Contents

AAPS Microdialysis Focus Group Steering Committee 2
Goals & Objectives

Microdialysis Technique Overview – Probe Calibration 4

“Special Feature”: Open Flow Microperfusion 9

“Pearls of Wisdom”: A Scientist Profile – Elizabeth de Lange, PhD 13

Role of Microdialysis in the Research of Young Scientists – 18
A Doctoral Candidate’s Profile – Nimita Dave, PhD

Microdialysis-Related Upcoming Meetings 20

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AAPS Microdialysis Focus Group
Leadership

The Microdialysis steering committee consists of a Chair, Chair-Elect, Past-Chair and 11 steering committee members. The leadership begins with serving as a Chair-Elect, then moving on to the Chair and ends with serving as a Past-Chair, each of which is a 2 year commitment. All steering committee members serve for 2 years. The current MD FG steering committee including its leaders boasts a diverse group including 3 graduate students, 1 clinical scientist, 4 members from academia, 4 members from the industry and 2 members from the Government.

The goals and objectives of the Microdialysis Focus Group include:
- Designing programming for AAPS Annual Meeting and NBC conference
- Attracting more members to the MD FG
- Encouraging student participation
- Collaboration with other FGs for joint programming

In 2013, the MD FG continues to pursue its goals and objectives through several avenues. We have active discussions via a teleconference held once every 2 months and are participating in social media to enhance our visibility to the larger scientific community (through a LinkedIn group) and to the AAPS membership (through a MD FG discussion board). MD FG representation at the NBC and Annual Meeting Jamborees, and consistent development of programs for AAPS meetings and AAPS co-sponsored meetings has become routine among MD FG steering committee members.

Probes magazine: The Microdialysis Focus Group steering committee proudly presents the third issue of the Focus Group magazine, “Probes”. This magazine provides an update of the activities of the MD FG. In support of the larger AAPS goal of enhancing student and young scientist participation, the profile of a Doctoral candidate is included in each issue. In this particular issue, we are pleased to present a summary of the graduate research work of Dr. Nimita Dave. Dr. Dave completed her Ph.D. in April of this year under the guidance of Dr. Pankaj Desai at the University of
Cincinnati. Of note, Nimita was honored at the 2012 AAPS Annual Meeting by receiving the PPDM section Poster Podium Award.

We also proudly present in this issue a profile of Dr. Elisabeth de Lange (in the section entitled, “Pearls of Wisdom”). Dr. de Lange is a recognized leader in the development and application of microdialysis to understand the PK/PD aspects of CNS agents. She is active in the leadership of AAPS, having served as a Chair of the Microdialysis Focus Group in 2007, she is currently the Past-Chair of the PPDM Section and Chair of Annual Meeting Programming Committee.

In recognition of Dr. Dave’s and Dr. de Lange’s recent accomplishments and leadership at AAPS, we dedicate this issue of “Probes” to them.

This issue also features a novel target site sampling technique called “Open Flow Microperfusion” under our “Special Features” section. This novel technique has now made possible sampling a large variety of molecules ranging from small molecules to large proteins and peptides.

On behalf of the design committee of this issue of “Probes” magazine, “ENJOY READING”!
Microdialysis Technique Overview - Probe Calibration

By Siva Ram Kiran Vaka, Ph.D, Scientist- Formulation R & D, Kashiv Pharma LLC, Piscataway, NJ.

Calibration of microdialysis probes is very important, as it determines the relationship between the measured concentration of a solute in the dialysate that is collected as it exits the probe vs. the solute concentration in the tissue fluid that is being sampled by the probe. The sampled tissue fluid is generally referred to as ECF (Extracellular Fluid). The figure below illustrates the general concept of microdialysis, illustrating liquid flow through a concentric probe (left), and the bi-directional, diffusion-driven, movement of solutes across the dialysis membrane (right).

The general equation that relates ECF and dialysate concentrations is:

\[ C_{\text{ecf}} = C_{\text{dialysate}} \times \frac{1}{\text{recovery}} \]

Thus, measurement of probe recovery is essential to probe calibration. There are several methods (in vitro and in vivo) reported in the literature with regard to the measurement of probe recovery. These are enumerated below.

