#### Traumatic Brain Injury (TBI)

A microdialysis catheter was placed in the penumbra surrounding a traumatic brain lesion. A decrease in CPP caused an increase in LP-ratio above the thin horizontal line, which is the threshold for ischemia (>25). A subsequent increase in CPP improves LP-ratio. The pattern repeats itself over time. The important finding is that a seemingly adequate CPP of e.g. 70 turns out to be greatly in adequate for maintaining capillary perfusion in the penumbra of this patient.Microdialysis alerted the staff to observe the ischemia of the brain tissue and gave them the chance to adjust the CPP in order to obtain adequate perfusion. (Courtesy of Prof. C-H Nordström and Prof. U Ungerstedt)





#### Vasospasmafter Subarachnoid Hemorrhage (SAH)

The graph shows a patient suffering SAH from a ruptured aneurysm. A microdialysis catheter was placed in the region of the parent vessel territory. LP-ratio initially decreased to below ischemic levels (shaded area). A sudden increase was followed by "pulsating" changes in LP-ratio, discriminating vasospasm from ischemia. Subsequently Glycerol values increased dramatically above normal levels (shaded area) which indicated damage to cell membranes. The Transcranial Doppler (TCD) indicates vasospasm considerably later than microdialysis. (Courtesy of Prof. C-H Nordström and Prof. U Ungerstedt)

#### Intraperitoneal Microdialysis Monitoring

Intraperitoneal metabolic sampling with microdialysis provides a promising diagnostic strategy. Analyzing lactate and lactate/pyruvate ratio offers several advantages in the critical periods postoperatively.

Lactate/pyruvate ratio over 20 and Intraperitoneal lactate values over 3.5 and 4 mM in the first 48 hours could in this study be an indicator of a surgical complication, such as anastomotic leakage. (Jansson K et al. J of Surgery and Surgical Research. 2019;)





#### Free Osteocutaneous Fibula Flap

Two hours post operatively the Microdialysis values indicated ischemia whereas no clinical signs of ischemia or venous obstruction were observed. During the following hours the Microdialysis values deteriorated with a high Lactate and low Glucose level. The decision was taken to re-operate, a venous thrombosis was found and a new anastomosis was performed. The flap survived.

(Courtesy of Dr. H Birke Sørensen)

#### Drug Monitoring with Microdialysis

Microdialysis catheter placed in in Subcutaneous Adipose tissue. Figure shows concentration difference of Linezolid in obese versus non-obese patients. (Simon P. et al. Journal of Clinical Medicine, 2020)



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## Microdialysis exploring tissue chemistry



# *L* dialysis

## Monitoring chemical events in individual tissues and organs

### The Microdialysis System

#### Overview

A any diagnostic and therapeutic decisions in clinical practice are based on measuring substances in blood, even though Mmost biochemical and pharmacological events take place in individual tissues and organs. Microdialysis offers a unique possibility to monitor tissue and organ chemistry and is rapidly making its way into clinical practice and medical research.

#### Metabolic tissue monitoring

Microdialysis enables monitoring of essentially any chemical event taking place in the interstitial fluid. Samples can be collected and analyzed continuously to get trends of in vivo tissue chemical changes. The advantage of microdialysis is the possibility to detect early signs of tissue ischemia. When the supply of glucose and oxygen is inadequate, it is followed by an instant increase in the ratio of Lactate and Pyruvate (LP-ratio), which is a well-known marker for tissue ischemia

#### Minimally invasive

A thin microdialysis catheter is introduced into the tissue and a microdialysis pump perfuses the interior of the catheter with a physiological fluid. The semipermeable membrane at the distal end of the microdialysis catheter functions like a blood capillary. Chemical substances from the interstitial fluid diffuse across the membrane into the perfusion fluid, which is ccollected in microvials and analyzed bedside as often as needed.

🖵 he basic setup for collecting microdialysis samples consists of a microinfusion pump and a microdialysis catheter. Perfusion fluid is pumped through the catheter into a microvial where the sample is collected and then transferred to the analyzer. The analysis results are displayed as trend curves on the screen.

