

Effects of Peripheral High Energy Missile Trauma on the Oxygenation of Lung Tissue in the Pig

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Abstract

The purpose of this paper was to study the effect of peripheral high energy missile trauma on oxygenation of the lung tissue. Eleven pigs were randomised to either high energy gunshot wound of the soft tissues of the thigh or sham exposure. Under anaesthesia and controlled ventilation, the carotid artery and the jugular vein were catheterised and a thoracotomy was performed. A Clark-type multiwire electrode was placed on the surface of the middle lung lobe for registration of the oxygen pressure fields of the lung tissue (P_tO_2). In animals subjected to missile trauma, an increased heterogeneity was seen in P_tO_2 1 and 2 hours after exposure, specially under hypoventilatory provocation. Furthermore, P_tO_2 values did not return to baseline when hypoventilation was followed by normoventilation, in contrast to what was seen in the sham exposed animals. No differences between groups were found in arterial PO_2 , O_2 -saturation, PCO_2 , pH or in pulse frequency. These findings of disturbance in oxygenation of pulmonary tissue, may represent an early phase in the development of a lung injury resembling the post-traumatic adult respiratory distress syndrome seen in man. The initiating events could be release of mediators from traumatised tissue and/or direct effects of the shock waves from missile impact, passing through the body.

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Introduction

The relationship between severe trauma and development of acute post-traumatic lung insufficiency manifested by dyspnoea, tachypnoea and cyanosis was first noted during World War II.¹ In the Vietnam War terms such as "shock lung", "Vietnam lung" and "DaNang lung" came to describe what later was to be known as Adult Respiratory Distress Syndrome (ARDS),² an entity which in peace-time USA affects maybe 150,000 patients per year and has a mortality of 50% to 70%.³ Initiating events in early onset ARDS, possible under battlefield conditions, are listed in Table I.

An experimental model to study biological effects of high energy missiles, using the hindleg of an anaesthetised animal as target, was described more than two decades ago⁴ and later developed into what is now referred to as the standardised "Swedish missile trauma model".⁵ Using this or similar techniques, it has been demonstrated that pressure waves generated at the moment and site (i.e. in the thigh) of missile impact, can travel through the body and be recorded in the abdominal⁶ as well as in the thoracic⁷ and cranial⁸ cavities. When

the missile impact also fractured the femur, radiologic and morphologic pulmonary changes corresponding to what is seen in human ARDS, were found in pigs. Furthermore, pulmonary trapping of platelets and fibrin was demonstrated.⁹ Interaction of leukocytes with the endothelium of the pulmonary vasculature has been proposed as one contributing factor in ARDS.¹⁰ Neutrophilic infiltrates, microthrombi and alveolar oedema and haemorrhage were recently reported in the lungs of dogs subjected to high energy gunshot wounds to the soft tissue of the thigh combined with haemorrhagic shock, but without skeletal damage.¹¹ With the use of a Clark-type surface multiwire electrode, the local tissue oxygenation can be measured in any tissue.^{12,13} We have recently demonstrated the possibility to record pulmonary tissue oxygen pressure (P_tO_2) fields in the anaesthetised pig using this type of electrode.¹⁴ We found that induction of hypoxic hypercapnia (hypoventilation) induced a left shift of the P_tO_2 histogram associated with low oxygenation of lung tissue itself. The aim of the present study was to evaluate whether a high energy gunshot wound to the soft tissue of the thigh would

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induce any changes in the oxygenation pattern of the lung tissue in a porcine model. It was also of interest to see how a hypoxic challenge (not infrequent in the clinical trauma situation) would affect the local oxygen utilisation of the lung tissue.

