# Routine Microcirculation Measurements in Intensive Care Unit Patients and Validation by PiCCO Technology. ROUMI-study

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With this project, we aim to validate Cytocam-IDF imaging as a routine monitoring tool in critically ill patients. To this end, we will compare Cytocam-IDF imaging to an invasive hemodynamic monitorization tool (PiCCO) in terms of comparability and…

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Other condition |
| **Study type** | Observational non invasive |

## Summary

### ID

NL-OMON49817

**Source**
ToetsingOnline

**Brief title**
Comparison and Validation of Cytocam-IDF imaging with PiCCO technology.

### Condition

- Other condition
- Heart failures

**Synonym**
Circulation, organ perfusion

**Health condition**

Bloedsomloop

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** HagaZiekenhuis
**Source(s) of monetary or material Support:** Eigen middelen

## Intervention

**Keyword:** Circulation, Intensive Care, Microcirculation, PICCO

## Outcome measures

### Primary outcome

2.1 Primary Objectives:

o To investigate the correlation of microcirculatory parameter MFI measured with Cytocam-IDF with Cardiac Index measured using the trans-pulmonary hemodilution technique PiCCO.

o To assess the association between the microcirculatory parameters and macro-hemodynamic parameters during admission and interventions such as fluid resuscitation and vasopressor/inotrope/vasodilator administration.

### Secondary outcome

o To investigate the value and feasibility of routine monitoring of sublingual microcirculation as an early warning of clinical deterioration/improvement before the diagnosis can be made with laboratory, vital and hemodynamic parameters in critically ill patients.

o To determine the usability of Cytocam-IDF in ICU practice, contribution for clinician's self-confidence, ease, time and cost.

o To investigate the correlation between micro- and macro-circulatory alterations with global metabolic parameters, health status,

laboratory/hemodynamic/vital parameters

o To investigate the predictive value of microcirculation monitorization on the occurrence of complications like acute organ failure (renal failure, hepatic failure, encephalopathy, etc.) frequently seen in patients with fluid overload which may be visualized by measuring TVD and PVD alterations and compare to possible PICCO parameters for fluid overload.

o To investigate the predictive value of microcirculatory alterations on patient survival.

o To create a cut-off range for total vessel density, perfused vessel density and proportion of perfused vessels

# Study description

**Background summary**

The microcirculation is the final destination of the systemic circulation and is comprised of microvessels with a diameter less than 20 µm consisting of arterioles, venules, and capillaries. Under physiological conditions, the microcirculation consists of about 10% of circulating blood and plays a vital role in oxygen transport to the tissue, carbondioxide ($CO_2$) removal, inflammation, hemostasis, and substrate and hormonal transport. Furthermore, capillaries are the primary interface between the circulating blood and the parenchymal cells. Hand-held videomicroscope (HVM) techniques are used to directly visualize the microcirculation of all organ surfaces. The sublingual area is the most commonly used target of HVMs due to its easy accessibility although other organ surfaces also in surgery have been explored. Sublingual area may represent the global microcirculation since it origins from the same point where the intestinal system stem from and blood supply of this area is provided by the arteria carotis which also provide blood to the brain.
HVMs are useful to directly monitor the convective and diffusive function of the microcirculation, which is quantified as the flow of red blood cells (RBCs) in the capillaries (mean flow index and proportion of perfused vessel (PPV)) and the density of perfused capillaries (also referred to as functional capillary density(FCD)), respectively. Blood flow in the microvessels indicates the quality of perfusion and is described as microvascular flow index (MFI).

Heterogeneity index (HI) is used to estimate the flow heterogeneity in the microcirculation specifically seen in conditions of sepsis and is calculated as the difference between the highest and lowest MFI divided by mean MFI. Overall, the perfusion of the tissues depends on the amount, distribution, and diameters of the capillaries. The density of the vessels is estimated as the proportion of total vessels present in the field of view. The total vessel density (TVD) is calculated as the total length of vessels divided by the total surface area of the field of view as units mm/mm2. Perfused vessel density (PVD) is estimated as the proportion of perfused vessels divided by the TVD. The perfusion of a tissue depends on the number, distribution, and diameters of the capillaries in combination with blood viscosity and driving pressure across the capillaries. There are two main hemodynamic principles governing how oxygen in red blood cells reaches the tissue cells; the first is the convection based on red blood cell flow, and the second is the diffusion distance oxygen must travel from the red blood cells in the capillaries to the parenchymal cells. Convection is quantified by measurement of flow in the microvessels, and diffusion is quantified by the density of the perfused microvessels (FCD). The convection and the diffusion are both deteriorated in the critically ill patients which in turn leads to impaired tissue oxygenation. Therefore, monitoring the microcirculation in combination with macrohemodynamic parameters provide a comprehensive evaluation of the cardiovascular system notability in critically ill patients.

