Can heat and cold be parameterized?
Clinical data of a preliminary study

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OBJECTIVE: The aim of this study was to demonstrate whether it is possible to objectively assess the effects of acupuncture by microcirculation-related parameters in the given clinical scenario, to evaluate the significance of the status of capillary perfusion prior to acupuncture for the treatment of a clinical cold pattern, and to evaluate the possible role of microcirculation-related parameters for the future parameterization of the traditional Chinese medicine (TCM) diagnosis.

METHODS: This prospective, uncontrolled, unblinded preliminary clinical trial included 32 elderly patients after surgical treatment for femur fractures. For acupuncture treatment the patients received acupuncture with the “leopard spot technique” on the stomach meridian (Liăngqí, S34/ST34). Measurements of microcirculation-related parameters (velocity, blood flow, haemoglobin, oxygen saturation) by white light spectroscopy and laser Doppler were performed prior to and after acupuncture treatment.

RESULTS: Two subgroups of patients after femur fracture could be identified: a low- and a high-perfusion group. Capillary flow velocity and blood flow were significantly augmented by acupuncture in the low-perfusion group only. In the high-perfusion group, there was no significant change of perfusion after acupuncture. The statistical analysis of all patients regardless of their pre-acupuncture perfusion status revealed no statistically significant alteration after acupuncture. The acupuncture effect may have been masked by the inhomogeneity of the overall group.

CONCLUSION: Microcirculation-related parameters may be valuable to measure acupuncture effects objectively and to characterize the vegetative functions prior to acupuncture so as to homogenize the comparison groups in clinical trials. In our example, a local cold pattern (low capillary perfusion of the leg) could be treated successfully by a point which enhances qi and blood flow, whereas in heat pattern (high capillary perfusion) this intervention had no such

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DOI: 10.3736/jcim20120508
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ISSN 1672-1977. Published by JCIM Press, Shanghai, China.
effect. Future studies may be directed to correlate the vegetative status as measurable by TCM vegetative parameters with the key symptoms of TCM diagnosis.

**KEYWORDS:** acupuncture therapy; microcirculation; femoral fracture; traditional Chinese medicine theories; blood flow velocity; hemoglobins; clinical trials

In current clinical acupuncture research, inclusion and exclusion criteria are conventionally based on the Western diagnosis only. Acupoints are selected according to the functional diagnosis of traditional Chinese medicine (TCM). Unfortunately, one Western diagnosis may represent a variety of TCM diagnoses resulting in a variety of possible treatment concepts for a given Western diagnosis. As a consequence there is great risk that the investigated acupuncture intervention might be suitable for some patients while not matching the TCM diagnosis of others. This might contribute to the fact that meta-analyses of acupuncture trials have so far not evaluated acupuncture treatments as being statistically significantly superior to controls[1,2].

It has been hypothesized by the Heidelberg (HD) Model[3,4] that the TCM diagnosis may be regarded as a vegetative functional status. Parameterization of the vegetative pretreatment status may therefore lead to better standardization and functional homogenization of patients in clinical trials, thus making them better comparable. Hence, there is a clear demand for measurable parameters that help parameterize the current vegetative state (the TCM diagnosis) of a patient in order to enable a more accurate definition of the study populations in acupuncture trials.

The backbone of TCM is the teaching of the eight guiding criteria which include “heat” (calor) and “cold” (algol), which refer to the dynamics of xue (blood). Xue is referred to as the “moved structural yin”. The functional power (energy) xue belongs, like qi or shen, to the almost untranslatable concepts of TCM[5,6]. Blood in TCM differs from the Western concept. According to the auxiliary vegetative definition of the HD Model, “xue is a form of ‘energy’ bound to circulating body fluids with functions such as warming, moisturizing, creating qi and nourishing a tissue”[3,4]. The functional status of this energy is evaluated by a variety of key symptoms, such as red tongue, fast pulse, and sparse, yellowish urine.

We have recently published a pathophysiological explanatory model for these clinical signs, which explains them as local and systemic indicators of enhanced microcirculation (MC)[7,8]. The HD Model leads to the hypothesis that “heat” is a state of augmented MC, whereas “cold” may represent a state of a low overall capillary perfusion (MC). Therefore, we tried to evaluate both the diagnosis of TCM (heat or cold states) as well as acupuncture effects by measuring MC-related parameters like capillary blood flow, velocity, oxygen saturation and haemoglobin content of the skin.

In our pathophysiological model of “heat” (calor), enhanced MC leads to the key symptoms of “heat” as taught in TCM: local signs of reddishness (tongue, skin) and a burning sensation like in a pre-inflammatory state. Systemic signs originate from a relative lack of fluid in central vessels, leading to higher pulse rate, sympathetic reactions (“liver” signs) and water-saving mechanisms (thirst, dry mouth and mucosa, dry constipation, sparse, yellow urine). The guiding criterion “cold” refers to the opposite state and symptoms, due to a general state of low perfusion (MC). The pathogenetic factor “cold”, however, refers to a reflex status with regional impairment of MC leading to loss of muscular power and stiffness, for example.

