Reviewer's report

Title: Brachial Artery Flow-mediated Dilation Following Exercise with Augmented Oscillatory and Retrograde Shear Rate

Version: 1 Date: 19 July 2012

Reviewer: Richard Ferguson

Reviewer's report:

General comments
This study sought to assess the impact of antegrade and retrograde shear stress on brachial artery dilatory function (FMD) following exercise. A further aim was to explore the role of oxidative stress in mediating FMD. The hypotheses are based on well define in vivo and in vitro observations and the study extends this work in an appropriate and well controlled human experiment. The finding that there is no dose-response relationship with the level of retrograde shear is novel. The manuscript is, for the most, very well written.

Title and abstract
The title accurately reflects the content of the manuscript and the abstract is nicely written and accurately conveys the main findings of the study.

Background
The background is focussed and provides a logical synthesis of the interrelationship between the potential negative effects of retrograde shear and the overriding beneficial effects of antegrade shear during exercise. The hypotheses are clear and well defined.

Methods
The methods are appropriate, using well established techniques of assessing brachial artery function (although these are not without their critics, the authors do allude to these limitations in the discussion). I have some suggested revisions indicated below.

Results
The data appear to be sound and the outcome measures are within the values expected. I do have some suggested revisions indicated below.

Discussion
The discussion is concise, articulate, well written and in line with the data presented. The pertinent physiological explanations are mostly well discussed and limitations are clearly established. I have some suggested revisions indicated below.

Major Compulsory Revisions
1. Methods, Paragraph 2 – Experimental design.
This point has not influenced my decision on acceptance, but it certainly needs addressing. It is just a bit more than a minor revision!

The experimental design is not well described and quite hard to follow, despite apparently being quite a straightforward design. There are obviously 4 experimental conditions; 20%, 40%, 60%, 60%+VitC. The way this section is written is rather confusing and is confounded by the different doses of placebo and VitC (500 or 1000mg). I am assuming consumption of the 1000mg placebo was because the VitC capsule happened to be 1000mg. This section needs re-organising to make the design more clear.

2. Results.
It might be a specific requirement of the journal but the textual commentary of the results are long and laborious, and it is often difficult to “see the wood for the trees”. The figures do help although I am confused as to why the 60% and 60%+VitC are presented on a separate figure. On the basis from the experimental design there are 4 conditions; 20%, 40%, 60%, 60%+VitC, it appears that the 60% data is being presented twice. Would it not be simpler and more appropriate to have all 4 conditions on the one figure? Or have I misinterpreted the experimental design?!

3. Discussion, paragraph 2 and 3.
It strikes me that much of the discussion is focussed on the fact that greater doses of retrograde shear do not induce a greater impairment of FMD. This is logical and fair enough. However, one could look at it the other way round in that a rather minimal “dose” of retrograde (i.e in the 20% condition; approx. 100 to 110 s⁻¹ in control and cuffed arm respectively), induces quite a substantial impairment of FMD, even with the overriding antegrade shear being present. I wonder if the authors could comment on this observation, if appropriate.

Minor Essential Revisions
1. Methods, paragraph 2 – Experimental design
Please indicate, with an average or range, the number of days each exercise session was separated by.

Discretionary Revisions
1. Methods, paragraph 1 – Subjects
It is perhaps more common to provide the subject characteristics here. They are currently provided in the Results, paragraph 1.

**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a
statistician.

**Declaration of competing interests:**

I declare that I have no competing interests