercises using therabands (T) and body weight (BW) as the primary resistance. The primary exercises used throughout the program included squats (T), lunges (T), hip abduction (T), shoulder press (T), latissimus dorsi pull-down (or seated row) (T), bicep curls (T), calf raises (BW), push ups (BW), tricep dips (BW) and lumbopelvic stabilisation exercises.

STATISTICAL ANALYSIS

For parameters of muscle function, within and between participant reliability was calculated using the coefficient of variance (CV) and intra-class correlation (ICC) respectively. Data were checked for normality of distribution by using the Komolgrov-Smirnov and Shapiro-Wilk tests and expressed as means ± SDs (95% CI) for normally distributed variables and medians (IQRs) (Q1-Q3) for non-normally distributed variables. Linear regression was used to determine the variance in RTD explained by peak torque and the variance in the linear phase of RTD explained by RTD at different time points. An independent samples t-test was used to report age-related difference in voluntary RTD. Pearson's r was used to report the association between linear phase RTD and performance in functional tasks. The treatment effect was calculated as the change in outcome measure from baseline to 12 week and presented as mean change and relative percentage change. These data were analysed by univariate ANOVA with treatment (PRO compared with PRO + PRT) as a fixed factor. To determine the influence of baseline RTD on the changes seen at 12 week, data were analysed by ANCOVA with group as a fixed factor and baseline RTD as the covariate. Baseline dietary intake and compliance to the dietary protein supplement were also used as co-variates to determine their effects on changes in RTD. Statistical analysis was performed by using PASW Statistics 22.0 for Windows (IBM SPSS, Inc.). Significance (2-tailed) was set at $P < 0.05$ for all analyses.

RESULTS

Physical characteristics for participants are displayed in **Table 1**. Reliability of estimate for peak torque measured from a MVC was excellent. Measurement of contractile RTD from the most linear slope of the torque-time trace could not be measured reliably nor could time to peak torque (TTPT) **(Table 2)**. Normalised for body mass, maximal knee extensor strength explained ~38% of the variance in maximal voluntary RTD. Peak isometric torque of the knee extensors was associated with voluntary RTD at time points ≥100 ms after the onset of contraction. The association between maximal RTD and RTD at different time points became stronger as time increased from the onset of contraction **(Table 3)**. Age-related differences are reported from participants who produced repeated measures of maximal knee extensor RTD (n=97) and knee flexor RTD (n=105) within a coefficient of variance of 10% or who had a single maximum RTD identified. In this sample the coefficient of variance improved to 4% for the knee extensors and flexors and the intra-class correlation coefficient improved to 0.990 and 0.986 respectively. On average, those in the 7th decade demonstrated a reduction in RTD in both the knee extensors and flexors ($P \leq 0.01$; **Table 4**). Maximal knee extensor RTD had a weak association with extended gait speed (r=-0.234; P=0.008) and no association with the number of chair rises completed in 30 seconds (r=0.076; P=0.540). Maximal knee extensor RTD did not change in response to 12 weeks of PRT **(Table 5)**.

Table 1. Physical characteristics of the participants (female; healthy; age range 50-70 years)

Age (years)	60.2 ± 5.2
Height (cm)	162.1 ± 5.5
Body mass (kg)	70.2 ± 12.9
BMI kg/m2	26.8 ± 5.0

Table 2. Reliability of estimate for torque and rate of torque development (RTD).

	Mean ± SD	CV (%)	ICC
Knee Extensor Torque (N•m)	84 ± 24	3	1.000
Knee Flexor Torque (N•m)	45 ± 12	3	0.993
Knee Extensor RTD (N•m s-1)	422 ± 187	17	0.840
Knee Flexor RTD (N•m s-1)	258 ± 104	14	0.768
Knee Extensor Time to Peak (s)	0.94 ± 0.47	25	0.067
Knee Flexor Time to Peak (s)	0.88 ± 0.51	24	0.083

Table 3. The association between RTD at different time points, peak torque and the linear phase of the torque time curve (n=26). *= statistical significance.

	Mean ± SD	Peak Torque (N•m)	RTD Linear Phase
		r2 (p-value)	r2 (p-value)
Knee Extensor RTD 0 – 50 (N•m•s-1)	263 ± 146	0.002 (0.848)	0.289 (0.006)*
Knee Extensor RTD 0 – 100 (N•m•s-1)	398 ± 168	0.221 (0.018)*	0.585 (<0.001)*
Knee Extensor RTD 0 – 200 (N•m s-1)	390 ± 150	0.701 (<0.001)*	0.627 (<0.001)*

Table 4. Age-related difference in RTD for healthy older women.

