ORIGINAL ARTICLE

Fatigue Characteristics during Maximal Concentric Leg Extension Exercise with Blood Flow Restriction

S. Fujita, A. E. Mikesky, Y. Sato, T. Abe

Int. J. KAATSU Training Res. 2007; **3**: 27-31

Correspondence to:
Satoshi Fujita, PhD, Department of Human and Engineered Environmental Studies, Graduate School of Frontier Sciences, The University of Tokyo, 5-1-5, Kashiwanoha, Kashiwa-shi, Chiba, 277-8563 Japan
fujita@k.u-tokyo.ac.jp

See end of article for authors' affiliations

Low-intensity resistance exercise combined with blood flow restriction has been shown to elicit hormonal and neuromuscular responses similar to those with high-intensity resistance exercise. However, muscle fatigue characteristics during resistance exercise with restricted blood flow have not been clarified. Therefore, we measured maximal voluntary torque values during isokinetic concentric leg extensions across 30 repetitions at 180°/s either with blood flow restriction (BFR) or without restriction (CON) in eight healthy adults. The exercise was performed at the rate of either 30 repetitions/minute (BFR30 and CON30) or 15 repetitions/minute (BFR15 and CON15) designed to allow different rest intervals between contractions. Muscle fatigue was quantified by two methods: slope of peak isokinetic torque values through the 30th repetition and percent decrease in force from the first 5 repetitions to the last 5 repetitions. At the rate of 30 repetitions/minute, both fatigue rates were similar between BFR and control group. On the contrary, both fatigue rates were significantly higher in BFR15 group than the CON15 group ($p<0.05$). The results indicate that during resistance exercise performed with longer inter-repetition rest intervals, blood flow restriction is more effective at inducing muscle fatigue and thus may increase the training response. Furthermore, inter-repetition rest intervals of less than 3.5 seconds can increase fatigue level regardless of muscle perfusion.

Key words: muscle fatigue, blood flow restriction, resistance exercise

INTRODUCTION

Numerous studies have indicated that low-intensity resistance exercise combined with blood flow restriction (BFR) leads to significant muscular hypertrophy (Burgomaster et al., 2000; Takarada et al., 2002; Takarada et al., 2000). Although the metabolic and hormonal responses to an acute bout of BFR have been explored extensively (Fujita et al., 2007; Takarada et al., 2000), the changes in muscular force output and fatigue response during BFR exercise have not been studied thoroughly.

Muscular fatigue is defined as the inability to sustain maximal force or power, and it may involve a number of neuromuscular or metabolic impairments (Allman and Rice, 2002). During maximal isometric contractions, the maximal force output declines progressively, and the decline in maximal force is even greater when the blood flow is restricted by cuff stenosis (Russ and Kent-Braun, 2003). Isotonic muscle exercise leads to an increase in blood flow in order to meet the higher metabolic demand caused by an elevated hydrolysis of ATP. However, maximal isokinetic contractions with short rest intervals between contractions may accelerate muscular fatigue due to greater metabolic demands and mechanical compression of the blood vessels as compared to exercise with longer inter-repetition rest intervals. As such, blood flow restriction during repeated maximal voluntary isokinetic contractions with cuff stenosis may lead to greater muscle fatigue.

It has recently been suggested that the more fatiguing the exercise, the greater the anabolic training stimulus(Cook et al., 2007). Muscle fatigue during a bout of resistance exercise is influenced by various factors, such as exercise intensity and overall amount of exercise (Hakkinen and Pakarinen, 1993). However, one recent study showed that under the same exercise load, the subject with the highest fatigue rate also demonstrated the highest increase in plasma growth hormone concentrations after a bout of low-intensity resistance exercise with BFR (Pierce et al., 2006). Since the acute increase in growth hormone is one of the potent anabolic stimuli for muscle growth (Healy et al., 2003; Liu et al., 2003; Pierce et al., 2006), characterizing the fatigue response associated with exercise with BFR has important implications. Therefore, the purpose of the current study was to investigate the muscle fatigue response during maximal voluntary isokinetic concentric contractions with blood flow restriction but different inter-repetition rest intervals.