Material and Methods

Swedish land race pigs ($n = 11$) weighing 21 ± 2 kg were used in the study. The experimental protocol was approved of by the appropriate Animal Ethical Committee (Umeå, Sweden, #A137/94). Animals were allowed to accommodate in an accredited animal facility for at least three days prior to the experiments. They were fed a standard diet and had free access to tap water. Animals were premedicated with intramuscular injections of Ketamine, 500 mg (Ketalar®, Parke Davis & Co, Pontypool, Gwent, Great Britain), Atropine, 0.5 mg (Kabi Vitrum, Stockholm, Sweden) and Diazepam 5 mg (Stesolid Novum®, Dumex, Denmark). Anaesthesia was induced with Pentobarbital Sodium 15 mg/kg (Apoteksbolaget, Umeå, Sweden) intravenously and maintained with continuous intravenous infusion of Ketamine (Ketalar®) 60 mg/kg/h using an infusion pump (Syringe Infusion Pump type 235, Atom Medical Corporation, Tokyo, Japan). The animals were tracheotomized or intubated orally and ventilated on room air with a Servo ventilator 900 B (Siemens-Elcoma, Sweden). The right common carotid artery and the left jugular vein were catheterised for blood sampling and fluid (Ringer Acetate, 10 ml/kg/h, Kabi Pharmacia, Sweden) administration. Arterial blood gases, pH, serum electrolytes, haemoglobin and haematocrit were measured (BGE analyser and CO-Oximeter 482, Instrumentation Laboratory Srl, Milano, Italy). A pulse oximeter (OxiCap 4700, BOC Ohmeda, Västra Frölunda, Sweden) was used to record pulse frequency. A thoracotomy was performed through the third right intercostal space and an electrode holder was sutured onto the pleural surface of the middle lung lobe. Animals were randomised to either high energy gunshot wound or sham exposure. The former was induced using the Swedish missile trauma model.⁵ Animals were positioned on their backs with the right hind leg suspended vertically. The weapon was a smoothbore rifle, calibre 6.2 mm, and the missiles were steel spheres (0 6.0 mm, mass 0.88 gram). The velocity of the missile just before impact was measured by means of two ring magnets, spaced 150 mm apart, connected to an electric counter and a pulse generator to measure the passage time of the missile, which struck the lateral aspect of the right thigh posterior to the femur and the femoral artery. The kinetic energy transfer from the missile to the tissues of the animal was calculated, considering the known characteristics of the missile, the velocity and the length of the trajectory.⁶ Animals randomised to

sham exposure went through the same procedure as animals randomised to gunshot wound, except the actual gunshot. The technique of recording lung P_{tO_2} has recently been reported elsewhere.¹⁴ Briefly, the Clark-type membrane-covered surface oxygen electrode (Mehrdracht Oberfläche, Eschweiler, Kiel, Germany) consists of eight platinum wires (0 15 μ m each) embedded in a glass cylinder.¹² The electrode was calibrated at 0% and 21% O_2 and recorded values were corrected for drift, temperature and atmospheric pressure. When placed in the holder on the lung surface, the electrode was rotated slightly 15 times in 2.5 minutes, thus recording 120 P_{tO_2} values for each measuring situation. Recordings were computer stored and analysed. The first P_{tO_2} measurement was performed after a 5-minute period of normo-ventilation (5.5 to 6.0 litres/minute; frequency 28/minute) followed by another recording after 3 minutes of hypoventilation (ventilator settings reduced 50%). Hereafter a 5-minute period of normoventilation followed, after which another P_{tO_2} measurement was carried out. Blood samples were drawn after all P_{tO_2} recordings. After this initial measuring cycle [1], animals were subjected to either gunshot wound (trauma) or sham exposure (control). Immediately thereafter, another measuring cycle [2] was performed and repeated one [3] and two hours [4] following trauma/sham exposure. After completion of the experiments, animals were terminated with an overdose of Pentobarbital intravenously.

Statistics

Results are given as descriptive statistics and thus expressed as mean $\pm$ standard deviation. For calculation of P_{tO_2} heterogeneity, the coefficient of variation (CV = standard deviation/mean) was used.¹⁶

Results

Six animals were randomised to gunshot and five to sham exposure. The impact velocity of the missile ($n = 6$) was 1494 ± 10 m/s. Trajectory length in the right thigh ($n = 6$) was 74 ± 8 mm giving a calculated energy transfer of 589 ± 42 joules in the exposed animals. A characteristic high energy missile trauma was seen in all six animals, with a small entrance and a large exit wound. All animals survived the exposure.

Arterial PO_2 and oxygen saturation decreased after hypoventilation in all animals and returned to baseline after the second normoventilatory period. PCO_2 showed the opposite pattern. Arterial pH decreased after hypoventilation and returned to baseline again after normoventilation. No differences in serum electrolytes, haematocrit and haemoglobin levels were seen between controls and exposed animals during the course of the experiment. Heart rate decreased somewhat over time in all animals. The same pattern was noted in every

measuring cycle in both traumatised and control animals, i.e. no differences were noted between groups.