	50 – 59y	60 – 70y	Δ	Δ%
Knee Extensor RTD (N•m•s-1) 95% CI	516 ± 188	369 ± 198	147±32; P<0.001 84 - 211	28
Knee Flexor RTD (N•m•s-1) 95% CI	273 ± 103	226 ± 105	47 ± 18; P=0.010 11 - 82	17

Table 5. RTD changes in response to 12 weeks of PRO and PRO +PRT.

	Baseline (Nm s-1)	Δ (Nm s-1)	Δ %
	PRO (n=28)		
Knee Extensor RFD 95% CI	421 (329)	21 ± 148 -36 - 78	13 ± 40 -2 - 28
	PRO + PRT (n=29)		
Knee Extensor RFD 95% CI or Q1-Q3	442 ± 199	64 ± 120 19 - 110	9 (42) -9.6 - 41

DISCUSSION

The first significant finding from this study was that maximal RTD as measured from the linear phase of the torque-time trace of an isometric MVC demonstrated poor within-participant reliability in healthy older women. RTD increased with time from the onset of contraction (0-200 ms) and became increasingly more dependent on maximal strength as the time from contraction increased. Maximal RTD was associated with RTD at all time points (0-50ms; 0-100ms; 0-200ms) and this association increased as the time from onset of contraction increased. Normalised to body mass, knee extensor torque explained 38% of the variance in maximal RTD **(Figure 2)**. On average, those in the 7th decade of life had lower (~23%) RTD compared to their younger counterparts in the 6th decade. Maximal knee extensor RTD had a weak association with extended gait speed and was not associated with chair rise performance. Maximal RTD did not change in response to PRT and PRO supplementation.

The variability in the measurement of contractile RTD from MVC's in which peak torque can be measured within an error of 3% is interesting. To explain whether the variance is arising from age-related difference in motor output variability or the method for determining RTD is challenging. It has been reported that older adults exhibit greater motor output variability **[24-26]**. Jakobi and Rice **[26]** reported no difference in central activation between younger and older adults when compared to their single best trial, however, when central activation was compared over 10 trials, a dramatic age-difference was observed (79 *vs.* 95% activation). Compared to young men who had knee extensor voluntary RFD assessed 200 ms after the onset of contraction **[13]**, there is greater variability around the mean in our sample of older women (842 ± 224 $N{\cdot}m{\cdot}^{s-1}$ *vs.* 422 ± 187 $N{\cdot}m^{s-1}$). The variability between groups is less in the assessment of MVC (211 ± 49 N·m *vs.* 84 ± 24 N·m). This would be consistent with a hypothesis that older adults are capable of maximal muscle recruitment which is reproducible but the speed of muscle contraction is more variable. In addition to an increase in older adult motor output variability, it should be acknowledged that the method for determining maximal RTD from an isometric contraction does require the subjective positioning of a line through the most linear phase of the torque-time trace which may also contribute to the variability of the measurement. We determined RTD at different time points from a sample (n=26) of knee extensor contractions in order to be able to make some comparisons with the data of Andersen and Aagaard **[13]**. This process involves using a standardised criteria to determine the onset of contraction before assessing Δ torque / Δ time i.e. RTD at specified time points. This procedure removes the subjective positioning of a line through the most linear phase and may provide pertinent physiological insights into muscle contraction at different time points. At present the reliability of these measures determined from a maximal voluntary isometric contraction in younger and older adults is unknown. Consistent with the work of Andersen and Aagard **[13]** we report RTD to become increasingly more dependent on MVC as the time from the onset of contraction increases. RTD at 50 ms was not associated with maximal muscle strength but strength could account for 22% and 70% of the variance in RTD at time points 0-100 ms and 0-200 ms after the onset of contraction. This suggests factors influencing maximal muscle strength such as the descending drive from the CNS to recruit more motor neurons and subsequently motor units, the number of sarcomeres in parallel and the force output per sarcomere are related to the RTD as time from the onset of contraction increases. The

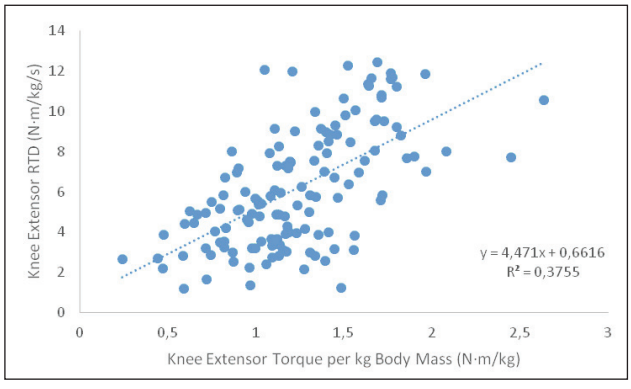

Figure 2. The relationship between maximal voluntary RTD and MVC.