1) **In vitro recovery:** Generally, probe recovery is measured as loss of solute from the perfusion solution or as gain of solute from a bulk solution sampled by the probe. The respective equations for these two recovery measurements are:

\[
\text{Recovery by loss (R}_L) = \frac{(C_{\text{perfusate}} - C_{\text{dialysate}})}{C_{\text{perfusate}}}
\]

\[
\text{Recovery by gain (R}_G) = \frac{C_{\text{bulk solution}}}{C_{\text{dialysate}}}
\]

It is essential that probe recovery by loss and gain be equivalent, since recovery by gain cannot be measured in vivo. There are several factors that influence probe recovery in vivo and which should be investigated *in vitro* first in order to optimize probe performance in vivo. These factors include perfusate flow rate, perfusate composition, characteristics of the semi-permeable membrane, probe geometry and tubing characteristics (length and diameter). Optimization of microdialysis conditions in vitro maximizes probe recovery and provides reasonable assurance of consistent probe performance in vivo.

2) **In vivo recovery:** The true relation between the dialysate and extracellular concentrations of a drug is dependent on the conditions in the tissue sampled and cannot be interpreted directly from the *in vitro* studies. This is because there are additional factors that play a vital role in determining solute recovery *in vivo*. These include diffusion of drug through the extracellular fluid of a tissue, uptake into cells, metabolic conversion, active transport across membranes, extent of tissue vascularization and blood flow.

Some of the commonly used calibration methods used in vivo are discussed below.

**a) Ultraslow flow rate method**

*In vivo*, if steady-state concentrations are present in the tissue, the flow rates can be changed from high to low. The resulting dialysate concentrations (recovery) are related to the flow rate; by regression, these recoveries will provide the true extracellular concentrations at zero flow rate. The major limitation of this method is the longer sampling time required and coincident loss of time resolution, as it
takes more time to collect sufficient sample volume to support measurement.

b) Retrodialysis (Reverse Dialysis) of the drug
In this method, the drug is added to the perfusate and its in vivo loss measured. Concentration of the drug in the extracellular fluid is calculated based on the in vivo recovery by loss of the drug, assuming that this recovery is equivalent to gain, which, as previously stated, cannot be measured in vivo. This method is relatively easy, so therefore is commonly used.

c) No-Net-Flux (NNF) method
This method involves consecutive perfusion of the probe with different drug concentrations, considering steady-state conditions of the drug in the tissue. Dialysate concentrations are measured and the difference between the perfusate and dialysate concentration is determined and plotted as a function of perfusate drug concentration. Regression analysis of the results yields the perfusate drug concentration that is in equilibrium with the surrounding tissue. A disadvantage of this method is that the animals used for calibration are not the same as those used in an experiment designed to measure systemic and ECF exposure simultaneously, so it is assumed that recovery is constant between probes and over time between animals.

d) Dynamic No-Net-Flux (DNNF) method
This method differs from NNF through the use of an inter-group rather than intra-group design. A group of animals are continuously perfused via a probe with one selected concentration instead of serial perfusion of individual animals with different concentrations. Different groups receive different concentrations and the data is combined at each sampling point. Regression of the mean data points obtained from the various groups at a particular time point will give the actual extracellular concentration with the associated in vivo recovery at that time. An additional limitation with this method is that it requires more experimental animals than the NNF approach.

e) Retrodialysis with internal standard
In this method an internal standard is added to the perfusate during the course of an experiment. The internal standard is selected so that it matches the characteristics of the drug as close as possible. In this
way, recovery by loss of the internal standard will predict the recovery by gain of the drug. The concentration of drug in the extracellular fluid \((C_{ecf})\) is determined by assuming that the ratio of \textit{in vitro} recovery of drug and internal standard will be the same \textit{in vivo}, and that the \textit{in vivo} loss of the internal standard is equal to the \textit{in vivo} gain of the internal standard. The following equation relates these various concentrations:

\[
(C_{ecf,drug}) = C_{dialysate,drug} \times \frac{1}{[\text{In vivo} \ L_{IS}]} \times [\text{In vitro} \ R_{drug}/ \text{In vitro} \ R_{IS}],
\]

where \(L_{IS}\) is the \textit{in vivo} recovery by loss of the internal standard,

\[
L_{IS} = (C_{perfuse,IS} - C_{dialysate,IS})/ C_{Perf,IS}.
\]

This method is more practical than reverse dialysis of the drug because the internal standard is perfused simultaneously with drug collection; whereas in reverse dialysis of drug, recovery and sampling for PK analysis following drug administration needs to occur separately, thus prolonging the entire experiment. This longer experimental time increases the chances of probe fouling and assumes that probe recovery remains constant over potentially several additional hours. Thus, retrodialysis with internal standard is quite common.

