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5 October 2013

To:

Editor-In-Chief
James C. Eisenach, M.D.
Editor-in-Chief, Anesthesiology
Department of Anesthesiology
Wake Forest University School of Medicine
Medical Center Boulevard
Winston-Salem, NC 27157

Sir:
Please find my submission entitled “Continual Reassessment Method for Dose-finding Studies” for consideration for publication in Anesthesiology as a Letter to the Editor. This submission is in response to a recent article published in Anesthesiology:

Kant A, Gupta PK, Zohar S, Chevret S, Hopkins PM. Application of the Continual Reassessment Method to Dose-finding Studies in Regional Anesthesia: An Estimate of the ED95 Dose for 0.5% Bupivacaine for Ultrasound-guided Supraclavicular Block.

Thanking you

Sincerely

Srinivas Mantha, MD
To:  
**Editor-In-Chief**  
James C. Eisenach, M.D.  
Editor-in-Chief, *Anesthesiology*  
Department of Anesthesiology  
Wake Forest University School of Medicine  
Medical Center Boulevard  
Winston-Salem, NC 27157

I am submitting the enclosed material for possible publication in *Anesthesiology*. It has not been submitted for publication nor has it been published in whole or in part elsewhere. I have read the manuscript, attest to the validity and legitimacy of the data and its interpretation, and agree to its submission to *Anesthesiology*. I acknowledge that I have read the Instructions for Authors and agree with its contents. I acknowledge that if the enclosed manuscript is part of a larger whole or if the primary analysis has been previously published, this must be explicitly stated in the manuscript and the previous publication cited.

**Conflicts of interest, sources of financial support, corporate involvement, patent holdings, etc.**  
Copyright transfer and the signatures of all authors will be requested prior to publication of accepted manuscripts.

**Signature : Srinivas Mantha**  
**Date 6th October 2013**

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   No

(2) Does any author or participant have any financial interest in the subject matter, materials or equipment discussed or in competing materials?  
   No

(3) Has the laboratory in which the research was performed been funded by, or has any participant in the planning, conduct, or reporting of the research been funded by or have financial interests in any source with a real or potential interest in the subject matter, materials, equipment or devices discussed or in any competing product or subject?  
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   No

If you answer yes to any of the above items, please provide details, including the name(s) of the supported authors as well as the corresponding names of the persons or organizations involved.
Continual Reassessment Method for Dose-finding Studies

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To The Editor

I read with interest the recent article by Kant et al.\(^1\), in which the authors used continual reassessment method (CRM) to determine dose-finding studies in regional anesthesia. Specifically, the methodology with Bayesian paradigm was used to estimate ED95 dose for 0.5% bupivacaine for ultrasound-guided supraclavicular block. The idea is novel and may be applied for relevant studies in our speciality in the future. Although, CRM was originally designed for dose-finding phase I trials in cancer drug research several modifications of CRM with different models have evolved over the past two decades. Kant et al.\(^1\) employed a modified version using a Bayesian approach with a power model. There seems to be discrepancy between the data for cohort 3 in the first dose range in Table 3 of the article and that depicted in Figure 2 related to clinical responses. The responses were shown as “Failure, Success” in the Table and as “Failure, Failure” in the Figure 2. I crossed checked the results of first dose range with a recently (September 2013) published R package “bcrm”.\(^2\) I was able to reproduce the results obtained by the authors when responses for cohort 3 were Failure, Success” i.e. as depicted in the Table. In other words, the representation of responses for cohort 3 in the Figure is incorrect. The package is freely available on Comprehensive R Archive Network (CRAN) [http://cran.r-project.org/](http://cran.r-project.org/) and can be accessed through Task Views → Clinical Trials → bcrm.
References