METHODS

Eight healthy subjects (4 females and 4 males) agreed to participate in the study. Each subject performed unilateral, isokinetic leg extension exercise across total of 30 repetitions with or without blood flow restriction using two different inter-repetition intervals of either 15 or 30 repetitions/minute. Each subject was tested for all experimental conditions on separate occasions. Unilateral leg extension exercise was carried out on a Biodex 3 isokinetic dynamometer (Biodex, Shirley, NY). Subjects were seated upright with a 100° hip angle on the dynamometer chair. Velcro straps were applied tightly across the thorax and pelvis with the distal leg fixed to the dynamometer lever arm. The axis of rotation of the dynamometer was aligned to the lateral femoral condyle, indicating the anatomical joint axis of the knee. Subjects performed a set of 30 maximum voluntary unilateral concentric leg extension at 180°/s angular velocity within a 100° range of motion (0°: full leg extension) while the torque was measured and recorded instantaneously.

For blood flow restriction, a lower extremity pressure cuff (Kaatsu-Master Mini, Sato Sports Plaza, Tokyo, Japan) was placed around the most proximal portion of exercising leg. While the subject was seated on a chair, the pressure cuff was inflated to 120 mmHg for 30 seconds, and the air pressure was released. The pressure cuff was then inflated four more times with each period being increased by 20 mmHg. Each period lasted 30 seconds and then the cuff was released for a 10 seconds between periods until a final pressure of 200 mmHg was reached. With the pressure maintained at 200 mmHg, the subjects then performed the set of leg extension exercises. For the control condition, the same exercise protocol was performed but without blood flow restriction.

Muscle fatigue was determined by two methods of calculation: the slope and fatigue index. The slope was determined by linear regression analysis of the peak torques for each repetition across the 30 contractions for each protocol. The slope from the calculated regression equation (N·m/rep) was used to quantify the muscle fatigue. The fatigue index (F.I.) was determined by the following formula to yield a percent decrease in isokinetic torque:

$$\text{F.I. }(\%) = 100 - [(\text{last 5 repetitions / first 5 repetitions}) \times 100]$$

All subjects gave informed, written consent before participating in the study, which was approved by the Ethics Committee for Human Experiments, The University of Tokyo.

All values were expressed as mean ± SEM. Comparison between gender on peak torque, F.I. and slope was performed with unpaired t-test. One-way analysis of variance (ANOVA) with repeated measures was used to compare the peak torque across 30 repetitions within each group. The fatigue rates (the slope and F.I.) between groups were assessed with one-way ANOVA. Post-hoc analysis with Tukey was performed when appropriate.

RESULTS

The age, height, body weight, and BMI of the eight subjects (4 females and 4 males) were 31±4 yr, 168±3 cm, 62.8±3.8 kg, and 22.1±0.8 kg/m^2, respectively. Gender differences in the single highest peak torque across 30 contractions were observed in two of the

Table 1. Single highest peak torque across 30 contractions (i.e. peak torque), slope, and Fatigue Index (F.I.) during maximal isokinetic leg extension exercise at 30 reps/min and 15 reps/min with blood flow restriction (BFR30 and BFR 15) as well as 30 reps/min and 15 reps/min without blood flow restriction (CON30 and CON15) between genders.
* Significantly different from males (P<0.05) Values are means ± SEM.

		Males	Fe males	*P* value
CON30	Peak torque (N·m)	164 ± 17	109 ± 10*	0.030
	Slope (N·m/rep)	-2.00 ± 0.43	-1.37 ± 0.23	0.240
	F.I. (%)	33 ± 4	31 ± 6	0.624
CON15	Peak torque (N·m)	151 ± 15	109 ± 9	0.054
	Slope (N·m/rep)	-0.72 ± 0.34	-0.53 ± 0.06	0.600
	F.I. (%)	14 ± 1	12 ± 6	0.776
BFR30	Peak torque (N·m)	157 ± 21	104 ± 10	0.066
	Slope (N·m/rep)	-2.24 ± 0.56	-1.70 ± 0.24	0.410
	F.I. (%)	41 ± 3	35 ± 4	0.339
BFR15	Peak torque (N·m)	155 ± 21	100 ± 7*	0.048
	Slope (N·m/rep)	-1.22 ± 0.50	-0.97 ± 0.14	0.640
	F.I. (%)	25 ± 3	21 ± 6	0.632