**General References**


**Special Feature**

**Open Flow Microperfusion**

By Frank Sinner, PhD, HEALTH Institute for Biomedicine and health Sciences, JOANNEUM RESEARCH, Graz, Austria

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**OFM concept and design**

Open flow microperfusion (OFM) is an *in-vivo* sampling technique that builds on the strengths of microdialysis (MD) as a continuous, minimally invasive interstitial sampling method (Pieber et al., 2012). But instead of a membrane, OFM uses probes with macroscopic openings to exchange substances via a liquid pathway. Transport is based on convection rather than diffusion so that the exchange is non-selective in either direction (Fig. 1). Since no dialysis or filtering occurs, OFM provides a diluted but otherwise unchanged sample of the surrounding interstitial fluid (ISF). Therefore, endogenous and exogenous substances present in the interstitial fluid of targeted tissues can be quantified without the risk of investigating an altered sample. The membrane-free OFM design also avoids problems such as membrane fouling, clotting or other limitations that can arise when sampling high-molecular-weight or lipophilic substances.

![Figure 1: Schematic drawing of the membrane-free OFM sampling principle (left). Schematic figure of the OFM system with a linear OFM probe (right)](image-url)
The inserted OFM probe is connected to a peristaltic pump via push-pull tubing. The OFM pump simultaneously pushes the perfusate into the OFM probe and pulls the OFM sample into an easily exchangeable vial. At the exchange area (enlarged section) all substances are exchanged freely between the ISF and the OFM perfusate.

**Key features of OFM and MD sampling systems**

<table>
<thead>
<tr>
<th>Component</th>
<th>OFM</th>
<th>MD</th>
</tr>
</thead>
<tbody>
<tr>
<td>probe</td>
<td>membrane-free</td>
<td>semi-permeable membrane</td>
</tr>
<tr>
<td></td>
<td>no nominal cut-off</td>
<td>different cut-offs available</td>
</tr>
<tr>
<td>sample</td>
<td>* unfiltered, diluted</td>
<td>* filtered, diluted</td>
</tr>
<tr>
<td></td>
<td>* long-term sampling</td>
<td>* membrane fouling or clotting</td>
</tr>
<tr>
<td></td>
<td>* low to high molecular weight compounds</td>
<td>* low to moderate molecular weight compounds</td>
</tr>
<tr>
<td></td>
<td>* low to high lipophilicity</td>
<td>* low to moderate lipophilicity</td>
</tr>
<tr>
<td></td>
<td>* high protein load in the sample</td>
<td>* none to low protein load in the sample</td>
</tr>
<tr>
<td>pump requirement</td>
<td>push-pull mode</td>
<td>push suitable for low molecular cut-off</td>
</tr>
<tr>
<td>analytics</td>
<td>sample pretreatment required</td>
<td>sample pretreatment optional</td>
</tr>
</tbody>
</table>

OFM represents a universal, continuous, tissue-specific sampling method with no nominal cut-off value, which thus provides the opportunity to investigate all substances regardless of their physico-chemical properties. All substances ranging from ions up to entire immune-competent cells are present in the collected OFM sample, which closely reflects the actual ISF composition around the probe. Since proteins and peptides are present but may not be the analyte of interest, the OFM sample requires specifically adapted analytical methods.

**OFM applications**

Stable sampling and quantification of lipophilic and high-molecular-weight substances in the ISF is currently realized in three tissues: adipose (aOFM, since 1995), dermal (dOFM, since 2006) and cerebral (cOFM, since 2008). aOFM has already been successfully used to quantify absolute concentrations of glucose, lactate, inulin and insulin for PK/PD studies or cytokines in inflammation studies (Bodenlenz et al., 2005; Ellmerer et al.,
1998, 2000; Pachler et al., 2007; Schaupp et al., 1999; Trajanoski et al., 1997). **dOFM** has been evaluated for applicability, tolerability, safety and performance (Bodenlenz et al., 2013). It has been used to sample topically applied drugs in lesional and non-lesional skin and to study cytokines and antibodies (Bodenlenz et al., 2012; Pieber et al., 2012; Dragatin et al. in prep). **cOFM** has been designed to monitor substance transport across the intact blood-brain barrier (BBB). Even two weeks after probe implantation the trauma layer around the cOFM probe is minimal and does not hinder sampling. Preclinical studies have shown BBB intactness after cOFM probe implantation (Birngruber et al., submitted) and successful transport of large molecules (nanocarriers) across the intact BBB (Birngruber et al., in prep).

