



## Response to “Letter to the editor regarding ‘Improvement of local microcirculation through intermittent Negative Pressure Wound Therapy (NPWT)’”



Dear Professor Boermeester, dear Professor Bader,

Thank you for your valuable feedback on our study “Improvement of local microcirculation through intermittent Negative Pressure Wound Therapy (NPWT)”.

Analysis of cutaneous microcirculatory changes during NPWT in humans has been quite challenging for different reasons. With our work we aimed to enrich the ongoing debate concerning the conflicting results from latest publications dealing with perfusion changes under an applied NPWT-dressing.

Various modalities have been introduced for the assessment of cutaneous microcirculatory changes. However, when it comes to analysis of gathered results, a one-dimensional approach like e.g. stand-alone Laser-Doppler Flowmetry (LDF) can be misleading. However, comprehensible analysis of combined LDF and white-light spectroscopy requires a detailed consideration of all the different parameters.

Like mentioned before, Kairinos et al. provided an explanatory framework, based on both profound physical principles and self-conducted research. One of the integral components of their explanation of how NPWT affects local circulation was, that compression of tissues results in a reduced perfusion. Beyond that, they stated that when tissue pressure was “not enough to totally occlude capillaries, then the Laser-Doppler records an increase in perfusion due to the increased velocity”, which they rated “not a true increase in perfusion” [1].

Our presented data (Table 1) further supports these considerations. When suction was applied the resultant tissue pressure (~30 mmHg) caused a compression of the local vasculature (no total occlusion) what lead to a (“not true”) increase in perfusion. This is comprehensible due to the constant levels of oxygen saturation during the “on phases” (During “off-phases” increase in perfusion is accompanied by an also increment of tissue oxygen saturation, therefore we rated this as a true increase in perfusion).

In our study the relative hemoglobin content increased when suction was applied. This was argued as an essential contrast to the considerations of Kairinos et al. who propagated a reduction of tissue blood content under an applied negative pressure dressing.

In one of the above-mentioned studies Kairinos et al. utilized a radioisotope that was applied intravenous after a circumferential

NPWT-dressing at the hand was activated. Subsequently the utilized gamma camera recorded a reduced perfusion in comparison to the contralateral hand (no suction) [2]. Kairinos et al. obviously neither performed direct measurements of the hemoglobin content under a semi-circumferential NPWT-dressing, like it was used in our presented study, nor they assessed the actual changes in local hemoglobin content right when the tissue was exposed to a certain pressure [1–3]. However, they completed their framework with the assumption that hemoglobin content also must be decreased when perfusion and therefore oxygen saturation are decreased due to the applied pressure.

We do agree with them. Vice versa, in view of our results during the “off-phases” measurements are completely in line with this assumption. Increased blood flow resulted in an improved oxygen supply due to a gradually increasing amount of hemoglobin (see Table 1 from 35 minutes to the end of measurements).

But changes in the relative hemoglobin content during the “on-phases” might appear rather irritating. Including all the other parameters we assume that the leap in relative hemoglobin content is the result of the above-mentioned change in the vessel diameter. The relative hemoglobin content is calculated from the amount of emitted spectroscopy light that is absorbed by the hemoglobin. Thus, absorption should be higher when vessel diameter is smaller, and concentration of erythrocytes is higher. Sole concentration of the same number of erythrocytes would not result in an increase in oxygen availability, like our measurements showed no increase in tissue oxygen saturation during the “on-phases”.

In conclusion, with regards to the “on-phases” the addition of further parameters in the assessment of microcirculatory changes under an applied NPWT-dressing further supports the hypothesis build up by Kairinos et al. to explain the changes in local perfusion.

Nevertheless, we would like to point out the remarkable improvement in cutaneous perfusion that could be achieved during the “off-phases” due to the utilization of an intermittent NPWT-protocol, in which context the application of combined LDF and white-light spectroscopy provided reliable data.

We hope our annotations and comments met your expectations and do contribute to the resolution of former contrasting results.

Sincerely,

## Appendix

Table 1

Detailed perfusion changes under the foam over the course of measurements ( $\Delta$  vs. BL), “on-phases” are marked grey, significant changes are marked bold, BL = baseline, CI = confidence interval, BF = blood flow, RBCV = red blood cell velocity, StO<sub>2</sub> = postcapillary oxygen saturation, rHb = relative hemoglobin content.

TIME	BF		RBCV		StO <sub>2</sub>		rHb	
	$\Delta$ vs. BL	CI	$\Delta$ vs. BL	CI	$\Delta$ vs. BL	CI	$\Delta$ vs. BL	CI
BL	1.000	-	1.000	-	1.000	-	1.000	-
5	<b>1.220</b>	1.042-1.399	0.995	0.938-1.051	0.952	0.889-1.015	<b>1.052</b>	1.013-1.092
10	<b>1.214</b>	1.047-1.382	1.021	0.938-1.103	1.010	0.936-1.083	<b>1.076</b>	1.044-1.107
15	<b>1.525</b>	1.111-1.938	1.077	0.925-1.229	<b>1.099</b>	1.035-1.164	<b>1.065</b>	1.024-1.106
20	<b>1.697</b>	1.130-2.264	1.135	0.946-1.325	<b>1.106</b>	1.018-1.194	<b>1.084</b>	1.033-1.136
25	<b>1.813</b>	1.123-2.502	1.159	0.931-1.386	<b>1.131</b>	1.022-1.239	<b>1.125</b>	1.058-1.192
30	<b>1.807</b>	1.158-2.457	1.153	0.938-1.368	1.099	0.984-1.214	<b>1.140</b>	1.068-1.211
35	<b>2.087</b>	1.327-2.848	1.212	0.959-1.465	<b>1.202</b>	1.110-1.295	<b>1.134</b>	1.067-1.202
40	<b>2.063</b>	1.348-2.777	1.202	0.977-1.427	<b>1.170</b>	1.071-1.269	<b>1.131</b>	1.058-1.205
45	<b>2.377</b>	1.446-3.309	1.274	0.983-1.565	<b>1.192</b>	1.072-1.311	<b>1.158</b>	1.074-1.242
50	<b>2.317</b>	1.414-3.221	<b>1.275</b>	1.004-1.547	<b>1.240</b>	1.097-1.382	<b>1.165</b>	1.084-1.246
55	<b>2.378</b>	1.400-3.356	1.272	0.988-1.556	<b>1.267</b>	1.080-1.455	<b>1.178</b>	1.093-1.263
60	<b>2.453</b>	1.421-3.486	<b>1.290</b>	1.006-1.574	<b>1.216</b>	1.082-1.350	<b>1.167</b>	1.087-1.248

## References

- [1] Kairinos N, et al. The flaws of laser Doppler in negative-pressure wound therapy research. *Wound Repair Regen* 2014;22:424–9.
- [2] Kairinos N, et al. Negative-pressure wound therapy II: negative-pressure wound therapy and increased perfusion. Just an illusion? *Plast Reconstr Surg* 2009;123:601–12.
- [3] Kairinos N, Solomons M, Hudson Da. Negative-pressure wound therapy I: the paradox of negative-pressure wound therapy. *Plast Reconstr Surg* 2009;123:589–98. discussion 599-600.

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