Bio-Medical Materials and Engineering 24 (2014) 2273–2281
DOI 10.3233/BME-141040
IOS Press

Quantitative evaluation of parkinsonian rigidity during intra-operative deep brain stimulation

Yuri Kwon[a], Sang-Hoon Park[a], Ji-Won Kim[a], Yeji Ho[a], Hyeong-Min Jeon[a], Min-Jung Bang[a], Seong-Beom Koh[c,*], Jong-Hyun Kim[d] and Gwang-Moon Eom[a,b*]
[a] *School of Biomedical Engineering, Konkuk University, Choonju, 380-701, Korea*
[b] *Research Institute of Biomedical Engineering, Konkuk University, Choonju, 380-701, Korea*
[c] *Department of Neurology, Korea University College of Medicine, Seoul, Korea*
[d] *Department of Neurosurgery, Korea University College of Medicine, Seoul, Korea*

Abstract. This study aims at the quantification of fine change in parkinsonian rigidity at the wrist during deep brain stimulation (DBS) using a portable measurement system and objective mechanical measures. The rigidity of fourteen limbs was evaluated during DBS surgery. The resistive torque to imposed movement was measured for every setting where a reduction in rigidity was perceived by a neurologist. Quantitative mechanical measures derived from experimental data included visco-elastic properties, work, impulse and mechanical impedance. Most mechanical measures could discriminate the optimal setting from baseline (electrode at stereotactic initial position without electrical stimulation) and the highest significance was achieved by viscous damping constant ($p<0.001$). Spearman correlation coefficients between mechanical measures and clinical score for multiple settings (averaged for 14 limbs) were 0.51-0.77 and the best correlation was shown for viscosity ($\rho=0.77\pm0.22$). The results suggest that intraoperative quantification of rigidity during DBS surgery is possible with the suggested system and measures, which would be helpful for the adjustment of electrode position and stimulation parameters.

Keywords: Intraoperative, quantification, rigidity, DBS surgery, Parkinson's disease

1. Introduction

Deep brain stimulation (DBS) of the subthalamic nucleus (STN) has been shown to be an effective treatment for Parkinson's disease (PD). With the progression of the disease, the efficacy of medication decreases and side effects increase [1]. STN-DBS has been shown to add improvement of parkinsonian symptoms, e.g. rigidity, bradykinesia and tremor, better than medication alone [1–3].

During surgery for DBS, placement of electrodes and optimization of stimulation parameters (setting) are critical for the success of the surgery. The optimal setting is determined based on the assess-

[*] Corresponding authors: Seong-Beom Koh, Department of Neurology, Korea University College of Medicine, Seoul, Korea. Tel.: +82-2-2626-3169; E-mail: parkinson@korea.ac.kr.
Gwang-Moon Eom, Research Institute of Biomedical Engineering, Konkuk University, Choonju, 380-701, Korea. Tel.: +82-43-840-3766; Fax: +82-43-851-0620; E-mail: gmeom@kku.ac.kr.

ment of the symptoms in response to the stimulation. The reaction delay of the symptoms to DBS is important, especially when multiple settings are tested in rapid succession. A commonly used symptom in this process is rigidity, because rigidity reacts to the change in DBS within a minute, shorter than those of other symptoms [4].

Parkinsonian rigidity is defined as the resistance of a joint to passive movement. When more force than might be expected is required to move a joint over a certain range, it is judged to be rigid. Commonly used criteria of the rigidity assessment are in the motor section (Part III) of Unified Parkinson's Disease Rating Scale (UPDRS). In UPDRS III, rigidity score is described in terms of the perceived resistance as 0: absent, 1: slight or detectable, 2: mild to moderate, 3: marked, and 4: severe. Although commonly used, UPDRS relies on raters' subjective and qualitative scoring based on their perception and clinical experience, hence the score differs among raters [5]. UPDRS has only 5 discrete scores and the resolution is limited for detecting small changes in symptoms [6]. If the severity of rigidity can be measured by scientific method rather than by the perception of human, it can be objectively quantified in a consecutive scale. New measures which are objective, quantitative and consecutive would be greatly helpful during DBS surgery, in the discrimination of fine change in rigidity induced by change in stimulation setting.

