# The interstitium: an analytical challenge

F. M. Sinner* T. Druml[*,**], C. Magnes*, M. Suppan*, M. Bodenlenz[*,**]; T. R. Pieber[*,**]

[*]Institute of Medical Technologies and Health Management, Joanneum Research Graz
[**]Department of Internal Medicine, Diabetes and Metabolism, University Graz

interstitial fluid (ISF) is accessible by using different techniques. The most commonly used sampling technique is microdialysis (MD) where substances are recovered from the ISF through a membrane. The resulting dialysate which is partially diluted with the used perfusate, is protein free or at least protein reduced, depending on the cut-off of the MD membrane used.
The open flow microperfusion (OFM) technique is an alternative to microdialysis. In contrast to MD catheters, OFM catheters have no membrane but perforation holes permitting the exchange between perfusate and ISF. Since there is no membrane discrimination, the resulting samples contain all analytes present in the ISF. In addition, there are no known phenomena such as membrane clogging, swelling, etc.

Nevertheless, ISF samples obtained by MD and OFM represent an analytical challenge for several reasons:

1) ISF samples are obtained at flow rates of 0.5-2 µl/min. To achieve a resolution of e.g. 10 minutes, all analytes of interest must be measured in sample volumes of 5-20µl.
2) ISF samples contain very low analyte concentrations.
3) Protein present in OFM samples and MD samples obtained using high cut-off membranes must be eliminated prior to analysis for some methods.

In this contribution, we will present different strategies to optimize analysis of low volume ISF samples. The presentation will cover the optimization of ELISA analysis, specialized enzymatic analysis (Cobas Mira) and GC-MS analysis. Method optimization for a variety of analytes like insulin, glucose, lactate, glycerol, free fatty acids, inulin as well as for stable glucose and mannit tracers will be presented. Selected data from in-house validation will be shown for these methods.