Response to Letter to Editor

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To the Editor:

The authors read with interest the letter from Pelleg¹ regarding the inherent clinical and physiological differences in the pharmacological properties of adenosine and adenosine triphosphate (ATP) and wish to clarify several points. Firstly, the paper by Prabhu et al in the Journal² was a clinical prospective study to determine an appropriate weight based dose of adenosine required to unmask dormant PV/LA conduction following acute pulmonary vein isolation rather than a head-to-head comparison between ATP and adenosine. Secondly, the pharmacological mechanisms responsible for the termination of AV node dependant SVT likely differ from those responsible for eliciting dormant conduction following PVI. The use of

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adenosine or ATP in unmasking dormant PV/LA conduction requires sufficient concentration to bind to specific atrial I_{KAdo} receptors on myocytes retaining functionality despite ablation. Use in the later instance occurs under entirely difference haemodynamic conditions to drug use during SVT and is designed to achieve a wholly different electrophysiological effect. In the Journal¹ we demonstrated that AV block was generally required to unmask PV reconnection. The extent to which the vagal component of ATP activity, contributes to its ability to unmask dormant conduction, rather than its active metabolite adenosine, to our knowledge has not been systematically explored. However given adenosine is effective at unmasking dormant PV conduction, with no or minimal direct effect upon cardiac vagal sensory nerve terminals, the vagal component is unlikely to be important. Indeed, in the case of ATP where AV block is mediated both directly by adenosine activity and by vagal effects, AV block may not be a suitable endpoint for sufficient dosing to unmask dormant PV conduction, compared to adenosine. Therefore, whether AV block is as reliable an indicator of an effective dose for ATP as it is for adenosine, cannot be conclusively determined from our study previously acknowledged in the limitations. For logistical and practical reasons, our study did not specifically analyse the dose/response relationship of ATP and dormant PV conduction. Nonetheless, as an easily measurable endpoint of drug activity, the occurrence AV block should be documented as a marker of an effective dose. We thank Pelleg and co for their interest in our study.

1. Pelleg A. Electrophysiologic effects of adenosine vs. ATP. J Cardiovasc Electrophysiol 2017;28:online correspondence.

2. Prabhu S, Mackin V, McLellan AJ, et al. Determining the optimal dose of adenosine for unmasking dormant pulmonary vein conduction following atrial fibrillation ablation: Electrophysiological and hemodynamic assessment. Dormant-af study. *J Cardiovasc Electrophysiol*. 2017;28:13-22

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