"This is the peer reviewed version of the following article: [Watterson PA, Nicholson GM. Reply from Peter A. Watterson and Graham M. Nicholson to Letter to the Editor from Anton Kordić and Vedran Deletis re "Nerve-muscle activation by rotating permanent magnet configurations" The Journal of Physiology 594(13):3843-3844 01 Jul 2016]which has been published in final form at [<u>http://onlinelibrary.wiley.com.ezproxy.lib.uts.edu.au/doi/10.1113/JP272330/abstract</u>]. This article may be used for non-commercial purposes in accordance with Wiley Terms and Conditions for Self-Archiving."

Reply from Peter A. Watterson and Graham M. Nicholson

Drs Kordić and Deletis (Kordić & Deletis, 2016) have raised important issues about the focality and controllability of the excitation method described in our recent paper entitled 'Nerve– muscle activation by rotating permanent magnet configurations' (Watterson & Nicholson, 2016), which we are pleased to discuss.

Firstly, Drs Kordić and Deletis rightly note that increasing the depth of penetration of the electromagnetic field into the body by increasing the device dimensions would also reduce the focality of the electric field. However, the following argument suggests that there is some opportunity for our first prototype device to be scaled up. Each of the two cylindrical magnets of the prototype had diameter and axial length both 30 mm and each magnet acts like a current carrying coil of 33 kA turns distributed across the cylinder surface (this is not an exact analogy as the magnet material has magnetic permeability slightly larger than that of air). On the mid-plane containing the rotation axis and perpendicular to the magnetisation directions, the current loops are squares of side 30 mm. As we remarked in the Discussion section of our paper, the two-pole magnetic configuration of our prototype resembles that of a figure-of-eight coil. Differences arise, however, from the magnet surface current being distributed across a cylindrical surface, with the mid-plane of that surface inevitably displaced by the magnet radius (plus containment sleeve thickness, gap and housing) from the skin, whereas the figure-of-eight coil mid-plane would be closer to the skin. Our magnet side length of 30 mm places the prototype configuration scale at the low end of the range of mid-diameters per coil for standard commercial figure-of-eight coils, which is 25–70 mm. This would suggest that our bipole magnet configuration could be roughly doubled in size, while still maintaining a useful focality. Drawbacks of such a size doubling, however, would include that the magnets would cost eight times as much, and greater care still would be needed in their handling, both during manufacture, from their attraction to each other, and generally, from their attraction to steel.

The effect on activation of lowering the frequency inversely with the increase in the device dimension, to keep the stress unchanged, depends on the nerve parameters, shape and surroundings as follows. Suppose firstly that the boundary and resistivity distribution of the conducting medium were to scale proportional to the device dimension L. In this case, the magnetic flux density **B** and the electric field **E** external to the nerve, as determined by eqns (2), (7) and (8) of our paper, are stretched in length scale in all directions, keeping their magnitudes unchanged. So E does penetrate further. For activation at a nerve end, if the diffusion term (the first term) of our eqn (13) is small (more precisely, if eqn (19) applies at all frequencies considered), then our eqn (21) shows that the membrane potential at the nerve end would be greater for the large device at low frequency compared to the nerve positioned proportionally closer to the surface for the small device at high frequency. The increase is only slight, however, if $\omega au\leq 1$, where ω is the high angular frequency and au is the nerve time constant. For activation due to a sharp bend in a nerve, when activation is governed only by the local E at the bend, activation would be neutral to the scaling if the bend radius is fixed. For activation along a nerve path which scales with the device dimension L (including a straight nerve), the gradient of **E** scales inversely with L, but the metric F of our eqn (11) is independent of L. We mentioned in the second to last paragraph of our paper that the application of F over a greater length would increase the membrane potential, but this actually only relates to the reduction in the effect of the diffusion term of eqn (13). Countering this is the effect of the temporal decay term, the third term of eqn (13), which would increase in relative significance as the frequency was reduced. If

the diffusion term is small (i.e. if eqn (19) applies), then by eqn (22), unless the high frequency limit applies (i.e. unless $\textcircled{IIT} \gg 1$ at all frequencies considered), the membrane potential would be reduced as the frequency is reduced. Now consider the actual case, of a nerve within a given human limb, whose boundary is, of course, fixed (rather than scaling with the device dimension). As the device dimension increases, if the sides of the limb are not distant from the device, then the effect of the boundary condition eqn (8) would become more significant, generally reducing **E**. The effect on activation of a nerve then follows as above but with the reduction in **E** lowering the membrane potential for each case.