The fundamental aim of resuscitation of critically ill patients from states of shock and severe inflammatory conditions is to restore tissue perfusion and oxygenation [10]. In order to maintain optimal tissue perfusion, large vessels should transmit the adequate blood from heart into the tissues. This transport is largely depends on the function of the heart, resistance of the vessels and the amount of the intravascular volume. Based on the guidelines regarding the resuscitation of shock, intravenous fluids and vasopressors are used to improve tissue perfusion by increasing heart contractility and vascular resistance, and expanding intravascular volume. Systemic macro-hemodynamic parameters such as blood pressure, heart rate, cardiac output, stroke volume, systemic vascular resistance are conventionally used to assess and monitor resuscitation success in routine clinical practice, assuming that tissue perfusion and oxygenation recover parallel to systemic hemodynamic parameters. However, only maintaining the tissue perfusion is not enough to achieve tissue oxygenation which may remain impaired despite the correction of systemic circulatory parameters. Unfortunately, normalization of routinely used macrocirculatory parameters may not always be accompanied with normalization of microcirculatory parameters resulting in an unknown under-resuscitation of the patient. Inconsistency between micro- and macrocirculation is a key feature of shock status has been recently defined as *loss of hemodynamic coherence*. Various studies have shown that improvement of the macrocirculation in conditions of shock can occur independently from the microcirculatory blood flow, especially in critically ill patients and has shown to be an independent predictor of organ dysfunction and adverse outcome. Direct visualization of sublingual microcirculation using hand-held video microscopes such as the Cytocam-IDF (Braedius Medical, Huizen

the Netherland) imaging device can be used to identify such loss of hemodynamic coherence and may provide an opportunity to monitor resuscitation therapy with vasopressors and fluids by potentially preventing unnecessary and inappropriate administration of large volumes of fluids and/or vasopressor therapy. The reason behind that is the published studies which showed the success of Cytocam-IDF in displaying loss of hemodynamic coherence in critically ill patients while macrohemodynamic parameters cannot. Moreover, Cytocam-IDF allows more physiologically based approaches for the diagnosis and treatment of intensive care patients.

For the reasons stated the importance of using the hand held video microscopes for measuring sublingual microcirculation has been underscored by intensive care specialist as witnessed the reason publication in Intensive Care Medicine of international guidelines for sublingual microcirculation measurement endorsed by the European Society of Intensive care Medicine. Despite the usefulness of microcirculatory monitoring in critically ill patients, however, it is as yet not part of routine monitoring in intensive care where systemic hemodynamic parameters are still the main variables being monitored, and for this reason, it requires validation. PiCCO monitorization is one of the most common invasive technique used to assess systemic hemodynamic status in severe critically ill patients. Although invasive hemodynamic monitorization is adopted as the gold standard in intensive care, during the few last years, monitorization of macro-hemodynamic parameters have evolved considerably from invasiveness to less or no invasiveness to decrease the complications like infection, bleeding, thrombosis, pneumothorax. In addition, continuous and real-time measurements of macro-hemodynamic variables are preferred to intermittent macro-hemodynamic parameters. Emphasizing non-invasive nature, easy to apply, and success in detecting hemodynamic coherence in critically ill patients, microcirculatory imaging with Cytocam-IDF becomes a candidate for integral hemodynamic monitorization. However, microcirculatory imaging has not been validated with an invasive hemodynamic monitoring tool such as PiCCO technology.

