REBUTTAL

## Rebuttal from Sanjiv M. Narayan and José Jalife

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Rather than disputing our position that 'rotors have been demonstrated to drive AF' (atrial fibrillation), Allessie & de Groot (2014) actually argue in its favour, with caveats that we will address. They now accept the unquestionable fact that a single rapid rotor *can* serve as a driver of AF. One small quibble with their welcome acceptance is the statement that the demonstration of rotors is limited to the sheep atria perfused with acetylcholine. Certainly, rotors have been demonstrated in AF in the absence of acetylcholine (Yamazaki *et al.* 2012) and have also been shown to drive AF in both paroxysmal and persistent AF (Filgueiras-Rama *et al.* 2012). In actual fact, rotors have been shown to maintain fibrillation in the atria and ventricles of a wide variety of species, including man (Noujaim *et al.* 2007).

Of more concern, however, is that Allessie & de Groot (2014) overlook a fundamental tenet of scientific enquiry – experiments in which interventions to eliminate a proposed mechanism successfully eliminate the disease should rise above descriptive mapping. Several groups around the world now show that intervention at electrical rotors can eliminate AF (Narayan *et al.* 2012; Haissaguerre *et al.* 2013; Lin *et al.* 2013; Miller *et al.* 2013). We welcome debate on how to extend these results to more patients, or whether differences in rotor stability reflect technical or other factors. However, we criticize discussions that essentially neglect a plethora of evidence that AF can be sustained by localized rather than spatially diffuse mechanisms. For instance, Allessie & de Groot (2014) fail to point out that several of the studies they cite as showing 'highly complex' activation varying 'from beat to beat' actually emphasized stable high-frequency sites consistent with drivers, and reproducible vectors consistent with activation from a driver in AF (Gerstenfeld *et al.* 1992; Sahadevan *et al.* 2004).

We are surprised that Allessie & de Groot (2014) still claim that we 'represent human AF by just a single map', and we therefore point to multiple maps and online videos of AF rotors in the CONFIRM trial (Narayan *et al.* 2012) and other studies. Their expectation of regular signals near a rotor core or 'anti-phase' signals at opposite equatorial points of a circular trajectory is a gross oversimplification of AF dynamics, in which rotors precess to produce variable electrograms (Zlochiver *et al.* 2008). This may explain difficulties in mapping AF by approaches designed for spatially coherent arrhythmias, including attempts to define timing sequences of complex electrograms. We accept that higher spatial resolution would be welcome, and are working to obtain this.

In conclusion, rotors have been demonstrated to drive atrial fibrillation in many patients and model systems. Future studies should define how remodelling contributes to rotor maintenance and fibrillatory breakdown.

### Call for comments

Readers are invited to give their views on this and the accompanying CrossTalk articles in this issue by submitting a brief comment. Comments may be posted up to 6 weeks after publication of the article, at which point the discussion will close and authors will be invited to submit a 'final word'. To submit a comment, go to http://jp.physoc.org/letters/submit/jphysiol;592/15/3171

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### Additional information

#### Competing interests

S. M. Narayan is co-author of intellectual property owned by the University of California Regents and licensed to Topera Inc. (Palo Alto, CA, USA). Topera does not sponsor any research, including that presented here. S. M. Narayan holds equity in Topera, and reports having received honoraria from Medtronic, St Jude Medical and Biotronik. J. Jalife serves on the Scientific Advisory Board of Topera, Inc.


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