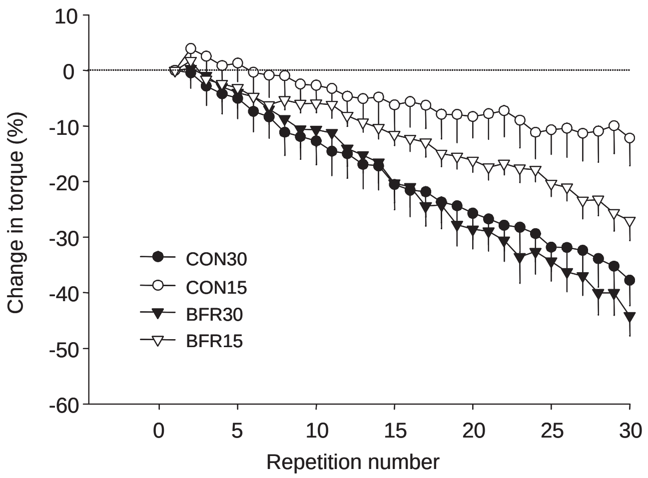

Figure 1. The percent change in maximal force output from the initial contraction during maximal isokinetic leg extension exercise at 30 reps/min and 15 reps/min with blood flow restriction (BFR30 and BFR15) as well as 30 reps/min and 15 reps/min without blood flow restriction (CON30 and CON15). Values are means ± SEM.

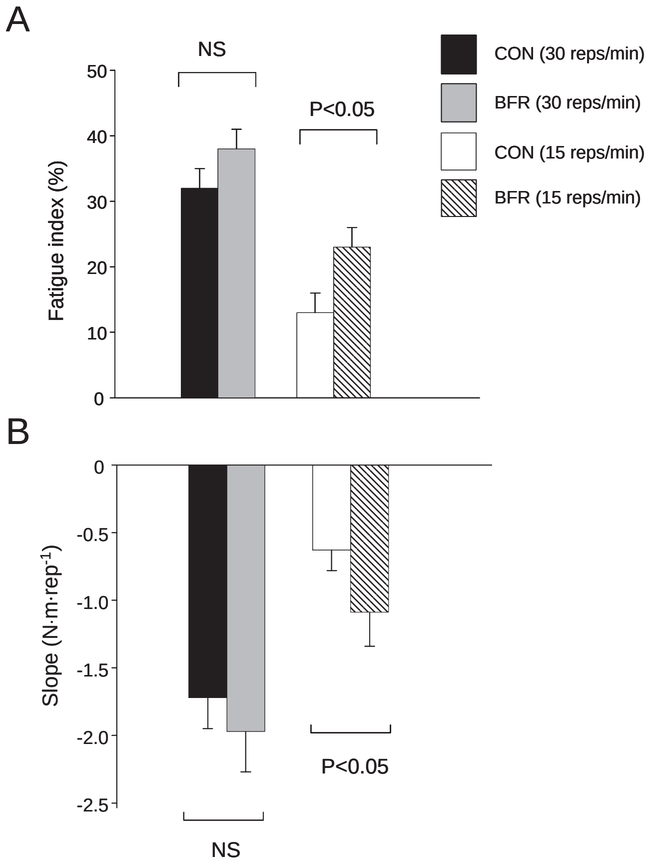

Figure 2. Percent decline in isokinetic torque (Fatigue Index.; Figure 2-A) and slope of peak torque across 30 repetitions (Slope; Figure 2-B) at 30 reps/min and 15 reps/min with blood flow restriction (BFR30 and BFR15) as well as 30 reps/min and 15 reps/min without blood flow restriction (CON30 and CON15). CON30 and BFR30 are significantly different from CON15 and BFR15 for both F.I. and slope (i.e. CON30 vs. CON15, CON30 vs. BFR15, BFR30 vs. BFR15, BFR30 vs. CON15; P<0.05) Values are means ± SEM.

repetitions/minute (reps/min) conditions. Peak torque was significantly higher in males for control exercise at 30 reps/min (CON30; $p<0.05$) and blood flow restriction exercise at 15 reps/min (BFR15; $p<0.05$) whereas the peak torque tended to be higher for control exercise at 15 reps/min (CON15; $p=0.054$) and exercise during blood flow restriction at 30 reps/min (BFR30; $p=0.066$) (Table 1). On the contrary, no significant gender difference in fatigue rates were observed when assessed by either slope of peak torque values (slope) or Fatigue Index (F.I.) (p=NS; Table 1). Therefore, both genders were combined for further comparison between 4 exercise protocols. No significant difference in single highest peak torque was observed for the combined gender data between groups (136±14, 130±11, 130±15, and 128±15 N·m for CON30, CON15, BFR30, and BFR15, respectively; p=NS). The peak torque decreased progressively across 30 contractions in all 4 groups (Figure 1).