To our knowledge, there has been no attempt to quantify rigidity during DBS surgery. Only reported are the assessment of DBS effect 0.25-6 yrs after surgery, by using measures such as mechanical work from torque-motor system [7] and the change in segmental EMG [4]. The reason for the lack of quantification trials during surgery may be the complex setting and bulkiness of these systems and also the limited validity of the suggested measures.

Previously, the authors have developed a portable system for the measurement of resistive torque in reaction to manually imposed wrist movements [8]. The viscoelastic properties derived from the system were shown to be reliable and, when tested on outpatients with PD.

The system was expected to be practical for use in an operation room, because it is small and easy to setup. Though limited to the outpatients with medication, viscoelastic properties could quantify the severity in rigidity. They were also expected to quantify the effect of DBS on rigidity during surgery. Therefore, we aimed to apply the system and measures to the DBS surgery. We evaluated the validity of the viscoelastic measures, as well as other mechanical measures, during surgery by comparison of the measures with the clinical score.

2. Methods

2.1. Subjects and experiments

Fourteen wrists of eight patients (mean age 57 yrs; 4 male and 4 female; mean disease duration 12 yrs) were tested during surgery (Table 1). Six patients received bilateral and two received unilateral surgeries. Patients were withdrawn from medication at least 12 hours prior to the surgery. Local anesthetic (lidocaine) was administered at the cutting region of scalp before opening of the skull. Electrodes were inserted in the subthalamic nucleus (STN) according to stereotaxis under the arousal condition. While the electrode is being advanced, the patient does not feel any pain due to an absence of nociceptors in the brain.

A setting during DBS surgery was composed by electrode position and stimulation parameters. Stimulation parameters refers to stimulation amplitude and type of pulse waveform (monopolor and bipolar). Starting from the initial position, multiple settings were tested with an external pulse generator. Pulse width and pulse rate were fixed to 60 microseconds and 130 Hz, respectively. Optimal setting was defined as one with the greatest reduction in perceived rigidity without adverse effects. Once the optimal setting was determined by a neurologist, the pulse generator, lead and brain electrode were implanted under general anesthesia.

This study was conducted in compliance with the Declaration of Helsinki and ethics committee approval was obtained for this study. All patients provided written informed consents.

2.2. Experiments and outcome measures

During surgery, rigidity at the wrist was repeatedly rated by a neurologist by using his own scale (modified rigidity score, hereafter). To describe small change in rigidity which is not represented by the original rigidity scale in UPDRS, the modified rigidity scale subdivided the scores. For example, the rigidity between 1 and 2 was defined as 1.5 and one between 1.5 and 2 was defined as 1.75 (Table 1).

Mechanical tests were repeated for every setting where a reduction in rigidity was perceived by a neurologist. For every setting of mechanical test, modified rigidity score was also rated. Baseline was defined as the setting where the electrode is located at initial position according to stereotaxis and no simulation was applied.

The measurement system was comprised by a handle for the application of wrist flexion/extension

Table 1

Patient characteristics

Subject	Gender	Age [yrs]	H&Y stage†	Duration [yrs]	MMSE score††	Limb	Clinical rigidity score¶		Stimulation Level [V]
							Baseline condition¶¶	Optimal setting	
1	M	58	3	12	26	L	3	1	2
						R	3	1	4
2	F	67	3	12	26	L	2	0	3
						R	2.5	0	3
3	M	58	3	21	26	L	2	0.5	4
						R	2	0	4
4	F	57	2	8	30	L	2.5	1	2
						R	3	1	2
5	F	65	2.5	10	23	L	1.75	0	3
						R	1.5	0	4
6	M	42	2.5	20	26	R	2	0	2
7	M	44	3	8	23	R	3	1	3
8	F	66	2	6	27	L	2	0	1
						R	3	0	3
Mean		57.1	2.6	12.1	25.9		2.4	0.4	2.9
SD		9.6	0.4	5.6	2.2		0.5	0.5	0.9

Note: † Hoehn and Yahr scale indicating progression of Parkinson's disease (stage 5 max);
††MMSE: Mini-Mental State Examination used to screen cognitive impairment (30 points max).
¶ The clinical rigidity score included mid-score between the scores defined in UPDRS part III, to describe small change in rigidity which is critical for determination of the optimal setting. See text for details.
¶¶ An electrode inserted at stereotactic initial position and no simulation applied

movement by an examiner, a bi-directional load cell for the measurement of resistive torque, a potentiometer for wrist angle measurement and an accelerometer for inertia calculation. Details of the system and the derivation of moment of inertia are described in the previous report [8].