The OFM concept has the potential to be optimized for use in many different tissues. By using OFM in bioequivalence and microdosing studies the time to market for active pharmaceutical ingredients can be shortened considerably.

**References**


Dr. Elizabeth (Liesbeth) de Lange received her PhD degree from Leiden University (The Netherlands) in 1992. She was a Post-Doctoral fellow at Leiden University from 1993 to 2001 and was appointed to Assistant Professor at Leiden in the same year. Presently, Dr. de Lange is Head of the Target Site Equilibration Group at the Division of Pharmacology of the Leiden - Amsterdam Center for Drug Research (LACDR).

She is a member of the Editorial Board of the Journal of Fluids and Barriers of the Central Nervous System (FBCNS), and a member of the editorial advisory boards for the Journal of Pharmaceutical Sciences (JPS) and Pharmaceutical Research (Pharm Res). She cofounded and was Co-Chair at the 1st, 2nd and 5th of the series of International Symposia on Microdialysis in Drug Research and Development, and was Chair of the 9th International Cerebrovascular Biology Conference (CVB) held in Leiden, The Netherlands, 2011. Furthermore, she is the 2013 Co-Chair and 2014 Chair of the Annual Meeting Programming Committee of the American Association of Pharmaceutical Scientists (AAPS), a member of the AAPS International Affairs Committee, and has been the Chair of the Section of Pharmacokinetics-Pharmacokinetics and Drug metabolism (PPDM) section of the AAPS (2012), and Chair of the Microdialysis Focus Group (2007). With her company “In Focus” (established in 2009) she provides courses, training and advice within her area of expertise on microdialysis, pharmacokinetics, pharmacokinetic-pharmacokinetic (PKPD) relationships,
blood-brain barrier (BBB) transport, and intra-brain distribution (www.infocus-ecmdelange.nl).

She founded the “BBB Nedwork Foundation” (Ned for “Nederland”, the Netherlands) for establishing a more interdisciplinary approach to gathering knowledge and to establish more interdisciplinary collaborations pertaining to the role of the BBB in CNS diseases and their treatment.

Dr. de Lange’s academic research program focuses on the development of generally applicable translational (physiologically based) PK-PD models for CNS drugs using advanced in vivo animal models and mathematical modeling techniques. This work involves identification and characterization of the rate and extent of key factors and their condition dependency. These key factors include the kinetics of the drug in plasma; passive and active drug transport into and out of the target tissue; drug distribution within the target tissue; drug equilibration to the target site; and the ability of the drug to interact with the target, in conjunction with biomarkers of the effect.

To that end her research has a comparative and integrative design to elucidate conditional influences on individual mechanisms, and includes the cycle of simulations – predictions - experimental testing - data modeling – simulations etc. Experiments typically involve monitoring techniques in (freely moving) chronically instrumented animals, including microdialysis. The microdialysis technique enables the measurement of free drug concentrations in a selected tissue, which is an indispensable tool in characterizing rate and extent of passive and active transport parameters, and is most valuable to reveal information on active concentrations at the target site. Moreover, the microdialysis technique can be used to monitor biomarker kinetics. Other frequently used in vivo techniques are electroencephalogram (EEG) recording and positron emission tomography (PET) scanning. Such techniques are applied in healthy animals, as well as in models of Parkinson’s disease and Epilepsy in which disease progression plays a role.
Abhay Joshi in conversation with Dr. de Lange

1. What are the key contributions of microdialysis in CNS Drug Research & Development?

- Important insights into neurochemistry

The microdialysis technique was developed about 30 years ago, actually as an improvement upon the push-pull technique to obtain information on the extracellular fluid in the brain (brain ECF), mostly focused on neurotransmitter functioning. Thus, changes in extracellular neurotransmitter concentrations upon administration of drugs could be observed, and led to many important insights regarding the effect of drugs on CNS neurotransmitter receptor systems in the CNS, in health and disease conditions.

- Concepts of importance of free drug concentration in CNS drug effects recognized

In the very early 90’s the microdialysis technique was broadened to the pharmacokinetic (PK) research field. Then, quantitative approaches were introduced, and drug concentration-time profiles of drugs could be obtained from the brain (but also many other tissues).