In Table II, P_tO_2 values and coefficient of variation (CV) are given. Pulmonary P_tO_2 decreased 49% (range 44% to 61%) in the control group after hypoventilation. Corresponding figures in the trauma group were 31% (27% to 64%). In the control group, P_tO_2 increased 15% (-16% to +50%) above baseline values after the second normoventilatory period. Corresponding values in the trauma group was -10% (-25% to +7%). Numerical P_tO_2

values in measuring cycles 1 and 2 were somewhat higher in the trauma group compared to the controls.

Figures 1 and 2 show summarised P_tO_2 histograms from all animals 1 hour after missile trauma/sham exposure. In the trauma group lung tissue oxygenation values were more scattered compared to controls. There were also a greater number of values close to zero during hypoventilation 1 and 2 hours after trauma compared to controls. The CV in the trauma group increased largely during hypoventilation compared to

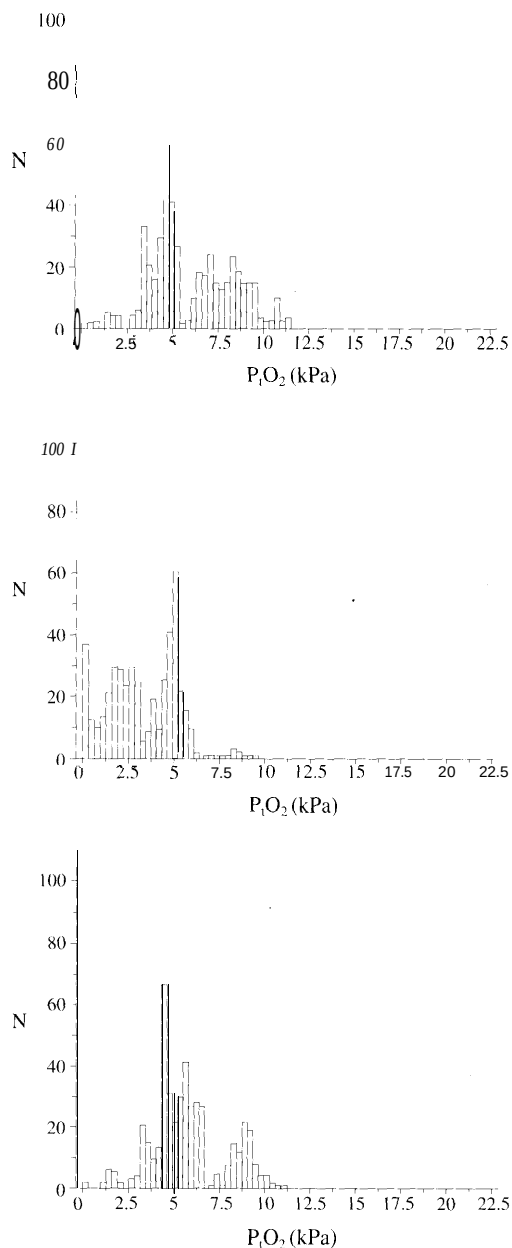


Fig. 1. Summarised lung tissue oxygen pressure (P_tO_2) distributions (PO_2 classes of 0.3 kPa) after 1 hour in the sham exposed (control) group ($n=5$) during normoventilation (upper histogram), hypoventilation (middle histogram) and a second period of normoventilation (lower histogram). N = number of sampled values.