We chose the clinical scenario of fractures of the femur for a number of reasons. According to TCM theory, fractures are normally related to the diagnosis of cold patterns which according to the HD Model of TCM may be regarded as a regional lack of MC[3,4]. Also in Western medicine fractures of the proximal femur are a common and important cause of functional impairment, immobilization and a general increase of morbidity in elderly patients[9,10]. Postoperative recovery is often complicated

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by multiple injuries and high rates of avascular
necrosis of the femoral head due to disrupted
blood supply and non-union, all associated with a
deficient capillary blood flow. We have previously
demonstrated that acupuncture may lead to mea-
sureable gait improvement within this scenario[13]
and it was hypothesized that this was at least partly
due to an augmented capillary flow in the leg
after acupuncture. In TCM, acupuncture is used
to reduce the aforementioned complications and
complaints. According to a contemporary inter-
pretation of the Shanghan lun[4], a regional lack
of MC induced by the factor algol provokes humoro-
vegetative reactions with a general increase in
MC, also known as “reactive heat”. This correlates
with typical pathophysiological changes as part of
what is known as the post-operative inflammatory
response in Western medicine[1,4,7,10,15].

Some studies have already investigated MC in a
TCM context using white light spectroscopy and
laser Doppler[16,20]. The aim of this study was to
demonstrate if it is possible to objectively assess
the effects of acupuncture by MC-related parameters
in the clinical scenario of fracture of the femur,
to evaluate the significance of the status of capillary
perfusion prior to acupuncture for the treatment
of a clinical cold pattern, and to evaluate the
possible role of MC-related parameters for the
future parametrization of the TCM diagnosis.

1 Materials and methods

1.1 Study design The study was a prospective,
uncontrolled, unblinded preliminary trial including
32 elderly patients (25 females) with a mean age
of (86.4 ± 6.3) years after surgical treatment of
femoral fractures. The patients received acupuncture
using the “leopard spot technique” on Liangqiu
(S34/ST34), while resting in a supine position.
Measurement of MC parameters (blood velocity,
blood flow, haemoglobin and oxygen saturation)
was performed using white light spectroscopy and
laser Doppler (O2C device, LEA Medizintechnik
GmbH, D-35394 Gießen, Germany). Measurements
of all four variables were taken at 3 and 6 mm
tissue depth, respectively. In order to determine
the difference between baseline (pretreatment)
and post-intervention values the average of 15 consecutive
measurements (30 s) were taken each before and
after treatment. The flow chart of this study was
shown in Figure 1.

1.2 Inclusion criteria We included geriatric
patients from a rehabilitation ward with proximal
fracture of femur and a report of gait impair-
ment. We excluded patients with dementia (score
of the Mini-Mental State Examination <24)[21]
as well as patients on anticoagulation therapy in
order to minimize the risk of secondary haemorrhage
after blood-letting acupuncture. An informed
consent had been obtained from all patients. An
ethical approval had been obtained.

Figure 1 Flow chart of this study

1.3 Outcome measures The following MC
parameters were measured by O2C: haemoglobin
content, oxygen saturation, blood volume flow
and blood flow velocity.

1.4 Statistical analysis For statistical analysis,
SPSS 17 software was used. The variables tested
were blood velocity, blood flow, haemoglobin
and oxygen saturation. The oxygen saturation was
given in percentages. All other units of measurements
were relative, namely, arbitrary units (AU). The
null hypothesis was that there were no significant
changes in the variables after the intervention.
The studied sample did not present a Gaussian
distribution; therefore, significant differences were
assessed using the two-sided Wilcoxon signed-rank
test. The study was tested at a 5% significance level.

2 Results

2.1 High-perfusion and low-perfusion groups
The analysis of MC data revealed that the pre-
treatment baseline values of the patients could be
divided into two groups according to blood flow
(Figure 2). There were 26 patients in the low-
perfusion group. Low perfusion was defined as
within two standard deviations from the mean in
approximation to a plausible definition of normal
values[21]. This low-perfusion status was considered
to be normal in the given clinical scenario. The
high-perfusion group comprised of 6 patients with
6- to 17-fold increase in comparison to the mean.

2.2 Blood flow in the low-perfusion group Regarding
the blood flow and velocity there was an objective
effect of S34/ST34 in the low-perfusion group that
could be measured by MC-related parameters. After
acupuncture treatment, the mean blood flow
increased by 50.4% from 44.69 to 67.21 at a
depth of 3 mm, and by 16.8% from 79.85 to
93.23 at 6 mm depth. Figure 3 displays the
distribution of blood flow measurements at baseline
and after acupuncture intervention. The differences
were statistically significant (P = 0.002 at 3 mm
depth and P = 0.012 at 6 mm depth).
2.3 Blood velocity in the low-perfusion group
Regarding velocity there was also a measurable effect in the low-perfusion group. After acupuncture treatment the mean velocity increased by 17.6% from 13.96 to 16.42 at a depth of 3 mm, and by 11.9% from 20.38 to 22.80 at a depth of 6 mm. The differences were statistically significant \( P < 0.001 \) at 3 mm depth and \( P = 0.006 \) at 6 mm depth. See Figure 4.

