Author's response to reviews

Title: Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer

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Author's response to reviews:

Reviewer's report

Title: Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer

Version: 2 Date: 16 August 2008

Reviewer: Seward B Rutkove

Reviewer's report:

In this straightforward, retrospective study, the authors identify that reductions in the BIA's phase angle hold prognostic significance in patients with non-small cell lung cancer. They identify that using a cut-off value for phase angle of 5.3, they can separate the groups into those with a longer survival from those with shorter. In addition, they identify that with each increase in phase angle of 1 degree, there is a 0.79 reduction in relative risk.

Major Compulsory Revisions:

1. It is unclear how the 5.3 degrees value for the univariate analysis was chosen. 5.3 WAS THE MEDIAN PHASE ANGLE SCORE OF OUR PATIENT POPULATION. PREVIOUSLY, IN OUR BREAST CANCER PAPER, WE HAD SIMILARLY USED THE MEDIAN SCORE AS THE CUT-OFF. WE HAVE ADDED THIS EXPLANATION UNDER THE METHODS SECTION.

2. There is a strong independent association between age and phase angle.

Thus, age must be clearly adjusted for in the multivariate analysis and discussed in the univariate (e.g. what was the mean age (±/SD) of the below and above 5.3 degree groups). If one corrects for age, do these effects still hold? ALL REQUIRED INFORMATION IS NOW INCLUDED UNDER THE RESULTS.
AFTER ADJUSTING FOR AGE, THE RESULTS WERE STILL THE SAME.

3. We are provided no information as to when in the disease course the phase angle was measured. Was it measured repeatedly? If so, which measurement was utilized for this analysis? PHASE ANGLE WAS MEASURED AT PRESENTATION TO OUR HOSPITAL. IT WAS NOT MEASURED REPEATEDLY. THIS INFORMATION HAS NOW BEEN ADDED TO THE METHODS SECTION.

4. What devices were used to do this measurement? Was there more than one? If so, were they calibrated to one-another? FOR DETAILED INFORMATION ON THE METHODS, KINDLY REFER TO OUR RECENTLY PUBLISHED PAPER ON BREAST CANCER (Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, Lis CG: Bioelectrical impedance phase angle as a prognostic indicator in breast cancer. BMC Cancer 8:249:.249, 2008). THIS IS WHAT WE HAVE BEEN REQUESTED BY THE EDITOR.

5. Was a linear Cox model utilized? If so, this is probably not accurate as there is a floor effect with phase angle rarely, if ever, reaching much below 2 degrees. So a degree difference in phase will may have a much greater relative risk between 2 and 3 degrees than 7 and 8 degrees. This point needs to be addressed. AS SUGGESTED, THIS POINT HAS BEEN ADDRESSED IN THE REVISED PAPER UNDER THE STUDY LIMITATIONS.

6. It would be helpful to provide a histogram of the phase angles across the group of patients studied here. AS SUGGESTED, HISTOGRAM HAS BEEN INCLUDED IN THE PAPER.

Minor Essential Revisions:
1. Phase angle is measured in degrees. The authors repeatedly use the term “phase angle score.” They should simply provide the phase angle in degrees. CHANGES MADE.

2. Standard deviations should be given for age and phase. AS SUGGESTED, STANDARD DEVIATIONS FOR AGE AND PHASE ANGLE HAVE BEEN PROVIDED.

Discretionary Revisions:
1. If the authors measured the phase angle more than once per patient, the relative declines in its value over time may be especially informative. WE ARE SORRY, WE DO NOT HAVE THIS INFO.