CNS drug efficacy is largely dependent on target site kinetics of the unbound drug which can be strongly influenced by transport across the blood-brain barrier (BBB) and intracerebral distribution. It is, therefore, essential to have information on the unbound CNS target site pharmacokinetics, as this may distinctively differ from (unbound) plasma pharmacokinetics.

For CNS drugs a very important barrier is the blood-brain barrier (BBB). The BBB may have a huge impact on the PK of a drug at a target site within the brain, relative to its PK in plasma. Having information on the free drug concentrations on either side of the BBB, enables the determination of two
distinct transport features being the rate as well as the extent of drug transport across this barrier.

Actually, to date, microdialysis is the only technique that can obtain quantitative information on the free drug concentrations at a particular region of the brain, which makes microdialysis data key in understanding PKPD relationships of CNS drugs. I would say that “microdialysis is where PK meets PD” and I believe that awareness of this unique feature will continue to gain appreciation.

Thus, key contributions of microdialysis in CNS drug research and development lies in the fact that microdialysis allows monitoring of free drug concentrations in the extracellular space of CNS sites, as well as detection of endogenous compounds as (potential) biomarkers of drug effects and/or disease.

2. What do you see as the major challenges with microdialysis?

One of the most important questions in microdialysis is how to relate the concentrations in the microdialysate to the true concentrations outside the probe as in vitro recovery is not equal per se to the recovery in vivo. Many calibration techniques and approaches have been proposed, with different levels of practicality and usefulness, to obtain quantitative information on extracellular concentrations as a function of time. [See the article “Probe Calibration” in the Microdialysis Technique Overview section on Page 4 of this issue of Probes for a comprehensive review of probe calibration and associated methodology.] Today we have built up enough experience to know how to obtain quantitative data using the microdialysis technique. Given this established capability, microdialysis is the only technique that provides data on the unbound concentration of compounds in extracellular fluid spaces in the body, being highly important information in drug development, as the unbound concentrations are the drivers for the effect.

- Quantitative aspect for “difficult” drugs

There are however situations in which quantitative approaches do not lead to very accurate estimations of actual extracellular concentrations. This holds for sticky compounds, including very lipophilic drugs. This means that the microdialysis technique is not generally applicable.
But, actually all monitoring techniques suffer from limitations. For example, Positron Emission Tomography (PET) only measures total concentrations of a positron-emitting-nucleus containing compound (and potential metabolites) as a function of time. Then, Nuclear Magnetic Resonance (NMR) based information on a magnetic nucleus containing compound is limited by availability of natural occurrence of this magnetic nucleus within the compound structure, or limitations on the inclusion of a magnetic nucleus into the structure, as well as limited sensitivity.

Of course limitations should be realized and addressed in interpretation of data generated. But I prefer putting the emphasis on the power of these techniques, combining them, and always trying to improve applicability.

Microdialysis is the current best technique to obtain information on the concentration of compounds in the extracellular space of tissues, and is therefore the current “gold standard” for obtaining such information!

3. Dr. deLange, we highly regard your Leadership Role with AAPS. What would be your advice to students and young scientists?

Learning and wishing to improve day-by-day, I aim to be a “dynamic and flexible leader”. I very much believe that stimulating people works much better than just telling them what to do, for those truly having passion for the task they have taken on. When this approach does not work, in exceptional cases I have to shift gears to another mode, getting a little more strict and hierarchical. And if things get “back in line” I continue to stimulate, and hopefully inspire others like they inspire me.

If I can say something to the youngsters, I would say that when it comes to personal attitude, I believe that being natural and true to oneself works out best. Also, realize that to achieve certain goals, it takes investment and focus. So, don’t try to be someone else. There are so many personality types that we all need to make the world go round. So, be yourself, follow your heart and passion, and work hard.

Note from Abhay Joshi: The interview with Dr. de Lange ended amicably and the steering committee thanked Dr. de Lange for sharing with us her “Pearls of Wisdom”.

17
Role of microdialysis in my PhD thesis research
Nimita Dave, Ph.D.

Dissertation Advisor: Pankaj B. Desai, Ph.D.
Professor of Pharmacokinetics and Biopharmaceutics,
The James L. Winkle College of Pharmacy,
University of Cincinnati, Cincinnati, Ohio.

Blood-brain and blood-tumor barriers, BBB and BTB, respectively, restrict access of drugs to CNS malignancies. For most anti-cancer drugs, there is limited quantitative information pertaining to the time course of absorption, distribution and elimination, and the resulting drug exposure to various parts of brain and brain tumor tissue.