Percent decrease in peak isokinetic leg extension torque across 30 repetitions (F.I.) was significantly attenuated when the leg extension was performed at 15 reps/min as compared to 30 reps/min during blood flow restriction (23±3 and 38±3%, for BFR15 and BFR30, respectively; $p<0.05$) (Figure 2-A). Similarly F.I. was significantly lower in CON15 than CON30 (13±3 and 32±3%, respectively; $p<0.05$). Although there was no difference in F.I. between control and BFR group when the exercise was performed at 30 reps/min, F.I. was significantly higher in BFR when the leg extension was performed at 15 reps/min ($p<0.05$).

Slopes of isokinetic peak torque values (slope) during leg extension exercise are shown in Figure 2-B, which was mirror image of F.I. Slope was significantly greater at 30 reps/min as compared to exercise at 15 reps/min for both control and BFR group. Whereas no significant difference was observed in slope between CON30 and BFR30, slope was significantly greater in BFR15 than CON15 ($p<0.05$; Figure 2-B).

DISCUSSION

The current study indicates that maximal force output decreases progressively during maximal voluntary leg extension exercise. Fatigue rates were significantly higher when the exercise was performed at 30 reps/min as compared to 15 reps/min. Furthermore, while the rate of fatigue was greater during blood flow restriction (BFR) when the exercise was performed at 15 reps/min, BFR did not further increase the fatigue rate when the exercise was performed at 30 reps/min.

Investigations using ^{31}P-NMR have indicated that during short-duration, high-intensity muscular contraction, muscle relies heavily on intramuscular phosphocreatine (PCr) for the source of high energy phosphates (Gaitanos et al., 1993; Yoshida and Watari, 1993). In the reaction, PCr ↔ creatine + inorganic phosphate (Pi), the forward reaction is controlled by myosin ATPase and sarcomere creatine kinase (CK), whereas reverse reaction is controlled by aerobic metabolism and mitochondrial CK (Mole et al., 1985). Consequently, hydrolysis of PCr and accumulation of inorganic phosphate (Pi) is further accelerated when the blood flow to the working muscle is restricted by a pressure cuff (Greiner et al., 2005; Greiner et al., 2007). Recent studies have indicated that the accumulation of Pi reduces the cross-bridge force production (Cooke and Pate, 1985; Millar and Homsher, 1990) and may contribute to muscular fatigue. Therefore, reduction in oxygen availability and Pi buffering capacity with limited muscular blood flow during exercise may contribute to greater muscular fatigue.

Muscular contraction at the rate of 30 reps/min induced significantly greater fatigue rates than 15 reps/min as indicated by the slope and F.I. Considering the exercise speed of 180°/s, each muscle contraction is about 0.5 second long, and there is about 3.5 sec rest period between contractions when the exercise was performed at 15 reps/min protocols. On the contrary, there is only 1.5 sec rest period between contractions at 30 reps/min. Therefore, it is possible that the exercising muscles were already in an ischemic condition at 30 reps/min due to a short rest interval between contractions. This may explain why further blood flow restriction during exercise had no significant impact on fatigue rates at 30 reps/min. On the contrary, rest intervals between contractions at 15 reps/min allowed greater muscular blood flow and recovery time in control group as compared to BFR group where the blood flow restriction persisted and accelerated the fatigue.

In the current study, we used two different indices of muscular fatigue, i.e. slope (N·m/rep) and fatigue index (F.I.). Since F.I. is calculated from the ratio of the average torque of the last five repetitions to the first five repetitions, variability in initial five torques may have considerable effect on F.I., hence the reliability of F.I. is questionable (Pincivero et al., 2003; Wretling and Henriksson-Larsen, 1998). In our current study, both calculations of fatigue rates drew essentially the same results.