In the mechanical test, measured was the resistive torque to six cycles of flexion and extension movement imposed at wrist. The movement was constrained on the horizontal plane by the custom-made device. Speed and inter-cycle interval were randomly chosen for every cycle to minimize subjects' anticipation. Time needed for one test was around 10 s, so that it neither burden patients nor significantly lengthened the total time for operation. The average number of mechanical tests per limb was 6.4 resulting in additional operation time around 1 min.

Quantitative mechanical measures were derived from the experimental data. Viscous damping constant (B) and stiffness (K) of the joint was derived from the fitting of spring-damper model to the experimental data [8]. Other mechanical measures in the literature were also calculated for comparison with viscoelastic properties. They included mechanical work (W: resistive torque integrated by angle) per cycle [7,9–13], mechanical impulse (I: resistive torque integrated by time) per cycle [9,11], and mechanical impedance (Z) [14]. Work and impulse are resultant quantities in contrast that the viscoelastic properties are causal factors. Impedance is a causal quantity but valid for a specific movement frequency.

Additionally, work was normalized by the angular range to exclude the effect of different excursion angles among trials and patients (Wnorm) [12]. Similarly, impulse was normalized by the excursion time to exclude the effect of different excursion time (Inorm). In the integration process to calculate impulse, original torque value in the direction of resistance (e.g. extension torque in case of imposed flexion) was used. It was to get the net resistive impulse (the resistive impulse subtracted by the assistant impulse), in contrast to the absolute torque of the literature [9,11].

2.3. Statistical analysis

In DBS surgery, rigidity is obviously expected to decrease at the optimal setting compared to baseline. For the quantitative measures to be useful in DBS surgery, they must, at least, be able to reflect the reduction in rigidity. In this context, quantitative measures were compared between baseline and optimal setting. The comparison was performed by Wilcoxin's signed rank test (because some measures were not normally distributed). Also, we counted the number of limbs, where each measure showed reduction from baseline to optimal condition. In view of multiple comparisons, null hypotheses of no difference were rejected if $p<0.01$ [15].

It is also desirable for the quantitative measures to reflect the fine change in rigidity for each setting. A neurologist commonly uses his/her own scale (modified rigidity score) during DBS surgery. The scale is often limb-specific, because a neurologist aims to compare the relative effects of different settings on the rigidity of one limb rather than to compare the rigidity among patients. In this context, it is proper to investigate the relationship between quantitative measures and modified rigidity score in each limb, so that Spearman rank-order correlation coefficient was calculated for each limb. In addition, the number of limbs with significant positive correlation was counted. Negative correlation was assumed useless, because it indicates the mechanical measure interpreted the higher (more severe) rigidity score as to be milder. In correlation analysis, the significance level was set to $p<0.05$ considering small number of data points per limb (6.4 ± 1.7 points).

All statistical analyses were performed using SPSS ver.16 for Windows (SPSS Inc., Chicago, IL, USA).

