Improving pre-analytical data quality with an automatized healthcare-integrated biobanking approach

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> "A major impediment to progress in the hunt for biomarkers is the
>
> lack of standardization
>
> in how specimens are collected, annotated, and stored."
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> *George Poste, Nature; 469: 156-57, 2011*

Introduction

Despite recent methodological advances in "omics-"technologies, the discovery of new biomarkers has been largely prevented by uncontrolled variability in the quality among and within existing biospecimen collections. In order to meet the quality requirements of liquid samples for high sensitive analytical technologies, such as mass spectrometry, recent efforts have mainly focused on the development of new biobanking infra-structure and on the standardization of pre-analytical protocols. With regard to the reproducibility of research results, not only the physical quality of samples but also the quality of their recorded data is crucial. Currently, pre-analytical information is often recorded manually. This type of recording is not only time consuming but also represents a considerable source of error.

Liquid Biobank Bern

Here, we present the healthcare-integrated biobanking process of the Liquid Biobank Bern (LBB), Switzerland. The LBB process is fully integrated into the routine processes and IT-landscape of the hospital. It takes advantage of multiple-interfaced IT systems (Fig. 1) and as such increases data quality by minimizing error rate through manual input of pre-analytical information.

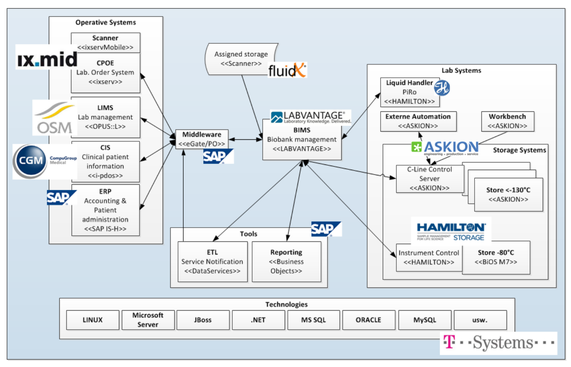


Figure 1: IT-landscape of the hospital integrated Liquid Biobank Bern.

Furthermore, the biobanking concept presented here allows for time efficient pre-analytical processes (Fig. 2).

The delay between sample collection and freezing has been shown to be a critical factor for sample quality, especially with regard to modern highly sensitive downstream analysis methods such as tandem-mass spectrometry (Fig 3).

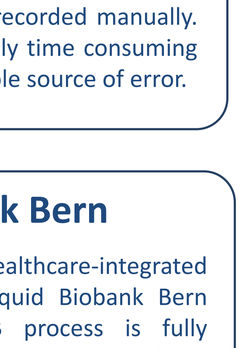


Figure 2: Target maximum delay between sample collection to freeze of the LBB.

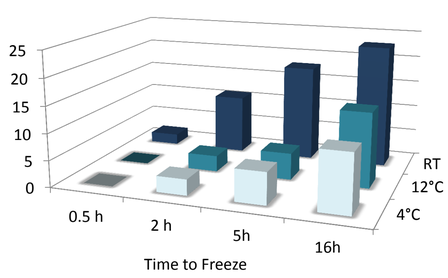


Figure 3: Percentage of significantly changed metabolite levels (262 metabolites in human EDTA-plasma) depending on temperature condition and duration of plasma before freezing. RT: Room temperature. Kamlage et al., Clinical Chemistry; 60(2): 399-412, 2014

Automated processing - Continuous tracking of time points set by barcode scans - interfaced data exchange

Consenting
ERP ⇔ CIS

Digitalized informed consent leads to automated information of the ward that biobank samples can be drawn

Sampling
CPOE ⇨ LIMS/BIMS

BedSideScan:
- Patient-to-Sample check of barcoded sample and patient wristband
- Start of sample documentation e.g. tracked time point of blood draw
- Automated activation of sample transport

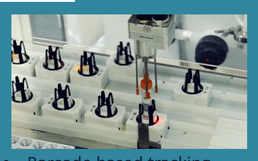
Transport
CPOE

Rapid sample transport from the blood draw...