2.4 Haemoglobin and oxygen saturation in the low-perfusion group
In the haemoglobin analysis there were no significant changes after acupuncture \( P = 0.757 \) at 3 mm and \( P = 0.751 \) at 6 mm. The oxygen saturation analysis revealed no relevant change. After acupuncture there was a 1% increase at 3 mm from 45.9% to 46.4% saturation \( P = 0.603 \) and an increase by 5.2% from 78.1% to 82.1% saturation at 6 mm \( P = 0.032 \).

2.5 High-perfusion group and total group
The presence of the high-perfusion group showed that different vegetative functional states may coexist within the same Western diagnosis. The statistical analysis of all patients (total group) regardless of their allocation to the low-perfusion or high-perfusion groups resulted in no significant alterations of blood flow, velocity, haemoglobin and oxygen saturation after acupuncture.

3 Discussion
Two groups of patients can be defined by MC-related values that show either low or high perfusion. According to TCM theory the complaints within this scenario are mostly due to cold patterns. The HD Model states that these correlate with impaired local MC, which is compatible with our results.

The point S34/ST34 is known to be suitable for cold patterns. As the low-perfusion group represents cold patterns, the enhancement of flow and velocity of MC in this group may reflect the suitability of this point for this condition as described in TCM theory, and the possibility of parameterizing this cold pattern by MC-related values within the chosen scenario.

Haemoglobin is predominantly located in venous branches of the capillaries. According to the HD Model this is correlated to the stagnation of blood, and this condition was not being treated so the result is compatible with the theory of TCM. The lack of effect therefore is as expected by the predictions of the functional hypotheses of the HD Model of TCM. Oxygen saturation levels also remained unchanged. This result was to be expected.
as even in the low-perfusion group the values were already high.

We hypothesized that the TCM diagnosis “heat” means high and “cold” means low perfusion. This means that S34/S34 is a suitable treatment rather than low perfusion. Mixing patients in whom the point is indicated with patients where it is not, may result in hiding existing acupuncture effects. According to the HD Model, not differentiating between with high-perfusion or low-perfusion patients is equivalent to mixing “heat” and “cold” patients. Consequently, the inclusion criteria should not only be defined by the Western diagnosis without regard to the given variety of TCM diagnoses (vegetative functional patterns), since this results in hiding the efficacy of acupuncture relating to the point[2]. This possibly illustrates a frequent principle in acupuncture studies failing to prove efficacy by defining the patient base regardless of the TCM diagnosis.

In order to determine whether heat and cold patterns may be distinguished by MC measurements, a careful examination should be carried out to correlate the classical diagnostic clinical patterns of the guiding criteria with MC-related parameters.

4 Conclusion

MC-related parameters may be worthwhile to measure acupuncture effects objectively and to characterize the vegetative functions (tissue regulation), as they are useful to define the vegetative pre-interventional state that in TCM is specified by a functional TCM diagnosis.

Future studies may be directed to correlate the vegetative status as measurable by objective vegetative parameters with the key symptoms of TCM diagnosis. Using MC-related parameters as inclusion criteria to homogenize the study groups functionally may drastically enhance the possibilities of acupuncture studies to detect existing acupuncture effects. Double- and triple-blinded studies may then be designed to exclude any doubts regarding placebo effects.

5 Competing interests

The authors declare that they have no competing interests.

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量化中医学中“寒”与“热”的初步临床研究

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目的：本研究探讨通过测量微循环相关指标客观衡量针刺效果的可能性，中医寒热刺治疗前后毛细血管灌注状态的意义，以及微循环相关指标在中医学诊断中的意义。

方法：本研究为前瞻性、非对照、不设盲临床研究。研究共纳入32例膝骨骨折手术后患者。这些患者均接受施于胃经梁丘穴的“医症点刺”针刺治疗。针刺治疗前使用舌光谱学及激光多普勒技术测量微循环相关指标如血流速率、血流量、血红蛋白含量、氧饱和度等。

结果：股骨骨折后，血流量、血流速度的不同。患者被分为两组，即高灌注组和低灌注组。高灌注组的毛细血管血流量及血流速率在针刺治疗后明显增加，而低灌注组则无明显改变。如果不考虑患者在针刺治疗前的灌注状态，统计分析表明所有患者针刺治疗前后的灌注状态均无明显改变，因此针刺的作用可能被患者的异质性所掩盖。

结论：微循环相关指标对于客观衡量针刺的治疗效果及描述针刺治疗前的营养性功能以评估比较不同组之间的差异具有重要意义。在本试验中，局部寒热（腹部的毛细血管低灌注）可以通过针刺补气血的胃经梁丘穴得到显著改善，而在热虚组（毛细血管高灌注）未见明显改变。未来的研究可以通过将中医学参数测量的营养状态与中医诊断中的主要证候相联系而得到更多结论。

关键词：针刺疗法；微循环；股骨骨折；中医学说；血流速度；血红蛋白类；临床试验