Several studies indicated that the muscle fatigue may be influenced by gender. In the current study we did not observe a significant gender difference in fatigue response during maximal isokinetic leg extension exercise, as assessed by two different calculations. Studies using muscle biopsies of the vastus lateralis have indicated that males show higher activities of several glycolytic enzymes than females (Hargreaves et al., 1998; Jaworowski et al., 2002; Melanson et al., 2002; Simoneau et al., 1985), whereas women exhibit greater activities of enzymes associated with carbohydrate (Melanson et al., 2002) and lipid oxidation (Hargreaves et al., 1998; Melanson et al., 2002). As such, females are more fatigue resistant than males at submaximal isometric or concentric contractions (Hunter and Enoka, 2001; Maughan et al., 1986), while gender difference in fatigue during maximal contractions tends to decline (Edwards et al., 1977; Maughan et al., 1986). On the contrary, one recent study demonstrated higher fatigue rates for knee extensor muscle during maximal concentric leg extension and flexion exercise across 30 contractions (Pincivero et al., 2003). In the current study, there was a significant correlation between the single highest peak torque and fatigue rates for CON30 ($r=-0.87$, $p=0.049$), and the single highest peak torque was greater in males than females. It is possible that in the current study we did not have enough statistical power to detect a gender difference in slope since we had only 4 subjects in each gender. Regardless, the impact of gender difference in fatigues should be minimal since each subject performed all four protocols.

In summary, the current study indicates that BFR during leg extension exercise elicits a higher decrement in maximal voluntary torque as compared to the control exercise when the contraction was performed at the rate of 15 reps/min. However, at a higher exercise rate (i.e. 30 reps/min), no effect of BFR was apparent. Thus it appears that when performing exercises with longer inter-repetition rest intervals (i.e. only 15 reps/min), blood flow restriction effectively increases the level of fatigue and thus may enhance the training effect. A secondary finding, which applies to resistance training in general, is that inter-repetition rest intervals of less than 3.5 seconds and in the range of 1.5 seconds can increase the fatigue level and potentially the training stimulus.

....

References

Allman BL, Rice CL (2002) Neuromuscular fatigue and aging: central and peripheral factors. Muscle Nerve **25**: 785-796

Burgomaster KA, Moore DR, Schofield LM, Phillips SM, Sale DG, Gibala MJ (2003) Resistance training with vascular occlusion: metabolic adaptations in human muscle. Med.Sci.Sports Exerc. **35**: 1203-1208

Cook SB, Clark BC, Ploutz-Snyder LL (2007) Effects of exercise load and blood-flow restriction on skeletal muscle function. Med.Sci.Sports Exerc. **39**: 1708-1713

Cooke R, Pate E (1985) The effects of ADP and phosphate on the contraction of muscle fibers. Biophys.J. **48**: 789-798

Edwards RH, Hill DK, Jones DA, Merton PA (1977) Fatigue of long duration in human skeletal muscle after exercise. J Physiol **272**: 769-778

Fujita S, Abe T, Drummond MJ, Cadenas JG, Dreyer HC, Sato Y, Volpi E, Rasmussen BB (2007) Blood flow restriction during low-intensity resistance exercise increases S6K1 phosphorylation and muscle protein synthesis. J.Appl.Physiol **103**: 903-910

Gaitanos GC, Williams C, Boobis LH, Brooks S (1993) Human muscle metabolism during intermittent maximal exercise. J Appl.Physiol **75**: 712-719

Greiner A, Esterhammer R, Bammer D, Messner H, Kremser C, Jaschke WR, Fraedrich G, Schocke MF (2007) High-energy phosphate metabolism in the calf muscle of healthy humans during incremental calf exercise with and without moderate cuff stenosis. Eur.J.Appl.Physiol **99**: 519-531

Greiner A, Esterhammer R, Pilav S, Arnold W, Santner W, Neuhauser B, Fraedrich G, Jaschke WR, Schocke MF (2005) High-energy phosphate metabolism in the calf muscle during moderate isotonic exercise under different degrees of cuff compression: a phosphorus 31 magnetic resonance spectroscopy study. J.Vasc.Surg. **42**: 259-267

Hakkinen K, Pakarinen A (1993) Acute hormonal responses to two different fatiguing heavy-resistance protocols in male athletes. J.Appl.Physiol **74**: 882-887

Hargreaves M, McKenna MJ, Jenkins DG, Warmington SA, Li JL, Snow RJ, Febbraio MA (1998) Muscle metabolites and performance during high-intensity, intermittent exercise. J Appl.Physiol **84**: 1687-1691