In my doctoral research, we identified a novel therapeutic target for brain tumors and assessed the activity of various investigational agents against this target. To support these investigations, we characterized the brain tissue/brain tumoral pharmacokinetics (PK) of the lead compound. We employed intracerebral microdialysis to assess/compare the normal and tumoral brain PK of the compound in Sprague Dawley rats. C6 glioma cells were orthotopically implanted into the right striatum, while the left striatum region served as the control/normal brain region. Dual probe intracerebral microdialysis was performed following tail vein injections of the drug to determine the unbound extracellular fluid (ECF) concentrations. Blood samples were simultaneously collected from jugular vein for 8 hrs after the injection and were corrected for protein binding. μPET/CT imaging of the rats was performed using $^{18}$F-FDG to evaluate changes in active tumor volumes pre- and post-treatment of letrozole. Also, brain tissues were collected at the end of the experiment for histological evaluations.

For quantitative pharmacokinetic analysis in the brain, a number of methods are employed. Analysis of brain tissue homogenates and CSF samples are the two most commonly used methods to obtain brain pharmacokinetic profiles of drugs. Tissue
sampling requires sacrifice of several animals per time point and only yields data on total drug concentrations (protein-bound plus unbound drug forms). CSF sampling does provide opportunity for temporal resolution of drug levels, but the method does not yield clinically relevant information. CSF concentrations may be applicable for target sites close to the ventricles, such as the meninges. However, for target sites within most other parts of the brain including brain tumors, CSF concentrations do not reflect the tissue availability of the drug. On the other hand, intracerebral microdialysis facilitates the measurement of local unbound drug concentrations in the ECF, which is the fluid compartment in the immediate vicinity of the cells. Intracerebral microdialysis can be used to monitor local concentrations of a compound in selected brain regions. This technique is also employed to investigate the differential uptake kinetics of drugs across the BBB and BTB. The primary advantages of microdialysis include minimal damage to the brain tissue and the BBB, and procurement of highly purified samples, thereby eliminating the need for tedious extraction procedures for bioanalysis. In addition, sampling can be performed continuously for hours after a single penetration of the tissue with the probe, without the need for withdrawing or handling any biological specimens. Also, combining the unbound drug concentration profiles obtained using intracerebral microdialysis with our in vitro cytotoxicity studies helped us identify the appropriate doses for our preclinical efficacy studies. μPET/CT imaging showed a marked reduction of active tumor volume after 8-10 days of treatment with the selected dose. Thus, employing intracerebral microdialysis in conjunction with cutting edge tools such as μPET/CT, immunohistochemistry, and cell proliferation markers facilitated conduct of critical PK/PD studies in support of a novel therapeutic approach for the treatment of brain tumors.

Publications –

**In Focus**
[Image: Right time, right place, right concentration.]

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**4th Annual Course on the BBB in CNS Drug Development**

*9 - 11th October, 2013, Leiden, The Netherlands*

**Aim**
This course will address the latest insights in the role and function of the Blood-Brain Barrier (BBB) in research concerning CNS drug development, CNS drug delivery and CNS diseases. It will provide profound insight in the complex function of the BBB with regard to transport kinetics in health and disease.

**Learning Objectives**
After having taken this course, the participants will

- have in-depth insight into mechanisms that contribute to BBB transport and intra-brain distribution, with special emphasis on drug delivery and active transport mechanisms
- know about the driving forces that determine whether or not a CNS drug will be at the right place, at the right time and at the right concentration
- be able to compare and choose between different methods for studying parameters that can be used to understand or even predict BBB transport and CNS distribution

For more information
see: [http://infocus-ecmdelange.nl](http://infocus-ecmdelange.nl)
email: [info@infocus-ecmdelange.nl](mailto:info@infocus-ecmdelange.nl)
- **Tuesday Afternoon Microdialysis Focus Group Business Meeting: November 12, 2013 (12:00 PM – 1:00 PM)**

- **Wednesday Afternoon Mini-symposia: Nov 13, 2013 (2:00 PM – 4:00 PM)**
  **Topic:** The value of real time target tissue concentrations in evaluating safety and efficacy of anti-infective drugs

- **Microdialysis Based Posters:** Please look at the final program for more information

**Other Meetings of Interest**

**Pharmaceutical Sciences beyond 2020 – The rise of a new era in healthcare**