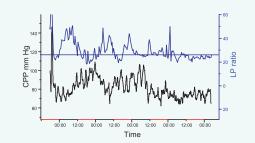
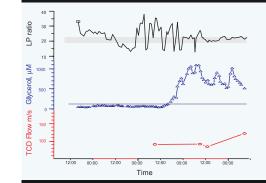
Graphically displayed results for easy interpretation

Traumatic Brain Injury (TBI)

 $A\,microdialysis\,catheter\,was\,placed\,in\,the\,penumbra\,surrounding\,a\,traumatic\,brain\,lesion.\,A$ decrease in CPP (blackline) caused an increase in LP-ratio (blue line) 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 inadequate 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)



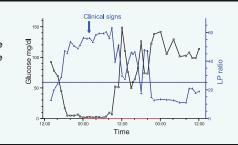


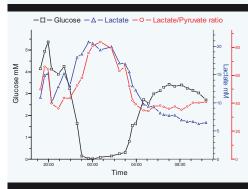
Vasospasmafter Subarachnoid Hemorrhage (SAH)

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 Ischemia after right sided Hemicolectomy

A dramatic decrease in Glucose and increase in LP-ratio, indicated severe ischemia of the gut, 5 hours before clinical signs were evident. An adjustment of oxygenation improved the condition and eventually brought Glucose and LP-ratio back to normal levels. (Jansson K et al. Scand J Gastroenterol. 2003;38:1007-1011)





Free Osteocutaneous Fibula Flap

 $Two \ hours \ post \ operatively \ the \ Microdialys is \ values \ indicated \ is chemia \ whereas \ no \ clinical$ 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.

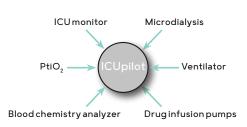
(Courtesy of Dr. H Birke Sørensen)

LABpilot - software for interpreting data

Visualize, compare and view your microdialysis data in a graphical user interface. Drag and drop any recorded variables into the same graph to enable faster interpretation. Formulate a hypothesis and test it immediately.

ICUpilot - software for multi modal monitoring

ICUpilot is a unique tool for multimodal point-of-care monitoring. ICU instruments (e.g. pulse, blood pressure, ICP, CPP) as well as your Microdialysis analyzer can be connected to a separate computer for on-line analysis and comparison of all data collected bedside during the entire treatment of the patient.



Courses and Symposiums

MDialysis offers regularly courses and symposiums for clinical researchers, surgeons, intensivists and nurses in different applications. For information and registration visit our web site www.mdialysis.com.

Bibliography

One of the first papers on microdialysis was published in 1974 by U. Ungerstedt and C.H. Pycock. Since then, more than 14,000 scientific papers have been published on the technique - among them some 2500 clinical investigations. You can find a regularly updated bibliography on clinical applications on our web site www.mdialysis.com

M Dialysis AB

M Dialysis is the leading company devoted to the development, manufacturing and marketing of the Microdialysis technique. The company was originally founded in 1984 under the name of CMA Microdialysis and was the first company in the world to market Microdialysis products and know-how. Consumables, instruments and computer software are developed and manufactured in Sweden with ISO 13485 certification. M Dialysis offers an extensive portfolio of CE approved and 510(k) cleared microdialysis products for clincal use in tissues and organs. The core technology and the essential peripherals are protected by US and International patents.

Microdialysis monitoring tissue chemistry



M Dialysis AB

Hammarby Fabriksväg 43 SE-120 30 Stockholm, Sweden Tel: +46 8 470 10 20 E-mail: info@mdialysis.se

US Office: 73 Princeton Street, North Chelmsford, MA 01863, USA Tel: (866) 868-9236, (978) 251-1940 Fax: (978) 251-1960, E-mail:usa@mdialysis.com www.mdialysis.com



Monitoring chemical events in individual tissues and organs Continuous in vivo sampling

Analyzer

.. Microdialysis can be used in essentially any tissue or organ

Many diagnostic and the rapeutic decisions in clinical practice are based on measuring substances in blood, even though most 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.

The 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.