Healy ML, Gibney J, Russell-Jones DL, Pentecost C, Croos P, Sonksen PH, Umpleby AM (2003) High dose growth hormone exerts an anabolic effect at rest and during exercise in endurance-trained athletes. J.Clin.Endocrinol.Metab **88**: 5221-5226

Hunter SK, Enoka RM (2001) Sex differences in the fatigability of arm muscles depends on absolute force during isometric contractions. J Appl.Physiol **91**: 2686-2694

Jaworowski A, Porter MM, Holmback AM, Downham D, Lexell J (2002) Enzyme activities in the tibialis anterior muscle of young moderately active men and women: relationship with body composition, muscle cross-sectional area and fibre type composition. Acta Physiol Scand. **176**: 215-225

Liu W, Thomas SG, Asa SL, Gonzalez-Cadavid N, Bhasin S, Ezzat S (2003) Myostatin is a skeletal muscle target of growth hormone anabolic action. J.Clin.Endocrinol.Metab **88**: 5490-5496

Maughan RJ, Harmon M, Leiper JB, Sale D, Delman A (1986) Endurance capacity of untrained males and females in isometric and dynamic muscular contractions. Eur.J Appl.Physiol Occup.Physiol **55**: 395-400

Melanson EL, Sharp TA, Seagle HM, Horton TJ, Donahoo WT, Grunwald GK, Hamilton JT, Hill JO (2002) Effect of exercise intensity on 24-h energy expenditure and nutrient oxidation. J Appl.Physiol **92**: 1045-1052

Millar NC, Homsher E (1990) The effect of phosphate and calcium on force generation in glycerinated rabbit skeletal muscle fibers. A steady-state and transient kinetic study. J.Biol.Chem. **265**: 20234-20240

Mole PA, Coulson RL, Caton JR, Nichols BG, Barstow TJ (1985) In vivo 31P-NMR in human muscle: transient patterns with exercise. J Appl.Physiol **59**: 101-104

Pierce JR, Clark BC, Ploutz-Snyder LL, Kanaley JA (2006) Growth hormone and muscle function responses to skeletal muscle ischemia. J.Appl.Physiol **101**: 1588-1595

Pincivero DM, Gandaio CM, Ito Y (2003) Gender-specific knee extensor torque, flexor torque, and muscle fatigue responses during maximal effort contractions. Eur.J Appl.Physiol **89**: 134-141

Russ DW, Kent-Braun JA (2003) Sex differences in human skeletal muscle fatigue are eliminated under ischemic conditions. J Appl.Physiol **94**: 2414-2422

Simoneau JA, Lortie G, Boulay MR, Thibault MC, Theriault G, Bouchard C (1985) Skeletal muscle histochemical and biochemical characteristics in sedentary male and female subjects. Can.J Physiol Pharmacol. **63**: 30-35

Takarada Y, Nakamura Y, Aruga S, Onda T, Miyazaki S, Ishii N (2000) Rapid increase in plasma growth hormone after low-intensity resistance exercise with vascular occlusion. J.Appl.Physiol **88**: 61-65

Takarada Y, Sato Y, Ishii N (2002) Effects of resistance exercise combined with vascular occlusion on muscle function in athletes. Eur.J.Appl.Physiol **86**: 308-314

Takarada Y, Takazawa H, Sato Y, Takebayashi S, Tanaka Y, Ishii N (2000) Effects of resistance exercise combined with moderate vascular occlusion on muscular function in humans. J.Appl.Physiol **88**: 2097-2106

Wretling ML, Henriksson-Larsen K (1998) Mechanical output and electromyographic parameters in males and females during fatiguing knee-extensions. Int J Sports Med. **19**: 401-407

Yoshida T, Watari H (1993) Metabolic consequences of repeated exercise in long distance runners. Eur.J Appl.Physiol Occup.Physiol **67**: 261-265

Author's affiliations

Satoshi Fujita, **Takashi Abe**, Department of Human and Engineered Environmental Studies, Graduate School of Frontier Sciences, The University of Tokyo, Chiba, Japan

Alan E. Mikesky, School of Physical Education and Tourism Management, Indiana University-Purdue University, Indianapolis, Indiana, USA

Yoshiaki Sato, Depertment of Ischemic Circulatory Physiology, The University of Tokyo, Tokyo, Japan