Sample size calculation:

Sample size calculation was performed prior to initiation of the study as part of the grant proposal. [1] We have added the sample size calculation as a supplement. Sample size was calculated for the **primary outcome of incidence of ROSC** with two different flush volumes, assuming 2-sided testing with alpha=5%. Assuming a 50% ROSC with 1 ml flush and 90% with 10 ml flush, we would be able to reject the null hypothesis with a sample size of 20 lambs for each flush volume with a power of 0.813**.**

We subsequently checked the power for two other outcomes – time to ROSC and epinephrine concentrations using this sample size (overall 40 lambs in the study).

Time to ROSC- flush volumes 1 ml vs. 3ml/kg: In a previously published study from our lab, the time to ROSC within each group was normally distributed with a standard deviation of 66 seconds (Vali et al JAHA 2017).[2] With 10 lambs in each group, this sample size would detect a difference of 90 seconds in time to ROSC with a power of 0.8 and a type I error probability of 0.05.

Epinephrine concentration: In the same study from our lab, the epinephrine concentrations within the 0.03 mg/kg group were normally distributed with a standard deviation of 132 ng/ml (Vali et al JAHA 2017).[2] With 10 lambs each in 0.03 mg/kg and 0.01 mg/kg groups (with different flush volumes), this sample size would detect a difference of 180 ng/ml in epinephrine levels with a power of 0.82 and a type I error probability of 0.05.

1. Dupont WD and Plummer WD, Jr. Power and sample size calculations for studies involving linear regression. *Controlled clinical trials*. 1998;19:589-601.
2. Vali P, Chandrasekharan P, Rawat M, Gugino S, Koenigsknecht C, Helman J, Jusko WJ, Mathew B, Berkelhamer S, Nair J, Wyckoff MH and Lakshminrusimha S. Evaluation of Timing and Route of Epinephrine in a Neonatal Model of Asphyxial Arrest. *Journal of the American Heart Association*. 2017;6:e004402.