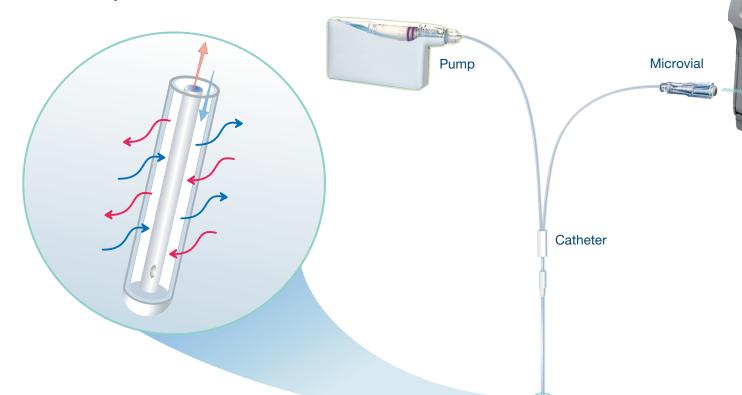
▲ Dialysis has designed different catheters approved for microdialysis in brain, adipose tissue, resting skeletal Muscle, intraperitoneal cavity, and hepatic tissue. Clinical research has been performed in many other tissues* and organs with local ethical committee approvals (marked with *).

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

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



Microdialysis Catheters

Catheters with different membrane and shaft lengths, as well as different membrane properties, are available for various applications. The membrane cut-off rare available n 20,000 & 100,000 Daltons, which means that large molecules, such as cytokines, can also be collected.

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

Bedside Analyzer

A dedicated bedside analyzer is rapidly analyzing the microdialysis samples. The analyzer has a touch screen showing the results as trend curves, making it easier to detect signs of tissue ischemia and other complications in order to identify patients at risk, guide therapy and determine the effect of the rapeutic interventions.

Markers for tissue energy metabolism, lipolysis and cell damage

· Glucose, Lactate and Pyruvate are markers for ischemia, hypoxia, mithocondrial dysfunction and hypoglycemia in peripheral

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.

rea is a marker for urea clearance during hemodialysis.

he benefit of monitoring tissue chemistry is to detect pathologic vents before they manifest themselves as clinical signs. This offers ar pportunity to start treatment hours or days earlier than when relying on clinical signs only,

Identifying brain ischemia

Adipose tissue

*Breast tissue

*Heart

*Kidney

*Knee

Intraperitoneal cavity

Resting skeletal muscle

Brain

Liver

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 Glycerol in these vulnerable areas makes it possible to continuously evaluate therapeutic interven- tions and decrease the risk of secondary insults. Monitoring of brain metabolism will permit • targeted therapy and may possibly minimize iatrogenic adverse effects by making better use of powerful therapies (Vespa P. Curr Opin Crit Care. 2006 Apr;12(2):119-23).

Saving free flaps

• Microdialysis is a clinically feasible and sensitive monitoring method for all kinds of micro vascular flaps, especially for those in which clinical observation is difficult or impossible Setala L et al. J Reconstr Microsurg. 2006 Feb;22(2):87-96). It is a reliable technique for early detection of ischemia after reconstructive surgery. When the delivery of Glucose and oxygen is reduced, there is an immediate increase of tissue Lactate and a decrease of Pyruvate and Glucose indicating signs of ischemia. Early detection of flap ischemia allows early surgical intervention.

Detecting complications after abdominal surgery

 Intestinal ischemia may be detected by placing a microdialysis catheter in the intraperitoneal • cavity. Clinical signs of peritonitis, bowel ischemia, and anastomosis leakage are preceded • by chemical changes, for example an increasing LP-ratio, which serves as an early marker of splanchnic ischemia (Jansson K et al. Scand J Gastroenterol. 2003;38:1007-1011).

Diagnosing post transplantation complications

Intrahepatic microdialysis is a new promising method for early detection of postoperative complications such as liver ischemia, graft rejection, or cholangitis after liver transplantation (Nowak G et al. Br J Surg. 2002; 89(9):1169-75)

Monitoring metabolic disorders

Microdialysis allows frequent sampling of substances involved in Glucose and lipid metabolism without removing any blood. This makes it possible to perform continuous monitoring • of Glucose, Lactate, Pyruvate, and Glycerol in new borne babies (Baumeister et al. Pediatrics • 2001;108;1187-1192), diabetic patients (Rajamand Net al. Diabetes, Obesity and Metabolism, 2005, 7, 525-535) and in critically ill septic patients (Levy B et al. Lancet 2005; 365: 871-75).