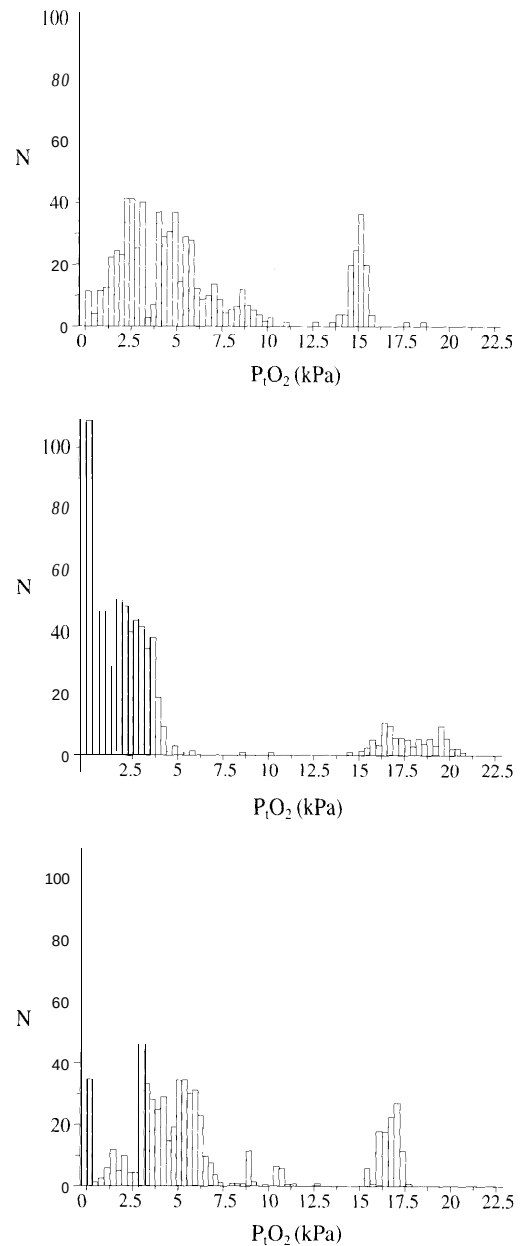


Fig. 2. Summarised lung tissue oxygen pressure (P_tO_2) distributions (PO_2 classes of 0.3 kPa) after 1 hour in the gunshot wound (trauma) group ($n=6$) during normoventilation (upper histogram), hypoventilation (middle histogram) and a second period of normoventilation (lower histogram). N = number of sampled values.

the control group. This CV increase persisted after 2 hours as well (Table II) which indicates an increased P_{tO_2} heterogeneity after the missile trauma.

Discussion

Pulmonary dysfunction after trauma and shock has been known for decades.^{1,2} Mechanisms involved include both local trauma to the lungs¹⁷ and trauma to distant sites resulting in secondary pulmonary changes, e.g. ARDS (Table I). Both cellular and humoral factors have been proposed to mediate these changes^{10,11,18-20} which may be parts of a generalised post-traumatic reaction.²¹

Although the Swedish Missile Trauma Model^{4,5} or similar techniques have been deployed in several different studies^{6,8,15,22} few of these have been focused on the lung and the possible development of ARDS-like conditions.^{9,11} In these studies changes in circulatory and non-circulatory parameters (e.g. fibrinogen, endotoxin and platelets) were noted 4 to 8 hours after the gunshot.^{9,11} Pulmonary microembolism⁹ and gut-derived endotoxaemia¹¹ were discussed as mediators of the lung changes. In the present study, we found disturbed pulmonary tissue oxygen pressure fields already 1 hour after high energy missile trauma to the thigh, but not immediately post exposure. Moore and co-workers¹⁸ found an increase of circulating primed polymorphonuclear neutrophils (PMN) 1 hour after the initiating insult (gut ischaemia) and lung injury 2 hours

after insult. In the present study PMN priming and/or activation could take place in the muscular tissue damaged by the missile and/or in the gut, possibly injured by shock waves passing through the abdominal cavity.⁶ Direct effects of the pressure waves on the lungs during the waves' passage through the thorax' cannot be ruled out, although the fact that the pigs were thoracotomized might counteract such effects.

The disturbed and scattered lung tissue oxygen pressure fields found after peripheral high energy missile trauma may be due to redistribution either of local microvascular blood flow in the lung or of ventilation on the alveolar level, or both. The animals were on a ventilator and no signs of impaired systemic ventilation were found in the arterial blood gases, except of course during hypoventilatory challenge. The increased P_{tO_2} heterogeneity seen, especially during hypoventilation, after missile trauma may reflect an insufficient local tissue oxygen utilisation.¹² This could be due to local metabolic effects caused by cellular dysfunction induced either by the shock waves passing through the thorax or by peripherally released circulating mediators. The somewhat higher P_{tO_2} values in the trauma group compared to the controls in measuring cycles 1 and 2 can be explained by the known variations in local mean tissue oxygenation between individual animals²³ and similar treatment groups.^{24,25} However, no increase in CV was noted earlier than in measuring cycles 3 and 4, where CV was found to be higher in the trauma group, especially after hypoxic provocation. An increase in this parameter indicates a disturbance in local tissue oxygenation.²⁶