... to the lab

- By central lab transport service
- Screen shows all pending biobank blood draws and corresponding ward

Processing
LIMS ⇨ BIMS



- Barcode based tracking
- Integration of sample processing into the routine workflow of the lab
- Exact time point of reception and centrifugation

Aliquoting
BIMS ⇔ Instrument Control

- Study specific automated aliquoting of primary biobank samples
- Exact time point of aliquoting
- Barcode scan of parent sample and aliquoted cryotubes

Controlled-rate freezing
BIMS ⇔ Instrument Control

- Standardized freezing curve per material type and volume
- Homogeneous nucleation
- Exact time point of freezing

Storage
BIMS ⇔ Instrument Control

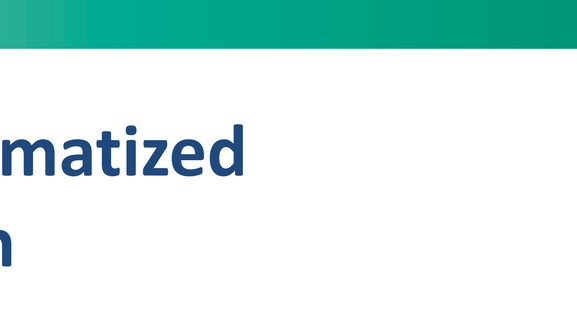
-80°C (-112°F)

-150°C (-238°F)

- ✓ Fully automated sample processing
- ✓ Capacity > 2 Mio. samples
- ✓ 3 redundant cooling systems
- ✓ Three systems; >150k samples
- ✓ Automated picking, manual backup
- ✓ LN2 cooling (direct line)

Process Monitoring

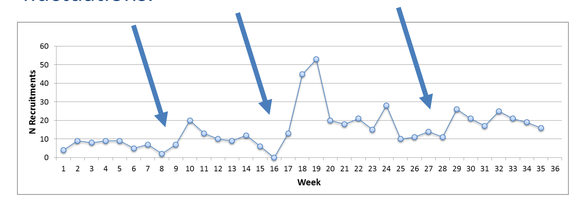
According to the current LBB performance statistics, 86% of the collected samples were processed within the anticipated time of one hour. The blue line indicates the target time period of 1h from blood draw to freeze. The corresponding SPREC performance statistics are given in Table 1.



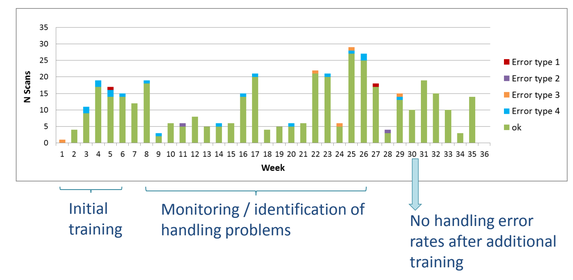
Parameter	Code	LBB samples
Pre-centrifugation delay	<2 h RT (A)	99.8%
Post-centrifugation delay	<1 h RT (B)	97.1%

Table 1: Percentage of samples within the anticipated codes A and B for pre- and post-centrifugation delay, respectively, of the STANDARD PRE-ANALYTICAL CODE (SPREC; Sabine Lehmann et al, Biopreservation and Biobanking. August 2012, 10(4): 366-374) V2.0.

Continuous recruitment performance monitoring anticipates early identification of potential bottlenecks in patient recruitment. Based on our analysis, the consenting procedure is the most critical step in recruitment. Arrows indicate analysis time points which led to minor adaptations of the process.
Continuous monitoring is essential because based on our experience, these processes may change over time unnoticed in the wards due to staff fluctuations.



The bedside scan data quality monitoring further emphasis the need for continuous monitoring. Each new ward which is included into the collection is closely monitored to discover potential handling problems during the sampling process. Data monitoring at the level of individual users (the user ID at each process step is recorded on data level) enables identification of individuals with further training needs.



Summary

- Collection and processing of biobank samples are integrated in the automated high-throughput processing of hospital routine samples.
- At every processing step from the blood draw to the storage, the sample and its derivatives are identified, tracked, and directed by their barcodes, and thus, electronically monitored and documented.
- All essential time points within the pre-analytical pathway are recorded automatically by the processing instruments.
- With this high-degree of IT integration of hospital routine and biobank processes, we achieve high data quality and rapid sampling processing: > 99.8% of samples achieve a SPREC pre-centrifugation delay A code; 96% being frozen within two hours after blood-draw and >86% even within one hour.