Next Generation HepQuant Tests for the Clinic and Clinical Trials: Within-Individual Reproducibility and Diagnostic Performance for Large Esophageal Varices

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Background

The HepQuant SHUNT Test:

- uses stable 24-13C-cholate (13C-CA) intravenously and 2,2,4,4-d4-cholate (d4-CA) orally to simultaneously measure portal and systemic clearances
- has been used in >26 clinical trials and studies
- encompasses all liver disease etiologies and stages

Aims

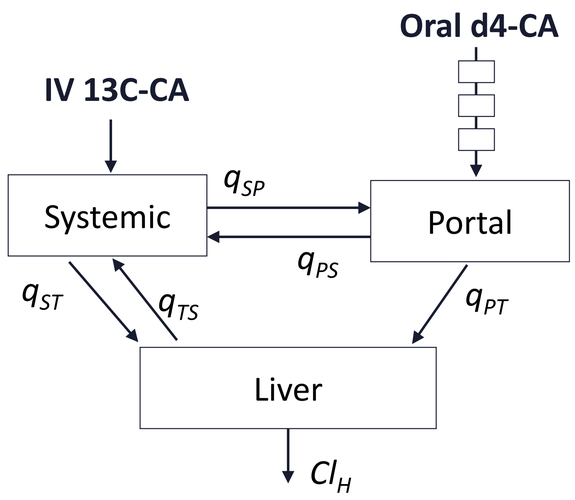
To enhance the Test and its performance by simplifying the sampling procedure and shortening the time of testing.

Herein we evaluate new versions of the Test: V1.1, V2.0, and DuO.

Methods

- In V1.0, the volume of distribution (Vd) is calculated from ln-linear regression of 5- and 20-minute [13C-CA] versus time.
- V1.1, V2.0, and DuO estimate Vd based on body weight and height [1], eliminating the requirement for the 5-minute blood sample.
- V2.0 (IV and oral) and DuO (oral only) is based on our published compartmental analysis [2] and further simplifies sampling requirements to 2 timepoints at 20 and 60 minutes.
- Test outputs include a Disease Severity Index (DSI) and portal-systemic shunting (SHUNT%).
- Reproducibility was assessed in 16 controls, 16 NASH, and 16 HCV subjects, each with 3 replicate tests conducted on 3 separate days [3].
- Differences in AUROC for predicting large esophageal varices (LEVs) were evaluated in HCV subjects from the HALT-C study (N = 217) [4] by the DeLong method [5, 6].