proportion of variance in RTD explained by maximal strength is lower than the 50 – 80% reported by Andersen and Aagard 90 ms after the onset of contraction. Furthermore, Andersen and Aagard report voluntary RFD to be highest at 0-50 ms and descending towards 0-200ms. We report the opposite trend as RTD is ~50% greater at intervals between 0-200ms compared to 0-50ms. These results suggest that RTD in the early stages of muscle contraction is lower than in young adults and also that factors influencing RTD 0-50 ms after the onset of contraction are less related to maximal strength. The lower RTD in the early phase of contraction may be due to age-related changes in the musculotendinous compliance **[27]**, such that a reduction in connective tissue stiffness may require a greater duration of muscle contraction in order to develop appropriate tension for force transmission **[28-30]**.

Maximal muscle strength accounted for ~38% of the variance in maximal RTD. The linear phase of the contraction would appear **(Figure 1)** to occur between 50-150 ms after the onset of contraction which would be in line with the trend of maximal muscle strength explaining 22-70% of the variance in RTD at time points 0-100 ms and 0-200 ms from the onset of contraction. As RTD was highest when estimated during the linear phase of contraction, we suggest this is the section of the torque-time trace where the rate of cross-bridge formation is greatest. The results further highlight that the method for determining RTD is key to the physiological interpretation. It would appear that RTD cannot be used as a broad based term as is the case with maximum torque derived from an MVC. In line with the age-related difference in peak torque and muscle quality we reported previously **[3]**, RTD was lower for women in the 7th decade of life compared to those in the 6th decade and this difference was greater in the knee extensors. The difference in knee extensor RTD was almost double (-28%) that of knee extensor torque (-15.7%) that we reported previously in the same sample of women. The preferential decline in the speed of muscle contraction is said to occur due to a reduction in the number of sarcomeres in series **[31]**, and a reduction in the maximum shortening velocity of muscle fibres **[32]**, thought to be caused by a decrease in myosin concentration and actins sliding velocity **[33]**. Type IIA muscle fibres are thought to be particularly affected by these changes with ageing **[34]**. The age-related difference in RTD in this study must be interpreted cognisant that it included participants with a coefficient of variance as high as 10% (~25- 42 N·m·s-1) which is as much as a third of the age-related difference.

Knee extensor RTD had a weak association with extended gait speed and no association with the maximum number of chair rises completed in 30 seconds. Furthermore, knee extensor RTD was not altered by 12 weeks of PRT despite improvements in peak torque, muscle quality and extended gait speed which have been detailed in our recently published manuscript **[16]**. The weak association with functional capability and the lack of change due to intervention may be linked to the time interval from which RTD was sampled (~50-150 ms) and the fact that the functional tests used and the exercise prescribed would likely require muscle contractions of >200 ms. The exercises in this intervention were performed to a count of 4 seconds for the eccentric phase and 2 seconds for the concentric phase. As part of the healthy ageing study we reported moderate correlations between knee extensor strength and the extended gait speed and chair rise tests reported in this manuscript **[17]**. As the variance in RTD explained by maximal muscle strength increases with time from the onset of contraction, it is likely that RTD sampled at later time points may have had an association with functional tasks and or been altered due to PRT. The associated increase in upper leg LTM and maximal strength with the PRT in this study may have arisen via an increase in the diameter of type IIA muscle fibre diameter but at the expense of a relative reduction in type IIX fibres characterised by a high RFD **[35]**. It is also possible that the increase in fascicle length and resultant increase in compliance cancels out the increased shortening velocity of muscle arising from having more sarcomeres in series **[29]**.

We report RTD from the most linear phase of the torque-time trace in the majority of this analysis. The associations reported in this study as well as the age and intervention related differences must be interpreted cognisant of the variability in the measure. A broader consideration for performing this form of analysis is that there is a significant researcher time cost. Exporting isometric contractions and quantifying RTD at different points or from the most linear slope of the time-torque trace is a laborious process. Given that this process produces values of limited reliability, researchers should consider alternate non-invasive measures of quantifying intrinsic muscle contractile properties such as Tensiomyography (TMG), Myotonometry (MMT) **[36]** and Mechanomyography (MMG) **[37]**.

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