Reviewer’s report

Title: Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIIB and IV non-small cell lung cancer

Version: 2 Date: 25 August 2008
Reviewer: Bruce Cornish
Reviewer's report:

The authors need to include details about the BIA instrumentation and measurement protocol. What were the electrode sites used for the BIA, at what frequency were measurements. The authors claim that the BIA was used to assess nutritional status but there is absolutely no mention of any other measures of nutritional status. FOR DETAILED INFORMATION ON THE METHODS, KINDLY REFER TO OUR RECENTLY PUBLISHED PAPER ON BREAST CANCER (Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, Lis CG: Bioelectrical impedance phase angle as a prognostic indicator in breast cancer. BMC Cancer 8:249,249, 2008). THIS IS WHAT WE HAVE BEEN REQUESTED BY THE EDITOR. SINCE OUR BREAST CANCER PAPER IS NOW PUBLISHED, WE HAVE INCLUDED THAT REFERENCE IN THE REVISED PAPER.

How is this manuscript different from their papers in advanced colorectal and pancreatic cancer? Is it simply the type of cancer that differs? YES, THIS IS JUST A DIFFERENT CANCER POPULATION.

Reviewer's report

Title: Bioelectrical impedance phase angle in clinical practice: implications for prognosis in stage IIIB and IV non-small cell lung cancer

Version: 2 Date: 1 September 2008

Reviewer: Ingvar Bosaeus

Reviewer's report:

This manuscript reports the prognostic role of BIA-derived phase angle in advanced NSCLC in a case series of 165 patients. Patients with a phase angle below the median (5.3) had a shorter survival that remained significant after adjusting for stage at diagnosis and prior treatment history. It is concluded that phase angle is an independent prognostic indicator in patients with stage IIIB and IV NSCLC, and that nutritional interventions targeted at improving phase angle could potentially lead to an improved survival in patients with advanced NSCLC.

This study extends previous observations, by the authors and others, on the relation between phase angle and survival in different forms of advanced cancer and other conditions. As previously stated by the authors (AJCN 2004;80:1634-38, Ref. 32), studies of various cancer types with large sample sizes are needed to further validate the significance of phase angle in cancer treatment settings. The study results are thus of importance in contributing to this. THANK YOU.

Comments:

As discussed on lines 158-166, previous reports have found a phase angle below the median of the study sample to be predictive of survival in lung cancer, colorectal and pancreatic cancer, but the median phase angle reported has
varied considerably, from 4.5 in the previous lung cancer report by Toso et al (Ref 33), to 5.6 in the authors´ previous report in colorectal cancer (Ref 32). In order to better understand what factors that may influence phase angle, it would be of interest to have more details on this. Was phase angle different in males versus females? In the reports discussed, was median survival time very different or similar? AS SUGGESTED, WE HAVE INCLUDED THE RELATIONSHIPS BETWEEN “AGE AND PHASE ANGLE” AND “GENDER AND PHASE ANGLE” UNDER THE RESULTS SECTION OF THE REVISED PAPER.

The conclusion in the abstract regarding nutritional interventions is not addressed in the discussion part, as far as I can see. Other factors than nutritional – such as metabolic changes driven by systemic inflammation – may be important in the development of cancer cachexia. Do the authors have any data on this. THANKS FOR THIS INTERESTING INSIGHT. WE ARE SORRY, WE DO NOT HAVE DATA ON THIS.

In the methods section, referral is made to a breast cancer manuscript, not available to me. I would prefer to have the methods used clearly described to enable the reader to make a judgment. Also, as in all BIA research, the specific equipment and measurement protocol used should be clearly described. FOR DETAILED INFORMATION ON THE METHODS, KINDLY REFER TO OUR RECENTLY PUBLISHED PAPER ON BREAST CANCER (Gupta D, Lammersfeld CA, Vashi PG, King J, Dahlk SL, Grutsch JF, Lis CG: Bioelectrical impedance phase angle as a prognostic indicator in breast cancer. BMC Cancer 8:249, 2008). THIS IS WHAT WE HAVE BEEN REQUESTED BY THE EDITOR. SINCE OUR BREAST CANCER PAPER IS NOW PUBLISHED, WE HAVE INCLUDED THAT REFERENCE IN THE REVISED PAPER.