

**Purpose:** Hepatic perfusion imaging could be valuable for assessment of therapeutic response and normal tissue toxicity in patients undergoing treatment for hepatic lesions. However, voxel-by-voxel estimation of liver perfusion using non-linear least squares (NLLS) fits of dynamic contrast-enhanced (DCE) CT or MRI data to a compartmental model with dual input functions is a computationally expensive process. The purpose of this study is to develop and evaluate efficiency, stability, and bias of three linear methods for computation of hepatic perfusion parameters.

**Method and Materials:** Through simple mathematical manipulation, the single compartmental model is converted into a linear equation (linear in three unknown parameters: arterial perfusion  $k_a$ , portal vein perfusion  $k_p$ , and the outflow rate  $k_2$ ). The ordinary least squares (OLS), total least squares (TLS), generalized linear least squares (GLLS), and NLLS methods were used for estimates of the perfusion parameters from simulated data that mimic normal liver perfusion. Gaussian-distributed random noise was added into the theoretic time-contrast concentration curves. The stability and bias of the three parameters were calculated from 5000 simulations as a function of contrast-to-noise ratio of the liver parenchyma,  $CNR_L$ , and the temporal sampling interval,  $\Delta t$ , for each of the four methods.

**Results:** Dependencies of the stability on  $CNR_L$  (varied from 10 to 20) and  $\Delta t$  (1 to 8 seconds) were similar among all four methods, with NLLS and GLLS having slightly better stability. The increase in bias with  $\Delta t$  was greater for NLLS and GLLS than for TLS and OLS, particularly for estimates of  $k_a$ . However, the computation time for NLLS was 10-100 times greater than for the linear methods.

**Conclusion:** This study suggests that the linear methods can achieve the stability and bias similar to or better than NLLS, but substantially reduce the computation time, making liver perfusion imaging practical for use in clinical trials.