In other studies of lung effects of peripheral missile trauma, the gunshot wound was combined with fracture of the femur or haemorrhagic shock.^{9,11} No such additional injuries were inflicted on the animals in the present study. No signs of circulatory shock were noted; in fact the heart rate decreased somewhat (approximately 35%) over time in traumatised as well as control animals. This decrease may be an effect of the anaesthetics used (Ketamine). No differences in the blood parameters measured (e.g. serum electrolytes and haemoglobin) were noted between the groups, indicating no

TABLE I: POSSIBLE CAUSES, UNDER BATTLEFIELD CONDITIONS, OF ARDS

Major and multiple trauma (missile or other)
Severe haemorrhagic shock
Multiple fractures with fat embolism
Severe thermal burns
Pulmonary contusion
Pulmonary blast injury ("blast lung")
Massive inhalation of smoke/toxic fumes
Massive inhalation of chemical warfare agents (e.g. sulfur mustard, phosgene)
Intracranial injury

TABLE II: THE DEVELOPMENT OF LUNG TISSUE OXYGEN PRESSURES (P_{tO_2}) (VALUES GIVEN AS MEAN±SD) AND COEFFICIENT OF VARIATION (CV) (MEAN VALUES GIVEN) IN THE CONTROL AND TRAUMA GROUP

	Measuring cycle 1			Measuring cycle 2			Measuring cycle 3			Measuring cycle 4		
	Normo	Hypo	Normo	Normo	Hypo	Normo	Normo	Hypo	Normo	Normo	Hypo	Normo
Control												
P_{tO_2} (kPa)	6.4±3.8	2.5±1.5	5.4±2.8	5.7±2.8	3.2±2.9	7.4±5.3	5.9±2.3	3.3±2.0	5.7±2.1	5.0±2.3	2.7±2.0	7.5±5.2
c v	0.59	0.61	0.52	0.50	0.92	0.72	0.39	0.60	0.35	0.46	0.74	0.70
Trauma												
P_{tO_2} (kPa)	9.8±5.2	5.6±4.0	7.7±3.9	8.0±4.5	2.9±1.9	6.0±3.2	6.0±4.5	4.4±6.1	6.4±5.1	4.0±3.5	2.5±3.2	3.9±3.7
c v	0.53	0.71	0.51	0.56	0.65	0.53	0.76	1.38	0.80	0.87	1.28	0.95

gross systemic effects of the trauma during the comparatively limited observation period.

Thus, using the standardised Swedish missile trauma model and the Clark-type multiwire surface oxygen electrode, we found that a high energy missile wound of the thigh resulted in disturbance of the oxygenation of lung tissue 1 and 2 hours after trauma in the pig. The energy transferred from the missile to the tissue was well defined and since the missiles were steel spheres, no missile deformation or tumbling occurred after impact. The disturbed oxygenation patterns were most evident during hypoventilatory provocation when a pronounced heterogeneity of P_{tO_2} values was found. Furthermore, in the traumatised animals, the P_{tO_2} reduction seen after hypoventilation was not reversed to baseline as in the control group where an increase above baseline actually occurred after the second normoventilation.

These findings may represent an early phase in the development of an ARDS-like condition. Release of cellular and/or humoral mediators from the wound area and/or from other peripheral tissues (e.g. intestines) is a possible initiating event. Shock waves from the impact can travel through both abdominal and thoracic cavities and thus induce injuries of the gut but also of the pulmonary tissue itself.

Further studies using this model are warranted to clarify the mechanisms behind the pulmonary changes seen after peripheral missile wounds and to evaluate possible prophylactic and therapeutic interventions.

