IVDr Research by NMR

- An Innovative Analytical Solution for Biobanking

NMR in the World of BioBanks

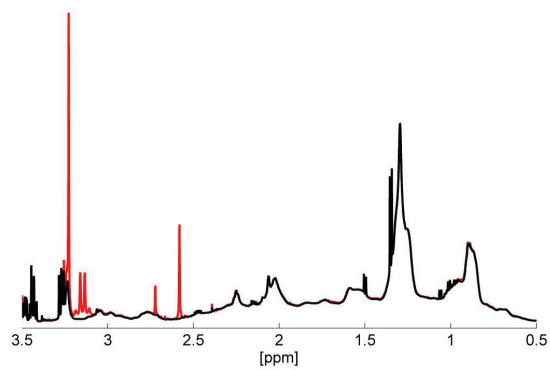
High Resolution NMR has rapidly developed into a leading tool for the analysis of body fluids and tissues. It is used in high-throughput push button automation to generate spectra, which are the input for automatic analysis to quantify markers or to be compared with statistical models of health or disease states. It also allows large scale epidemiological studies due to its outstanding instrumental reproducibility and transferability from lab to lab. Combining this with Standard Operation Procedures and a standardized instrumental platform allows to integrate data generated all over the world with data from a biobank network.

How Does NMR Relate to Biobanks and their Daily Work?

NMR can be used as QC for input of samples into the biobank and at the same time with the same measurement create additional value in terms of analytical information:

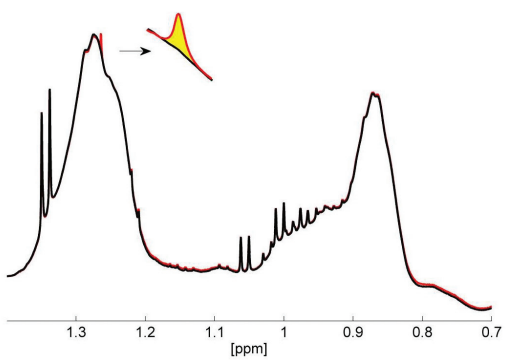
- Validate the type of sample e.g. EDTA Plasma (see Figure 1), Citrate Plasma and Quality Control to check for contamination and impurities (see Figure 2)
- Produce NMR spectra for input into the biobank information for each sample, NMR spectra are produced under standard conditions and can be used for integrated spectral bases from different biobanks worldwide
- Generate a lipoprotein subclass panel with 114 parameters (serum/plasma)
- Add a List of quantified parameters in urine including concentration distributions

Figure 1



Identification of EDTA Plasma - see signals in red

Figure 2



Identification of contamination with disinfection material, see yellow labeled peak

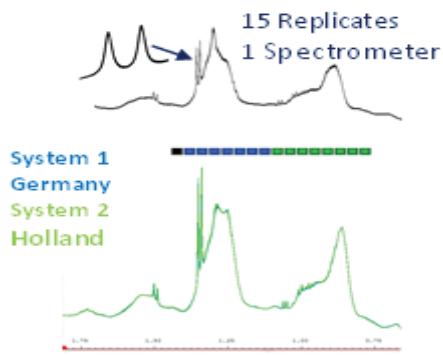
Suitability of NMR for Spectral Database Usage and Data Exchange

Reproducibility and transferability of the NMR analysis under identical SOPs and using a standardized NMR platform is shown in Figure 3. Aliquots of Serum samples have been prepared and measured, showing in the upper part the overlay of spectra of 15 replicates prepared and measured individually one instrument, while the lower spectrum shows the overlap of 8 spectra each measured in 2 locations on identical machines under the same SOPs using replicate samples. As can be seen there is a perfect overlap of all spectra. This is the proof, that spectra from different biobanks can be used for integrated statistical analysis. For new studies therefore spectra can be used instead new aliquots to be taken from the biobank.

Add Value to the Biobank with Analytical Data

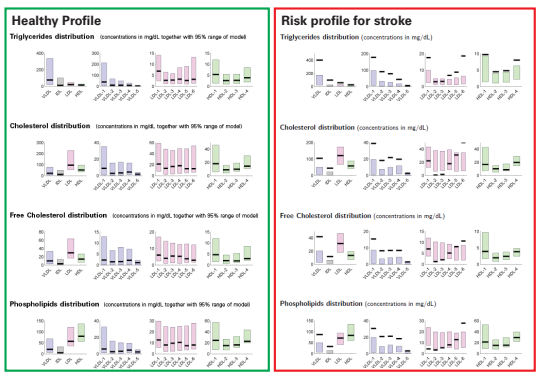
For every Biobank, the value also lies in the metadata associated to the samples stored. This can be patient data, lifestyle information, but also analytical data, like lipoprotein concentrations including in plasma/serum including subclasses and concentration of endogenous metabolites in urine. Using directly the spectra acquired for quality control, these analytical results can be generated automatically including concentration distributions calculated from all biobank samples analyzed. Since many samples are analyzed in a biobank it is possible to define normal concentrations in the cohort investigated. Figure 4 shows an excerpt of the lipoprotein subclass analysis obtained from 2 samples, one from a healthy subject and one from a person who had a stroke 3 days after sample collection, clearly showing the deviations, which are indicative of a risk profile. Figure 5 shows an excerpt from the quantification of endogenous metabolites including the cohort concentration distribution with the actual sample shown in the profile as a stick. Further analytical analysis is available on request.

Figure 3



^{1}H NMR in Serum at 600 MHz

Figure 4



Lipoprotein subclass analysis comparing healthy (left) and risk profile (right)

Figure 5

Compound	Concentration[1]		LOD	Reference Distribution
	mmol/L	mmol/mol Crea	mmol/mol Crea	
Creatinine	6.9			
Creatine	2.51	361	90	≤ 90 — 503
D-Glucose-beta	≤ LOD	≤ LOD	100	≤ 100 — 209
D-Galactose-alpha	≤ LOD	≤ LOD	50	≤ 50 — 394
D-Lactose	≤ LOD	≤ LOD	275	≤ 275 — 428
Alanine	≤ LOD	≤ LOD	110	≤ 110 — 279
Lactic Acid	≤ LOD	≤ LOD	100	≤ 100 — 152
Acetic Acid	≤ LOD	≤ LOD	90	≤ 90 — 288
Succinic Acid	0.51	74	20	≤ 20 — 272
Citric Acid	6.08	876	490	≤ 490 — 1076
Dimethylamine	0.43	63	20	29 — 155
Trimethylamine	≤ LOD	≤ LOD	35	≤ 35 — 118

Excerpt Report Endogenous compounds in urine

Bruker BioSpin

Providing NMR Solutions for Metabolomics

NMR is an advantageous technique for metabolomic research, providing high reproducibility, simple sample preparation and the ability to measure different small molecule metabolites simultaneously. Today, new advances in software and hardware platforms have made NMR more effective, easier to use and more cost efficient. Discover for yourself how NMR can help illuminate metabolic networks.

Bruker BioSpin

info@bruker.com
www.bruker.com