Frozen Sample Aliquotter

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introduction

Banked biosamples are invaluable to biomedical research. Optimal processing, preservation and sampling are crucial to protect their biochemical composition and molecular integrity lest a study's results be compromised.

Exposing frozen samples to repeated freeze-thaw cycles to aliquot them may damage their fidelity in unpredictable ways -- degrading critical biological molecules and damaging antibodies of interest – and increase potential data variation. Freeze-thaw processing is highly manual and many samples become unusable due to inadequate handling.

To guarantee access to quality samples biobanks face critical cost/efficiency trade-offs between freezing and storing samples in fewer larger volumes (exposing them to freeze-thaw cycles) or small-volume cryo-tubes (increasing storage requirements and associated costs).

the Frozen Sample Aliquotter

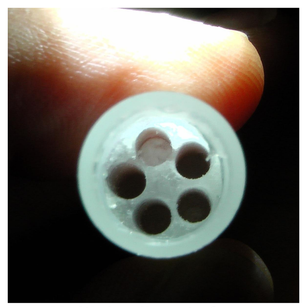
The Automated Frozen Sample Aliquotter enables the hands-free extraction of multiple homogenous and volumetrically-uniform frozen aliquots from one frozen plasma or serum sample without thawing it.

The Automated Frozen Sample Aliquotter is a specialized robotic drilling system that cores a specimen under ultra-cold conditions and deposits the frozen core into a separate cryovial for downstream analysis. The parent samples and the extracted cores remain frozen through the process. Any sample remaining in the parents may be returned to storage still frozen.

By eliminating a number of freeze/thaw cycles the Automated Frozen Sample Aliquotter helps biobanks to store samples in larger volumes while protecting sample integrity, standardizing aliquot processing and increasing lab efficiencies through automation

key design requirements

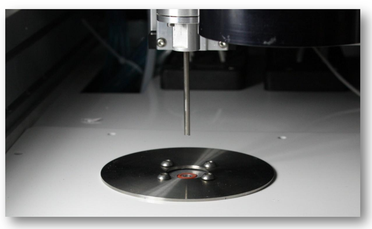
- Extract multiple frozen cores from a single frozen sample
- Maintain samples at & below -65C
- Maintain volumetric uniformity
- Ensure sample core homogeneity
- Ensure no carryover contamination between samples
- Deliver hands-free operation (after sample preparation and loading)



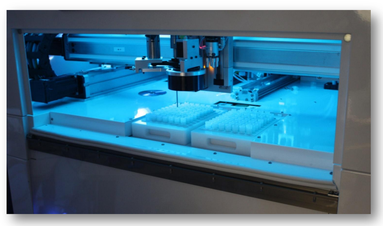
Multiple aliquots from one tube of frozen sample

key system components

- Coring probe
- Systems to manage samples (select tubes, de-cap/ re-cap tubes; move tubes in/ out of coring zone)
- Auto-dispensing of frozen cores into destination tubes
- Integrated automated cleaning to eliminate carryover contamination
- Thermal control systems



Proprietary Coring Probe and fully automated and integrated automated cleaning system



Temperature and humidity controlled deck keeps samples at < -65C during processing

testing

representative cores with low variability

The Rhode Island BioBank completed an independent evaluation using a test platform of the system to assess the degree to which frozen cores extracted with the system are representative of sample controls and whether material remaining in a sample after coring is representative of the controls. Using EDTA plasma from human donors the evaluation demonstrated that the technology can extract multiple frozen, consistently homogeneous cores which give reproducible results with very low variability when analyzed for common analytes.