Table 2

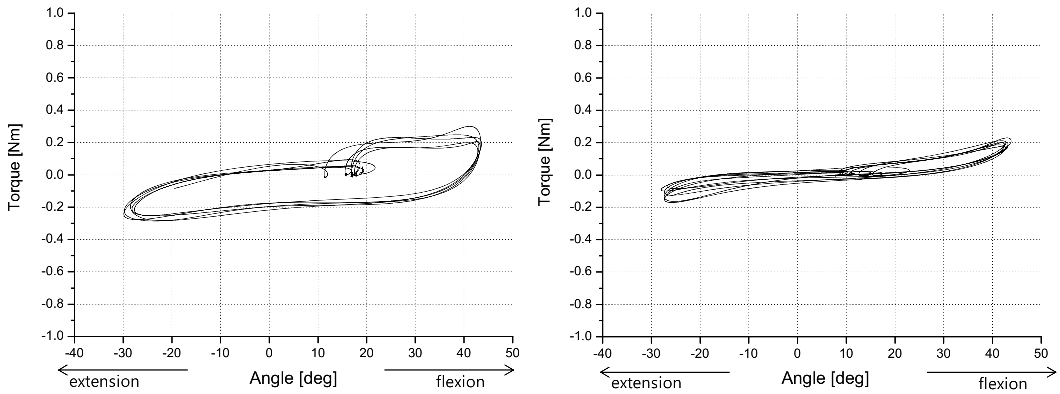
Quantitative mechanical measures on baseline and optimal conditions

Measure		Baseline condition†		Optimal setting		Difference	Limbs with reduction in each measure		Performance††
		mean	(SD)	mean	(SD)	(p value)	# of limbs	% total limbs	
Clinical score		2.38	(0.54)	0.39	(0.49)	**	14	100%-	-
B	[Nm/rad/sec]	0.14	(0.15)	0.07	(0.06)	**	14	100%	Good
K	[Nm/rad]	0.72	(0.64)	0.48	(0.48)	*	13	93%	Moderate
W	[Nmrad]	0.49	(0.67)	0.27	(0.36)	*	13	93%	Moderate
W_{norm}	[Nmrad/rad]	0.33	(0.32)	0.19	(0.20)	*	13	93%	Moderate
I	[Nms]	0.56	(0.70)	0.23	(0.23)	**	14	100%	Good
I_{norm}	[Nms/s]	0.11	(0.12)	0.05	(0.04)	*	13	93%	Moderate
Z	[Nm/rad]	0.87	(0.75)	0.56	(0.54)	0.51	13	93%	Poor

Note: **p<0.001, *p<0.01;

†electrode inserted at stereotactic initial position and no simulation applied

††Good: p<0.001; Moderate: 0.001≤ p<0.01; Poor: 0.01≤ p



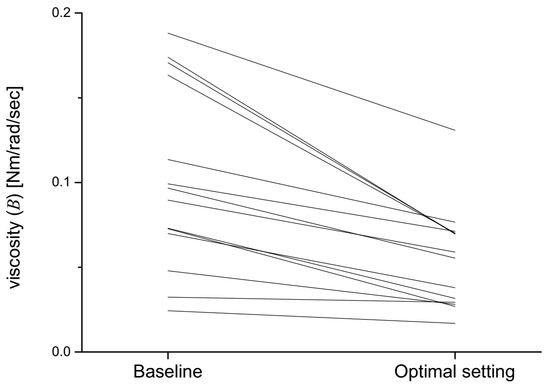
(a)Baseline (clinical rigidity score: 2.5) (b) Optimal setting (clinical rigidity score: 1)

Fig. 1. Representative torque-angle trajectories (subject 4, left limb).

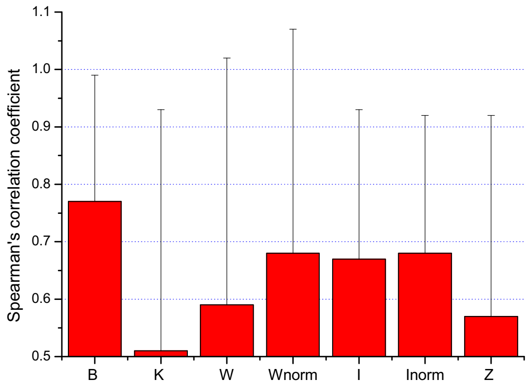
3. Results

Figure 1 shows the representative torque-angle trajectories for the baseline and optimal settings. It is noted that the slope (corresponding to the stiffness) and the area of the trajectories (corresponding to the work done by viscous damping constant) at the optimal setting are reduced from those of the baseline, as the modified rigidity score reduced from 2.5 to 1. This implies that stiffness and viscous damping constant would be related to the change in rigidity during surgery.