Whether or not a magnet configuration and dimension can be found to penetrate to sufficient depth at sufficient frequency to stimulate nerves in the brain remains to be determined. As we mentioned in the final paragraph of our paper, even if it is found possible, the high frequency likely to be needed with rotating magnet devices may well be precluded if it causes seizures. The safety guideline given in Table 4 of Rossi *et al.* (2009) for excitation by a figure-of-eight coil asserts that even just 25 Hz should only be applied for up to 1.28 s at motor threshold, and only for up to 0.24 s at 130% of motor threshold.

Secondly, Drs Kordić and Deletis remark that the rotating magnet method 'disables the control of magnetic induction duration (because of sustained sinusoidal excitation)' and that 'it will be close to impossible to control them and to make short trains of pulses which is the standard methodology for excitable tissue stimulation'. For a rotating magnet device at a given location, the amplitude of the electric field generated is proportional to the rotation speed (by our eqn (5)). Thus the amplitude is proportional to frequency, and they cannot be separately controlled, for a device in a fixed position. It is possible, however, to reduce the amplitude, at a given frequency, by moving the device away from the tissue.

The following indicates how rapidly the rotation speed might be accelerated and decelerated to introduce a 'burst' of excitation. How far above and below the threshold frequency is needed to reliably turn activation on and off would have to be trialled for a given nerve/muscle, but suppose the threshold frequency were 300 Hz and cycling between 270 Hz and 330 Hz was sufficient. Consider a cycle of period 1 s, comprising 0.2 s at 270 Hz, then a rise over 0.4 s to 330 Hz, followed immediately by a fall over 0.4 s back to 270 Hz, for which the burst duration (frequency above 300 Hz) would be 0.4 s. The prototype bipole rotor has a rotational inertia of 4.6×10^{-5} kg m² (calculated). To accelerate the rotor linearly from 16,200 r.p.m. (for 270 Hz) to 19,800 r.p.m. (for 330 Hz) in 0.4 s would require a torque of 4.3×10^{-2} N m, and an average additional power of 82 W. The increase in rotational kinetic energy associated with this power would be recovered by regenerative braking during the deceleration. The reaction torque on the housing would need to be resisted by fixing the housing. The motor winding of the prototype (Fig. 2B of our paper) was only designed for the very small steady state torque plus gradual acceleration, as the winding and motor controller were chosen to demonstrate how light and cheap the motor drive could be. Detailed electromagnetic finite element analysis and thermal calculations would be needed to optimally design a winding for this high acceleration torque, but approximate calculations based on the prototype winding suggest that it should be possible to provide such a winding with copper loss in the range 5–15 W, with resulting temperature rise, assuming a cooling rate typical for fan cooling, of about 20–60°C, around the limit of what would be acceptable.

Another method to oscillate the excitation amplitude would be to shuttle the device linearly towards and away from the skin surface, without changing the rotation speed. The prototype device has a mass of 0.54 kg (rotor plus housing). Consider a cycle of period 50 ms, comprising

10 ms with the device stationary at a distance just over 10 mm away from the skin, producing no activation, then a triangular velocity profile to move the device 10 mm to a position adjacent to the skin in 20 ms, followed immediately by a negative triangular velocity profile to move the device back away 10 mm in another 20 ms. The acceleration amplitudes would be 100 m s⁻², the maximum speed 1 m s⁻¹, and the force amplitudes to move just the device mass 54 N. Several manufacturers sell linear actuators capable of this drive cycle, with the allowance needed for the extra force to accelerate the actuator mover's mass (e.g. LinMot P01-48×240/30×180 if fan cooled, made by NTI AG, Spreitenbach, Switzerland). However, drawbacks of this method would include: the cost of the extra linear actuator and electronic controller; vibration fatigue; and that the device could not be pushed against the body. For some sites on the body, a gap might need to be maintained to avoid repeated impact between the device and the skin, but if there were only soft tissue under the skin, some level of repeated indentation should be allowable.

In summary, the above preliminary calculations suggest that for the prototype device, a burst frequency of about 1 s⁻¹ appears feasible using oscillation of the rotor speed, at little extra cost. A burst frequency of about 20 s⁻¹ appears feasible using a reciprocating oscillation, though at additional cost. The frequency is limited in the former method and there are drawbacks of the second method. So although neither method looks ideal, at least they offer two possible options to provide a burst mode delivery of excitation using rotating magnet devices.

Additional information

Competing interests

P.A.W. declares a potential financial interest in being the inventor of the related patent application (Watterson, 2012, in References section of original paper), owned by his employer, the University of Technology Sydney.

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