## Research highlights

* Perfusion as measured within traditional one-compartment models is a discretization dependent measure.
* One-compartment models over-estimate perfusion by a factor of between ~20-40% for image devices of clinical resolution.
* The reason for the observed over-estimation is due to volume normalizing flow is not relating to the correct distribution volume.
* Traditional compartment models should not be applied in coupled systems of feeding flow.
* Our findings suggest a careful interpretation of perfusion maps within clinical research studies.