Table 2 shows the performance of each measure in differentiating the optimal setting from the baseline. Modified rigidity score at the optimal setting decreased from that at baseline in all limbs (from 2.38 to 0.39). Viscous damping constant (B) decreased from the baseline to the optimal setting in all limbs (Figure 2(a)) resulting in the best performance (p<0.001) among measures. Impulse (I) showed similar performance with viscous damping constant. Stiffness (K), work (W), normalized work



(a)



(b)

Fig. 2. Changes in viscous damping constant from baseline to optimal setting (14 limbs) (a) and correlation of mechanical measures with clinical rigidity score (b).

(Wnorm) and normalized impulse (Inorm) could also differentiate baseline and optimal setting ($p<0.01$), but they increased in part of the limbs contradictory to the clinical decision that the rigidity decreased in all limbs.

Figure 2(b) and Table 3 describe the correlation of each measure with modified rigidity score for multiple settings. Viscous damping constant had the best correlation ($\rho=0.77\pm0.22$) with clinical measures and the greatest number of limbs with significant positive correlation (57%). The other measures showed 'moderate' or 'poor' performance. Normalization of work and impulse (Wnorm and Inorm) slightly improved correlation but the performance was still moderate ($0.6< \rho<0.7$).

In summary, the overall performance was the best for viscous damping constant, as it was rated 'good' in Tables 2 and 3. Impedance had the worst performance ('poor' in both tables). The other measures had 'moderate' or 'poor' performance at least in one of two tables.

Table 3

Correlation of each measure with clinical rigidity score

Measure	Spearman correlation (ρ)			Limbs with significant positive correlation†		Performance††
	Mean	(SD)	CV	# of limbs	% total limbs	
B	0.77	(0.22)	29%	8	57%	Good
K	0.51	(0.42)	81%	5	36%	Poor
W	0.59	(0.43)	73%	2	14%	Poor
W_{norm}	0.68	(0.39)	57%	7	50%	Moderate
I	0.64	(0.44)	69%	4	29%	Moderate
I_{norm}	0.67	(0.35)	52%	4	29%	Moderate
Z	0.57	(0.35)	62%	5	36%	Poor

Note: †Average number of data points in one limb was 6.4(SD: 1.7).
††Good: mean $\rho > 0.7$; Moderate: $0.6<$ mean $\rho \leq 0.7$; Poor: mean $\rho \leq 0.6$

4. Discussion

The main finding of this study was that parkinsonian rigidity during DBS surgery could be quantified by mechanical measures from a simple and portable system. The best measure was viscous damping constant in that it best represented the reduction in clinical score of rigidity from baseline to optimal setting (Table 2), and also the changes in clinical score of rigidity for multiple settings (Table 3). Though post-surgery assessment of rigidity has been reported in the literature, intra-operative quantification was tried for the first time in this study, which would have clinical significance. The success of the suggested system for use in an operation room comes from the small size, comfortable setup, and intuitive operation of the system (similar to the clinical testing method).

The success of viscous damping constant in quantification of intra-operative assessment of rigidity may be related to the pathophysiology. Parkinsonian rigidity is sensitive to the velocity of imposed movement at the wrist [10,11] as well as at the other joints [16,17] and it is believed to be related to enhanced long-loop (long-latency) reflexes mediated by the sensorimotor cortices [18]. The viscous damping constant was suggested to reflect the velocity-dependency of long-loop reflexes [8]. Good correlation of viscous damping constant with modified rigidity score in outpatients with normal state of medication was reported, where the effect of DBS was not considered [8,12]. This relationship also holds for the intraoperative assessments in this study. Stiffness showed poor correlation with clinical score during operation (Figure 2(b) and Table 3), though it showed good correlation in outpatients [8,12]. From these results, neurologists' rating of rigidity seems to depend much on the sensation of the resistance in reaction to the imposed movement speed, irrespective of the interventions.

