Author's response to reviews

Title: The role of cervical Electrical Impedance Spectroscopy in the prediction of the course and outcome of induced labour.

Authors:

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Author's response to reviews: see over
Dear Editor

Re: MS: 2090185586226580
Research article: The role of cervical Electrical Impedance Spectroscopy in the prediction of the course and outcome of induced labour. Roobin J Jokhi, Brian H Brown and Dilly OC Anumba.

Thank you for your e-mail of 9th July 2009 in respect of the above manuscript communicating your willingness to consider publishing the manuscript subject to adequate responses to referee comments. I attach our detailed responses in response to the few outstanding comments by the referees. I am uploading the revised manuscript that takes into account these comments as requested.

Thank you for reconsidering publication of our manuscript.

I look forward to hearing from soon.

Kind regards.

Yours sincerely

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Reviewer 1

We thank this reviewer for his comments and respond to these as follows:

1) Length of labour is problematic as an outcome as it is susceptible to clinical management bias. As cervical dilatation of at least 3 cm is part of the definition of labour, it is possible women with a more favourable cervix by Bishop score may be assessed earlier in the induction cycle (e.g. for amniotomy). Therefore diagnosis of the "start" of spontaneous labour maybe brought forward in those with a higher Bishop score and lengthening length of labour will no impact on induction to delivery interval (as demonstrated).

Response: We agree that the determining the length of labour is problematic as the true onset of labour is never known, this being a retrospective diagnosis based on an assessment when the cervix has already progressed beyond 3cm dilatation and uterine contractions are regular, of a frequency more than 2 every 10 minutes. This problem is not unique to this work but is one encountered by all researchers and clinicians attempting to estimate the duration of labour. We also agree with the reviewer’s comments regarding the distinction between the duration of labour and the induction-delivery interval. It is for this reason that we present data on both parameters so that the reader can appreciate both features of induced labour reported in this series and judge the relative performance of clinical assessment and spectroscopy for both parameters. We have incorporated an additional sentence in the discussion acknowledging these caveats since the reviewer feels very strongly about this.

2) There is a strong argument for censoring cases of Caesarean delivery for non-reassuring fetal status in labour particularly as a significant number of labour induction were indicated by a suspicion of fetal compromise. In these cases labour induction is akin to an "oxytocin stress test".

Response: This reviewer had made this observation before and we fully took this view into account by comparing the performance of the Bishop score to cervical spectroscopy for predicting the success of vaginal delivery, thereby censoring Caesarean delivery as an outcome measure. We agree with the reviewer that caesarean delivery is a subjective, complex and multi-factorial indication for discontinuing labour. This is the very reason we have now avoided this as an outcome as he had suggested previously. Indeed we had also stated in the manuscript that “women whose sole indication for abdominal delivery was suspected fetal compromise were excluded from analysis”

3) The multiplicity of analyses of different probes, different frequencies for each probe against many different clinical outcomes is still a concern with regard to statistically spurious results.

Response: We studied probes of 4 different dimensions but detected significant results with only the 12mm probe at a very specific frequency range. Our modelling studies had predicted that cervical stromal changes were most likely to be identified by this probe which delivered the highest stromal fraction of injected current at and these frequencies. These electrical frequencies at which we detected significant results also demonstrated differences in cervical resistivity with parity and duration of labour. It would therefore be extremely unlikely that our observations simply occurred by chance. It is noteworthy that this probe dimension, at exactly these frequencies, has also demonstrated the best repeatability and reproducibility (inter-class coefficient of correlation >0.95, coefficient of variation <5%) of all probe designs employed in our experiments, consistent with our clinical observations in this study. This robust data on repeatability of the 12mm probe compared to smaller dimension probes is now published in a sister biomedical engineering journal (see Jokhi RP, Ghule VV, Brown BH, Anumba DO. Reproducibility and repeatability of measuring the electrical impedance of the pregnant human cervix-the effect of probe size and applied pressure. Biomedical Engineering Online. 2009 Jun 17;8:10).

4) PPV is typically higher with Bishop score than CR across Tables 4-6 for the various outcomes considered. Therefore as a clinical tool (as opposed to ROC/AUC analyses differences), it does not at present appeared superior to Bishop Score.

Response: The positive and negative likelihood ratios are the best summary indices of prediction in this setting. Whilst the BS demonstrated mainly non significant but slightly higher PPV and +LR than CR across clinical outcomes, the latter demonstrated better –LR and NPV than BS. We completely agree with the reviewer’s comment that at present CR does not appear superior to the BS, a position reflected in our discussion of the results and our conclusion. Ongoing device designs are currently geared at employing biophysical principles to attempt to improve CR clinical performance.
Response: We thank this reviewer for his commendation of our work. He has suggested minor revision of our comment on negative cervical smears prior to the study and we have amended the manuscript accordingly.