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REFERENCES

1. Buford T H, Burbank B. Traumatic wet lung: Observations on certain physiologic fundamentals in thoracic trauma. *J Thorac Cardiovasc Surg* 1945; 14:415-25.
2. Ashbaugh D G, Bigelow D B, Petty T L, Levine B E. Acute respiratory distress in adults. *Lancet* 1967; 2:319-23.
3. Hyers T M. Adult respiratory distress syndrome: definition, risk factors, and outcome. In: Zapol W M, Lemaire F, editors. *Adult Respiratory Distress Syndrome*. New York, Basel, Hong Kong: Marcel Dekker Inc, 1991:23-36.
4. Rybeck B. Missile wounding and hemodynamic effects of energy absorption. *Acta Chir Scand* 1974; 450(suppl):5-32.
5. Schantz B. Is the missile wound a model suitable for general trauma studies? *Acta Chir Scand* 1982; 508(suppl):159-66.
6. Tikka S, Cederberg A, Rokkanen P. Remote effects of pressure waves in missile trauma: The intra-abdominal pressure changes in anaesthetised pigs wounded in one thigh. *Acta Chir Scand* 1982; 508(suppl):167-73.
7. Berlin R. Energy transfer and regional blood flow changes following missile trauma. *J Trauma* 1979; 19:170-6.
8. Suneson A, Hansson H-A, Seeman T. Peripheral high-energy missile hits cause pressure changes and damage to the nervous system: Experimental studies on pigs. *J Trauma* 1987; 27:782-9.
9. Jansson I, Lovén L, Rammer L, Lennquist S. Pulmonary trapping of platelets and fibrin after musculoskeletal trauma: An experimental model. *J Trauma* 1985; 25:288-98.
10. Worthen G S, Lien D C, Tonnesen M G, Henson P M. Interaction of leukocytes with the pulmonary endothelium. In: Ryan U S, editor. *Pulmonary Endothelium in Health and Disease*. New York, Basel: Marcel Dekker Inc, 1987:123-60.
11. Yao Y M, Sheng Z Y, Tian H M, Wang Y P, Yu Y, Fu X B, et al. Gut-derived endotoxemia and multiple organ failure following gunshot wounds combined with hemorrhagic shock: An experimental study in the dog. *J Trauma* 1995; 38:742-6.
12. Kessler M, Hoper J, Krumme B A. Monitoring of tissue perfusion and cellular function. *Anesthesiology* 1976; 45:184-97.
13. Gustafsson U, Torsell L, Sjöberg F, Sollevi A. Effect of systemic adenosine infusion on capillary flow and oxygen pressure distributions in skeletal muscle of the rabbit. *Int J Microcirc Clin Exp* 1993; 13:1-12.
14. Kjellström B T, Gustafsson U. Microvascular lung tissue oxygenation pressure distributions in the anaesthetised pig: A preliminary report. *Int J Microcirc Clin Exp* 1995; 15:148.
15. Janzon B. High-energy missile trauma. A study of the mechanisms of wounding of muscle tissue. Stockholm, Sweden: Swedish National Defense Research Establishment (FOA); 1983. FOA Report No. B20043.
16. Duling B R, Damon D H. An examination of the measurement of flow heterogeneity in striated muscle. *Circ Res* 1987; 60:1-13.
17. Hellinger A, Konerding M A, Malkusch W, Obertacke U, Redl H, Bruch J, et al. Does lung contusion affect both the traumatised and the noninjured lung parenchyma? A morphological and morphometric study in the pig. *J Trauma* 1995; 39:712-9.
18. Moore E E, Moore F A, Franciose R J, Kim F J, Biffl W L, Banerjee A. The post-ischemic gut serves as a priming bed for circulating neutrophils that provoke multiple organ failure. *J Trauma* 1994; 37:881-7.
19. Williams J J, Moalli R, Calista C, Herndon J H. Pulmonary endothelial injury and altered fibrinolysis after femur fracture in rabbits. *J Orthop Trauma* 1990; 4:303-8.
20. Bult H, Heiremans J J, Herman A G, Malcorps C M A, Peeters F A M. Prostacyclin biosynthesis and reduced 5-HT uptake after complement-induced endothelial injury in the dog isolated lung. *Br J Pharmacol* 1988; 93:791-802.
21. Gosling P, Sanghera K, Dickson G. Generalised vascular permeability and pulmonary function in patients following serious trauma. *J Trauma* 1994; 36:477-81.
22. Almskog B A, Haljamäe H, Hasselgren P O, Nordstrom G, Seeman T. Local metabolic changes in skeletal muscle following high energy missile injury. *J Trauma* 1982; 22:382-7.
23. Thorborg P, Lund N. Serotonin as a modulator of skeletal muscle oxygenation: effects of ketanserin and ritanserin on oxygen pressure distributions. *Int J Microcirc Clin Exp* 1989; 8:191-203.
24. Thorborg P. Skeletal muscle oxygenation and microflow [thesis]. Linköping, Sweden: University of Linköping, 1989.
25. Gustafsson U. Microcirculation in skeletal muscle during hypoperfusion [thesis]. Linköping, Sweden: University of Linköping, 1995.