#### Microdialysis Catheters

Catheters with different membrane and shaft lengths, as well as different membrane properties, are available for various applications. The membrane cut-off are available in 20& 100 K Daltons, which means that both small metabolites as well as large molecules, such as cytokines, can be collected.

#### Pumps

There are two different pumps for clinical use, one with a fixed standard flow rate of  $0.3 \,\mu\text{L/min}$  and one with an adjustable flow rate of  $0.1 - 5 \,\mu\text{L/min}$ . Low flow is used to obtain high recovery of the substances and high flow makes it possible to use shorter sampling intervals.

#### Microdialysis Analyzer

The ISCUSflex Microdialysis analyzer is rapidly analyzing the microdialysis samples. The analyzer has a touch screen showing the results as trend curves, for easy detection of tissue ischemia and other complications in order to guide therapy and determine the effect of therapeutic interventions.

#### Markers for tissue energy metabolism, lipolysis and cell damage

Glucose, Lactate & Pyruvate are markers for ischemia, hypoxia, mithocondrial dysfunction and hypoglycemia in peripheral & central tissues

Glycerol is a marker for lipolysis in adipose tissue and cell membrane damage in most other tissues.

Glutamate is a marker for cytotoxicity in brain tissue.

Urea is a marker for urea clearance during hemodialysis or can be used as reference marker.



A Microdialysis Catheter (1) is inserted into the tissue and connected to the 106 or 107 Microdialysis Pump (2). Perfusion fluid from the pump equilibrates with the extracellular fluid through the dialysis membrane of the catheter. Samples are collected in Microvials (3), and rapidly analyzed in the ISCUS<sup>flex</sup> Microdialysis Analyzer (4).

Dialysis has designed different catheters approved for microdialysis in brain, adipose tissue, resting skeletal muscle, intraperitoneal Mcavity, and hepatic tissue. Clinical research has been performed in many other tissues and organs with local ethical committee approvals (marked with \*below).

#### Identifying brain ischemia

By introducing microdialysis catheters into the brain after severe trauma or subarachnoid hemorrhage, it is possible to monitor brain tissue metabolism in the tissue at risk, i.e. the penumbra of a lesion or a region affected by vasospasm. Changes in the LP-ratio and Glucose in these vulnerable areas makes it possible to continuously evaluate therapeutic interventions and decrease the risk of secondary insults. Consensus statement from the 2014 International Microdialysis Forum. Hutchinson PJ et al. Intensive Care Med. 2015 Sep

#### Saving free flaps

Intraperitoneal cavity maxillofac Surg. 2019 Aug.) Liver **Resting skeletal** muscle

Adipose tissue

Brain

Skin

\*Bone



\*Heart \*Kidney

\*Knee \*Lung

#### Monitoring post transplantation complications tion Surgery of Liver or Pancreas (Kjøsen G et al. PLoS One. 2021 Mar 11)

Microdial ys is allows frequent sampling of substances involved in Glucose and lipid metabolism without remov-involved involved in Glucose and lipid metabolism without remov-involved involved involved in Glucose and lipid metabolism without remov-involved involved involved in Glucose and lipid metabolism without remov-involved involved inving any blood. This makes it possible to perform monitoring of Glucose, Lactate, Pyruvate, and Glycerol in various research fields such as Ortopheadic Surgery, Drug Monitoring and Metabolic research

The benefit of monitoring tissue chemistry is to detect pathological events before they manifest themselves as clinical



Postoperative monitoring of free flaps using a microdialysis decision algorithm allows early diagnosis of anastomotic complications. It is a clinically feasible and sensitive monitoring method for microvascular flaps, allowing surgical revision to be undertaken before clinical alteration takes place. (Birekenfeld et al J Cranio-

#### Detecting complications after abdominal surgery

Intestinal ischemia may be detected by placing a microdialysis catheter in the intraperitoneal cavity. Intraperitoneal Microdiaysis studies have found high values of lactate and lactate/pyruvate ratio in anastomotic leak patients after the fourth postoperative day. (Jansson K et al. Scand J Gastroenterol. 2019 Oct).

Microdialysis is a new promising method for early detection of postoperative complications after Transplanta-

#### Microdialysis monitoring within Clinical research and Drug Development