Work and impulse are resultant quantities from resistive torque. Specifically, work integrates resistive torque over displacement angle and impulse over displacement time. Hence, variation in movement range and time would affect work and impulse. Slight improvement of their correlation by normalization (Table 3) may be due to negation of the variations in range and time (resulting in the resistive torque averaged for range and time, respectively). The inherent problem of work and impulse is that the resistive torque depends on the speed of imposed movement [10,11,16,17], so that work and impulse (even after normalization) also depends on the speed. The variation in speed in multiple trials in the surgery of each limb may have degraded the ordered relationship of work and impulse with modified rigidity score. To maintain constant velocity, a large-scale torque motor can be used, but it makes the system bulky, expensive and difficult to manipulate [12]. Moreover, a good coupling of torque motors to the patient's extremities lead to a worse correlation with clinical evaluation, likely because it constrains the patient even further [19], and a constant velocity makes the measures to lose the velocity dependence which is an important feature of rigidity.

Mechanical impedance is an attractive measure in that it is a causal quantity representing combined impedance of viscous damping constant and elastic stiffness. However, its performance was the worst in both Table 2 and Table 3. The inherent problem of impedance is that its mechanical meaning is valid for a specific (mean) frequency of cyclic movement. Because the speed varies during one trial as well as between trials, its consistency would be poor and it would have resulted in poor correlation with clinical score. Similarly to the case of work and impulse, maintaining a constant frequency would lose the velocity dependent feature of rigidity.

Limitations of this study include moderate number of limbs (14 limbs). It is common that DBS surgery is performed only for patients of advanced disease stage with the presence of disabling motor fluctuations, prolonged off-medication periods and significant dyskinesias in the on-medication status, but without significant cognitive dysfunction or concomitant medical or neurological disorders [20]. Therefore, patients satisfying the inclusion criteria are only small portion of those with PD, so that the number of limbs included in the literature related to DBS effect after surgery [4,7] was smaller (10-13 limbs) than this study. In spite of the limitation, significance shown in Tables 2 and 3 is statistically meaningful, so that 14 limbs of this study appear to be acceptable.

Another limitation is the moderate number of data per limb (6.4±1.7 points) which was resulted from limited number of DBS settings per limb during operation. This resulted in the insignificance of correlation in part of the limbs (Table 3). Trying extra settings to increase the number of data per limb may increase the significance of correlation. However, it would be ethically improper because it increases the operation time and burden to patients, and therefore, moderate number of data points per limb was inevitable. Nevertheless, the correlation performance of viscous damping constant was good enough (ρ =0.77±0.22) which is argued to be meaningful.

In this study, the passive movement was generated by an examiner. This may result in small range of velocity which is not desirable for the determination of viscoelastic constants. An automated system which is capable of generating wider range of velocity is recommended to confirm the results in future study.

5. Conclusion

Quantitative investigation of rigidity during DBS surgery was performed for the first time in this study. Results show that the rigidity during DBS surgery can be quantified the best by viscous damping constant among mechanical properties. Moreover, the measurement system (dispensed with torque motor) was practical enough to be used in an operation room. The suggested system and measure are expected to be a useful help during DBS surgery for the adjustment of electrode position and stimulation parameters.

References

[1] M. Horstink, E. Tolosa, U. Bonuccelli, G. Deuschl, A. Friedman, P. Kanovsky, J.P. Larsen, A. Lees, W. Oertel, W. Poewe, O. Rascol and C. Sampaio, Review of the therapeutic management of Parkinson's disease, report of a joint task force of the European Federation of Neurological Societies (EFNS) and the Movement Disorder Society-European Section (MDS-ES), part II: late (complicated) Parkinson's disease, Eur. J. Neurol. **13** (2006), 1186–1202.

[2] D.E. Vaillancourt, J. Prodoehl, L. Verhagen Metman, R.A. Bakay and D.M. Corcos, Effects of deep brain stimulation and medication on bradykinesia and muscle activation in Parkinson's disease, Brain **127** (2004), 491–504.

[3] M.M. Sturman, D.E. Vaillancourt, L.V. Metman, R.A. Bakay and D.M. Corcos, Effects of subthalamic nucleus stimulation and medication on resting and postural tremor in Parkinson's disease, Brain **127** (2004), 2131–2143.

[4] J. Levin, S. Krafczyk, P. Valkovic, T. Eggert, J. Claassen and K. Botzel, Objective measurement of muscle rigidity in Parkinsonian patients treated with subthalamic stimulation, Mov. Disord. **24** (2009), 57–63.