	T-Chol	Trig	Glucose	IgG	Average
Reproducibility Study (few donors, many repeats)					
Cores vs. Controls	105%	108%	104%	108%	106%
Remainders vs. Controls	97%	100%	94%	100%	98%
Diversity Study (many donors, few repeats)					
Cores vs. Controls	101%	105%	102%	101%	102%
Remainders vs. Controls	98%	99%	99%	98%	98%
Reproducibility Study Coefficient of Variation (CV) (few donors, many repeats)					
Cores	4.4%	6.1%	6.6%	4.6%	5.4%
Remainders	1.9%	4.7%	3.5%	3.0%	3.3%

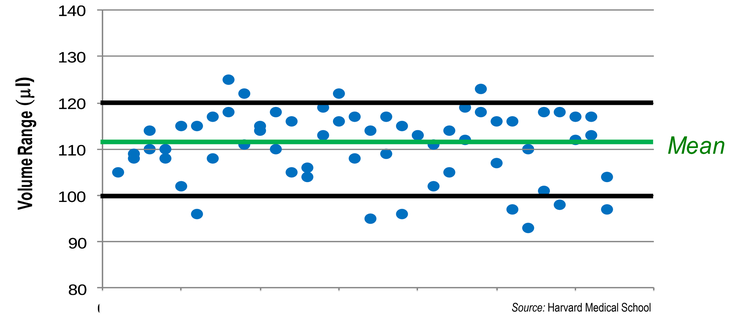
NOTE: All results were normalized using the assay results from the controls

Source: R.I. Biobank, Children's Hospital Boston

volumetric uniformity

Harvard University Medical School tested the technology's capability to extract volumetrically-uniform frozen cores. Using 63 full 1.8 ml cryotubes of frozen bovine serum the evaluation confirmed the technology's effectiveness by the uniformity of the frozen cores, the vast majority of which equaled or exceeded a targeted 100µl volume threshold.

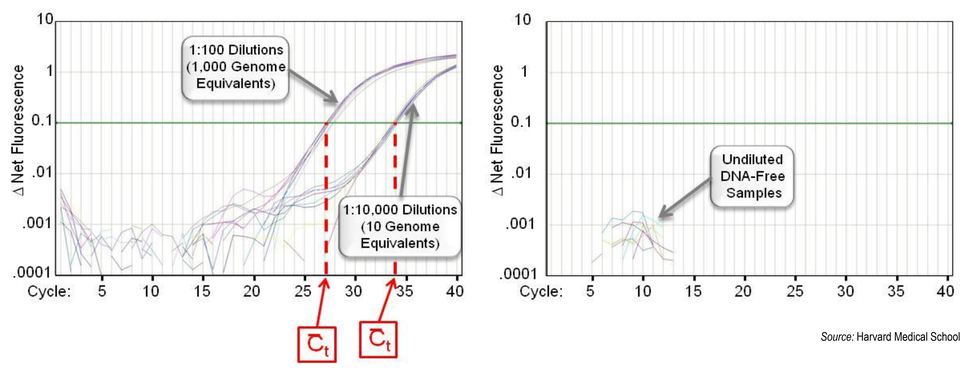
n=63
Mean core in test = 111µl
Design point =110µL +/-10µL
(to account for under-filled tubes)



Source: Harvard Medical School

elimination of carryover contamination

Harvard University Medical School tested the system's effectiveness in eliminating sample-to-sample carryover. The technology was used to extract 32 frozen cores from frozen bovine serum samples containing DNA and 32 cores from identical DNA-free controls, in alternating succession, with a cleaning protocol in between. Measurements of DNA content by RT-QPCR revealed no traces of DNA in the control cores while revealing the expected DNA amounts in the DNA-containing cores. Analysis of high-copy DNA demonstrated the cleaning Protocol effectively reduced DNA carryover by more than a million-fold. Samples 1-8 (1:100 and 1:10,000 dilutions) were amplified with primers specific for a sub-region of the DPH3 gene (Fig. A). The analysis threshold line is depicted in dark green (Δnet fluorescence = 0.1), mean Ct values (where dashed red line crosses the x-axis) are the cycles that correspond to the average point at which the amplification plots cross the threshold line. Amplified DNA-free controls 1-8 contain no DNA (Fig. B). (*Biopreservation and Biobanking*, vol.9, Number 4, 2011)



Source: Harvard Medical School

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