Compartmental Model

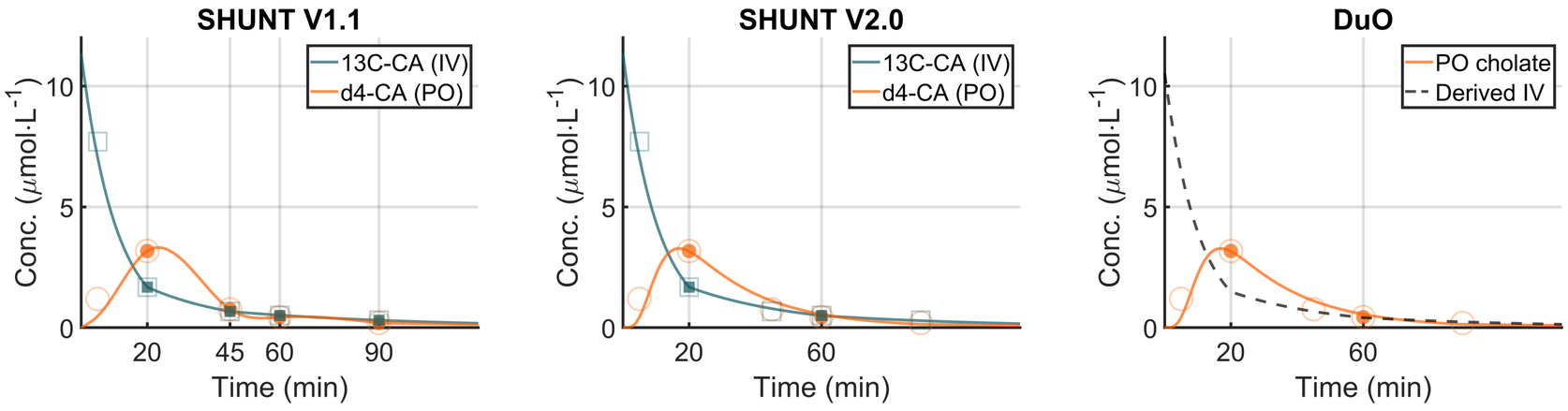


q = flow rates between compartments

Cl_H = total hepatic clearance

Results

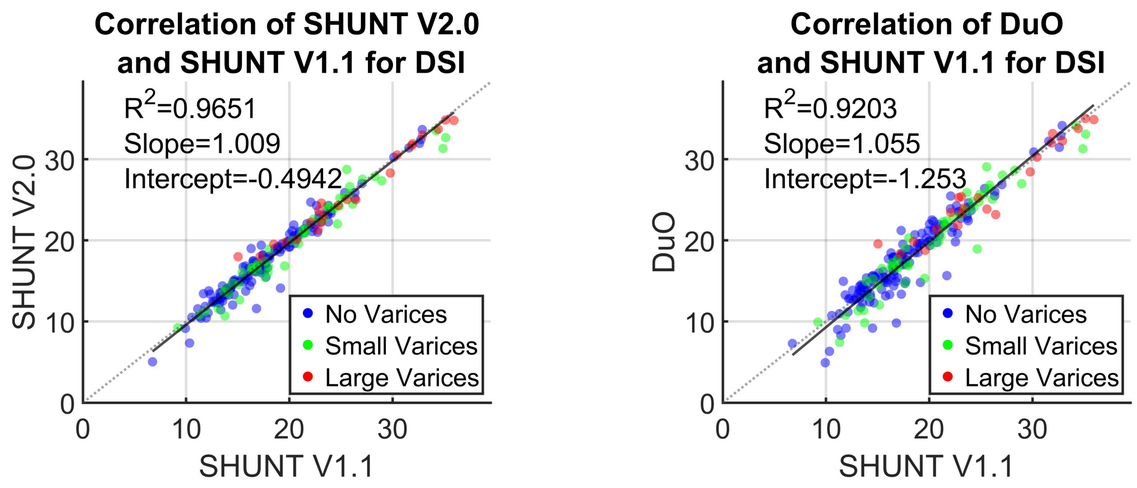
Next generation Tests accurately reproduced systemic and portal clearance curves but require fewer blood samples and less time.



Next generation Tests demonstrated similar, if not improved, reproducibility and diagnostic performance to V1.0.

	Reproducibility (N=48 Control, NASH, HCV)			Diagnostic performance of in the prediction of LEVs (N=217)	
Test Parameter & Method	**CV (%)**	**ICC**	**p value**	**AUROC**	**p value**
Disease Severity Index (DSI)					
V1.0	11.07%	0.94	**< 0.001**	0.82 (0.72-0.90)	-
V1.1	9.59%	0.95	**< 0.001**	0.82 (0.71-0.89)	0.4896
V2.0	10.37%	0.94	**< 0.001**	0.84 (0.75-0.90)	0.1028
DuO	10.64%	0.93	**< 0.001**	0.84 (0.77-0.91)	0.3425
Portal-systemic Shunt (SHUNT%)					
V1.0	14.93%	0.74	0.2120	0.80 (0.66-0.89)	-
V1.1	11.95%	0.85	**< 0.001**	0.84 (0.74-0.90)	**0.0337**
V2.0	12.65%	0.84	**0.0011**	0.83 (0.73-0.91)	0.1060
DuO	9.18%	0.90	**< 0.001**	0.87 (0.81-0.92)	0.0572

V2.0 and DuO show excellent agreement with the reference method V1.1 for determination of DSI.



Conclusions

The next generation HepQuant SHUNT tests:

- **simplify the test administration by eliminating the 5-minute sample (V1.1)**
- **reduce the total samples required to 2 (V2.0 and DuO)**
- **shorten the time from 90 minutes to 60 minutes (V2.0 and DuO)**
- **eliminate need for IV injection (DuO)**

These improvements should enhance operator performance, resource utilization, and patient acceptance, allowing for greater utilization of HepQuant for measuring liver function and physiology.

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Transforming Liver Health

References

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Disclosures

MPM is a paid consultant for HepQuant LLC. SMH and GTE are employees and equity members of HepQuant LLC. All authors have provisional patents pending. HepQuant tests are not FDA approved and are for investigational use only under FDA guidelines for investigational device exemption (IDE).