To use a new technique, parameter or device as a monitoring method in clinical practice, it should fulfil the conditions safety, efficacy, effectiveness, and efficiency. Once the technique meets these conditions, clinical appraisal and efficacy are possible. Efficacy indicates whether the technique indeed measures what it claims to measure, and this has been shown in several studies in the literature. A gold standard should exist to evaluate the efficacy of the measurement, and currently, this can only be a systemic hemodynamic variable such as cardiac output or mean arterial pressure. Based on such information the clinical utility of the technique on the diagnosis of circulatory compromise can be evaluated. Another crucial point to be evaluated is the safety. Due to its non-invasive nature (an optical measurement under the tongue), however, Cytocam-IDF imaging is not associated with any adverse effect. Measurement of the microcirculation using the device requires only a disposable sterile cap to be placed on the light guide of microscope making it a cheap technique to implement. The technique is easy to use and can also be used by nurses and circulation practitioners.

With this project, we aim to assess the correlation of PiCCO technology and Cytocam-IDF imaging as a routine monitoring tool in critically ill patients with circulatory compromise. To this end, we will compare Cytocam-IDF imaging to an invasive hemodynamic monitorization tool (PiCCO) in terms of comparability and linearity in critically ill patients. In addition, we will create a cut-off range for total vessel density, perfused vessel density and proportion of perfused vessels since there has been no range defined yet so as to assess the severity of the microcirculatory dysfunction. Therefore, we sought to examine the most common parameters used in PICCO viz. cardiax index and (stroke) volume index to respectively microvascular flow index (MFI) and the vessel density parameters of sublingual microcirculation viz. total vessel density and perfused vessel density. To our knowledge, this study is the first that compares microcirculatory parameters with the invasive macro-hemodynamic parameters obtained by a gold standard and invasive technique in critically ill patients.

### Study objective

With this project, we aim to validate Cytocam-IDF imaging as a routine monitoring tool in critically ill patients. To this end, we will compare Cytocam-IDF imaging to an invasive hemodynamic monitorization tool (PiCCO) in terms of comparability and linearity in critically ill patients.

### Study design

o Single-centre, prospective, observational study in the adult Intensive Care Unit.

### Study burden and risks

Assessment of sublingual microcirculation is a non-invasive procedure which takes a few minutes to perform associated with no risk or burden to the patient. Additional blood tests will not be required. The patients will have been treated and diagnosed using conventional modalities

## Contacts

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**Scientific**

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# Trial sites

## Listed location countries

Netherlands

# Eligibility criteria

**Age**
Adults (18-64 years)
Elderly (65 years and older)

## Inclusion criteria

o Should be under PiCCO monitorization with routine clinic indication
o Should be older than 18 years
o Be suitable for monitoring in the intensive care unit
o Eligible for sublingual microcirculatory evaluation (not to have maxillofacial injury, bleeding in the mouth)

## Exclusion criteria

o <18 years old
o Woman of childbearing potential with a positive pregnancy test
o Refusal to participate in the study or demand to end study for any reason
o Resistance during the measurements of sublingual microcirculation will lead to end of the study.
o Moribund
o Intra-cardiac shunts, aortic aneurysm, aortic stenosis, mitral or tricuspid insufficiency,
o Pneumonectomy, macro lung embolism

# Study design

## Design

**Study type:** Observational non invasive

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| Masking: | Open (masking not used) |
| Control: | Uncontrolled |
| Primary purpose: | Diagnostic |

## Recruitment

NL

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| Recruitment status: | Recruiting |
| Start date (anticipated): | 30-05-2020 |
| Enrollment: | 30 |
| Type: | Actual |

# Ethics review

Approved WMO

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| Date: | 23-12-2019 |
| Application type: | First submission |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

Approved WMO

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| Date: | 29-07-2020 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

Approved WMO

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|---|---|
| Date: | 15-04-2022 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br>metc-ldd@lumc.nl |

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| Approved WMO Date: | 17-03-2023 |
| Application type: | Amendment |
| Review commission: | METC Leiden-Den Haag-Delft (Leiden)<br><br>metc-ldd@lumc.nl |

# Study registrations

## Followed up by the following (possibly more current) registration

No registrations found.

## Other (possibly less up-to-date) registrations in this register

ID: 23604
Source: NTR
Title:

## In other registers

| Register | ID |
|---|---|
| CCMO | NL70350.098.19 |
| OMON | NL-OMON23604 |