In vivo måling af kapillærgennemstrømningsforhold under stigende håndgrebsbelastning ved hjælp af kontrastforstærket ultralydsteknik

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ABSTRACT August 2011:

Introduction: It is well known that exercise increases muscle blood flow and improve oxygen extraction, ultimately enhancing muscle oxygen supply. However, there is a large variation in oxygen extraction capacity (OEC) during exercise, which may be due to capillary transit time heterogeneity (CTTH). By means of a relatively newly developed contrast enhanced ultrasound technique (CEUS), accurate measurements of these vascular parameters (OEC and CTTH) can presumably be obtained, both at rest and during exercise.

Aim: The aim of this master thesis is to attempt to evaluate in vivo changes of capillary flow patterns in response to graded handgrip muscle work in 10 healthy subjects by means of CEUS. Furthermore, it is also the aim to demonstrate that CTTH is associated to oxygen extraction during graded handgrip muscle work – as far as is known, the first time that the vascular parametric model has been applied to CEUS. Additionally, mean transit time (MTT), muscle blood volume (MBV) and muscle perfusion (abbreviated MP – blood volume per unit tissue volume per unit time) were also measured. Secondly, beetroot juice was given to all subjects in order to test whether its high content of nitrate may reduce the oxygen extraction at the same work rate (80% of maximal handgrip force). This is believed to be regulated by pericytes.

Methodology: The study was performed in 10 volunteers. At the initial examination day, their individual maximal handgrip force was tested. This specific measurement was used to calculate 25% and 80% of their individual handgrip force, used on the subsequent experiment day. Capillary flow patterns of the flexor muscles in the forearm were measured, using CEUS. The contrast agent (SonoVue®), whose rheological property corresponds to red blood cells, facilitates an accurate measurement of hemodynamic parameters during rest

and exercise (25% and 80%). Additionally, after exogenously administered beetroot juice each subject repeated their individual 80% handgrip force.

Results: In response to graded handgrip muscle work, it is demonstrated that OEC gradually increases (rest to 25%: increasing from 0,30±0,03 to 0,42±0,04 ($p<0.05$); rest to 80%: increasing from 0,30±0,03 to 0,59±0,03 ($p<0.01$); from 25% to 80%: increasing from 0,42±0,04 to 0,59±0,03 ($p<0.01$)). Additionally, it is also demonstrated that CTTH gradually decreases in response to graded handgrip muscle work (rest to 80%: decreasing from 3,91s±0,88s to 1,73s±0,25s ($p<0.01$); 25% to 80%: decreasing from 3,42s±0,56s to 1,73s±0,25s ($p<0.01$)). Between rest and 25% handgrip muscle work, no significant change ($p>0.05$) is demonstrated. Furthermore, it is also shown that MTT gradually increases in response to graded handgrip muscle work (rest to 80%: increasing from 2,35s±0,24s to 4,00s±0,29s (<0.02); from 25% to 80%: increasing from 3,24s±0,49s to 4,00s±0,29s ($p<0.01$)). Between rest and 25% handgrip muscle work, no significant change ($p>0.05$) is observed. Most of the changes in MBV and MP were also associated with statistical significant increases. From rest to 25% MBV increased by 304%, and from rest to 80% MBV increased by 379% (both $p<0.01$). Between 25% and 80%, no significant change ($p>0.05$) is demonstrated. Between rest and 25%, MP increased by 195% ($p<0.01$). Between rest and 80%, MP increased by 316% ($p<0.01$). Additionally, a statistical significant increase was seen between 25% and 80% handgrip forces in MP of 62% ($p<0.01$).

No significant changes ($p>0.05$) between 80% handgrip muscle work with or without beetroot juice supplement were seen in any hemodynamic parameter.

Conclusion: On the assumption that this vascular parametric model is correct and it works with CEUS, it has been demonstrated in this master thesis that graded handgrip muscle work is associated with reduced CTTH and increased OEC (R^2-value of 0,96). Additionally, it has been demonstrated that graded handgrip muscle work is related to increased MBV, MP and MTT. Applying beetroot juice did not reveal any significant changes between 80% handgrip muscle works. Though not measured in this master thesis, pericytes possibly play a pivotal role in the regulation of capillary perfusion, thus potentially affecting CTTH and the efficacy of OEC.