[5] A. Machado, A.R. Rezai, B.H. Kopell, R.E. Gross, A.D. Sharan and A.L. Benabid, Deep brain stimulation for Parkinson's disease: Surgical technique and perioperative management, Mov. Disord. 21 Suppl. **14** (2006), S247–S258.

[6] M.M. Koop, N. Shivitz and H. Bronte-Stewart, Quantitative measures of fine motor, limb, and postural bradykinesia in very early stage, untreated Parkinson's disease, Mov. Disord. **23** (2008), 1262–1268.

[7] M.B. Shapiro, D.E. Vaillancourt, M.M. Sturman, L.V. Metman, R.A. Bakay and D. M. Corcos, Effects of STN DBS on rigidity in Parkinson's disease, IEEE Trans. Neural. Syst. Rehabil. Eng. **15** (2007), 173–181.

[8] B.K. Park, Y. Kwon, J.W. Kim, J.H. Lee, G.M. Eom, S.B. Koh, J.H. Jun and J. Hong, Analysis of viscoelastic properties of wrist joint for quantification of parkinsonian rigidity, IEEE Trans. Neural. Syst. Rehabil. Eng. **19** (2011), 167–176.

[9] R. Xia, K. Markopoulou, S.E. Puumala and W.Z. Rymer, A comparison of the effects of imposed extension and flexion movements on Parkinsonian rigidity, Clin. Neurophysiol. **117** (2006), 2302–2307.

[10] R. Xia, J. Sun and A.J. Threlkeld, Analysis of interactive effect of stretch reflex and shortening reaction on rigidity in Parkinson's disease, Clin. Neurophysiol. **120** (2009), 1400–1407.
[11] V.S. Fung, J.A. Burne and J.G. Morris, Objective quantification of resting and activated parkinsonian rigidity: A comparison of angular impulse and work scores, Mov. Disord. **15** (2000), 48–55.
[12] B. Sepehri, A. Esteki, E. Ebrahimi-Takamjani, G.A. Shahidi, F. Khamseh and M. Moinodin, Quantification of rigidity in Parkinson's disease, Ann. Biomed. Eng. **35** (2007), 2196–2203.
[13] D. Powell, N. Hanson, A.J. Threlkeld, X. Fang and R. Xia, Enhancement of parkinsonian rigidity with contralateral hand activation, Clin. Neurophysiol. **122** (2011), 1595–1601.
[14] S.K. Patrick, A.A. Denington, M.J. Gauthier, D.M. Gillard and A. Prochazka, Quantification of the UPDRS Rigidity Scale, IEEE Trans. Neural. Syst. Rehabil. Eng. **9** (2001), 31–41.
[15] J. Chae, G. Yang, B.K. Park and I. Labatia, Delay in initiation and termination of muscle contraction, motor impairment, and physical disability in upper limb hemiparesis, Muscle Nerve **25** (2002), 568–575.
[16] H.M. Lee, Y.Z. Huang, J.J. Chen and I.S. Hwang, Quantitative analysis of the velocity related pathophysiology of spasticity and rigidity in the elbow flexors, J. Neurol. Neurosurg. Psychiatry **72** (2002), 621–629.
[17] M.K. Mak, E.C. Wong and C.W. Hui-Chan, Quantitative measurement of trunk rigidity in parkinsonian patients, J. Neurol. **254** (2007), 202–209.
[18] M. Hallett, Parkinson revisited: Pathophysiology of motor signs, Adv. Neurol. **91** (2003), 19–28.
[19] A. Prochazka, D.J. Bennett, M.J. Stephens, S.K. Patrick, R. Sears-Duru, T. Roberts and J.H. Jhamandas, Measurement of rigidity in Parkinson's disease, Mov. Disord. **12** (1997), 24–32.
[20] C. Hamani, E. Richter, J.M. Schwalb and A.M. Lozano, Bilateral subthalamic nucleus stimulation for Parkinson's disease: A systematic review of the clinical literature, Neurosurgery **56** (2005), 1313–1321.