TISSUE OXYGENATION DURING EXPERIMENTAL ARTERIAL GAS EMBOLISM

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ABSTRACT

Tissue oxygenation during experimental arterial gas embolism
Microvascular hemodynamic responses to arterial gas embolism (AGE) and local oxygen tensions (PO_2) have never been evaluated in vivo using intravital microscopy. Perfluorocarbon (PFC) has been advocated as a potential treatment of AGE. We have developed novel instrumentation and methodology to image and analyze AGE and PFC action in real time in the microcirculation of living rodents.
Rats were anesthetized and the cremaster muscle was prepared for intravital microscopy. Measurements were made before and after embolism protocol. Microvascular diameter, RBC velocity, blood flow and microvascular PO_2 were determined. All systemic parameters were continuously stored in computer via data acquisition system.
Blood pressure and heart rate were not significantly different before and after AGE. The first attempt of microembolization (15µL) did not result in arteriolar occlusion and multiple attempts were needed. Control diameter and blood flow averaged 53 25 µm and 13 10 nl/s, respectively. After AGE, these parameters changed to 53 24 µm and 1 3 nl/s. Arteriolar PO_2 averaged 59 19 mmHg during control and dropped to 34 27 mmHg (upstream) and 24 22 mmHg (downstream) after AGE. Eleven interstitial PO_2 changed from 44 22 to 23 20 mmHg and did not follow the drop recorded in the embolized arteriole when the PO_2 in nearby flowing vessels remained high. Our observations suggest that 1- arteriolar entrapment of air bubbles seems to be associated with prior endothelial cell damage due to first air bubble passage, 2- redistribution of blood in the muscle prevented severe hypoxia in some tissue areas after AGE, 3- PFC may be delivered by flowing blood vessels to tissue areas where blood flow is compromised due to partial or total microvessel occlusion, providing additional oxygenation.
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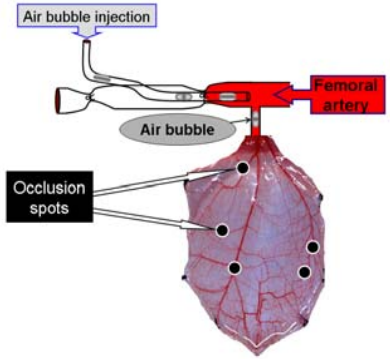
INTRODUCTION

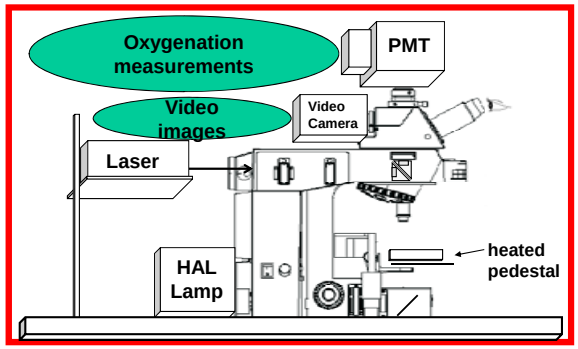
Decompression Syndrome is caused by the formation of air bubbles in blood and tissue due to a sudden change in ambient pressure. Air bubbles are typically formed in the venous circulation (venous gas emboli), but arterial gas emboli may also be associated. **Arterial Gas Embolism** (AGE), due to microbubble generation, can cause ischemia in the tissue/organ, in which the air bubbles are trapped, that leads to hypoxia and ultimately cell death. Understanding microvascular changes following AGE requires the knowledge of microvessel topology and geometry, blood flow, and oxygen tension levels (PO_2). We have developed novel instrumentation and methodology to image and analyze AGE and PFC action in real time in the microcirculation of living rodents.

METHODS

Intra- and extra-vascular PO_2 were measured by the *phosphorescence quenching technique*. Baseline measurements were made before and after bubble lodging. Perfluorocarbon (PFC) emulsion (Oxycyte, Oxygen Biotherapeutics, Inc.) was injected and studied *in vivo*.

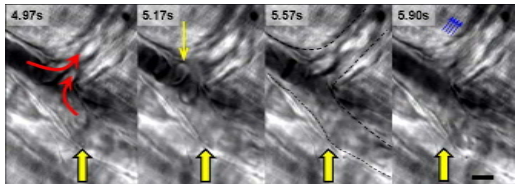


▶A microcannula positioned in the femoral artery directly injects air bubbles into ipsilateral exteriorized cremaster of an anesthetized rat. Selected arterioles were occluded to limit the networks that could be reached by the bubble injection.

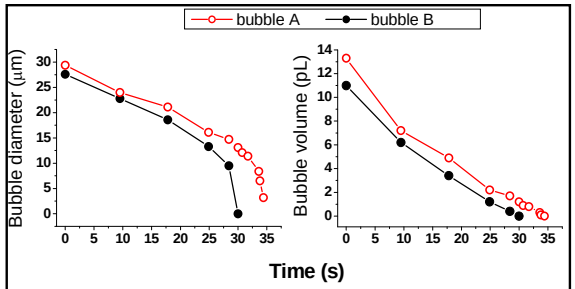


▶Schematic drawing of the system used to simultaneously collect systemic (mean arterial pressure, heart rate, central venous pressure, respiratory rate), microcirculatory data (arterial diameter, red cell velocity, intra- and extravascular PO_2) and bubble dynamics (volume and reabsorption time).

RESULTS



▶ Snapshots from a venule *in vivo* after PFC injection, showing the flow of PFC particles along the luminal surface of the endothelial layer. Vertical block arrow (yellow) on all the frames point to one of the particles moving on the endothelial surface.



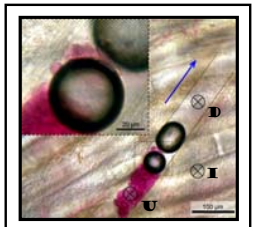
▶ Absorption of air bubbles of different sizes over time.

Emboli size and PO_2 measurements before and after AGE

	Arterioles			Associated Interstitium		Air Bubble	
	BL (mmHg)	Upstream (mmHg)	Downstream (mmHg)	BL (mmHg)	Embolism (mmHg)	L/D ratio	Volume (nL)
Mean	59.4	33.5	23.6	44.3	23.1	7.7	1.5
SD	19.0	26.6	21.8	22.1	20.3	6.2	2.4
n	16	16	9	11	11	8	8

Microhemodynamics measurements before and after AGE

	Baseline			Upstream			Downstream
	Diameter (µm)	RBC velocity (mm/s)	Blood flow (nl/s)	Diameter (µm)	RBC velocity (mm/s)	Blood flow (nl/s)	Diameter (µm)
Mean	53.3	8.1	12.8	53.0	0.9	1.3	56.6
SD	24.6	4.3	10.2	23.6	1.9	2.7	32.0
n	16	13	13	16	13	13	9



▶ Arterioles *in vivo* after AGE. Note the gap between air bubble and endothelium and that no RBCs are seen after the bubbles, suggesting plasma flow. The circles indicate interstitial (i), upstream (U) and downstream (D) locations where PO_2 was measured.

CONCLUSIONS

- We assessed the adequacy of intravital microscopy for studying and measuring PO_2 following AGE in the rat cremaster microcirculation, providing high resolution observations;
- Despite bubble lodging in some arteriolar networks, some interstitial areas did not become fully hypoxic due to some O_2 supplied by nearby vessels;
- Different therapeutics can be tested using this model, such as the use of Perfluorocarbon to improve tissue oxygenation and air bubbles reabsorption.

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