Author's response to reviews

Title: Photodynamic diagnosis of shed prostate cancer cells in voided urine treated with 5-aminolevulinic acid

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Version: 2 Date: 24 June 2014

Author's response to reviews: see over
Reviewer's report
Title: Photodynamic diagnosis of shed prostate cancer cells in voided urine treated with 5-aminolevulinic acid
Version: 1 Date: 22 February 2014
Reviewer: Kenneth Iczkowski

Reviewer's report:
This article is on a well-done study that should generate significant interest. A few revisions are needed.

Minor Essential Revisions

1. It is misleading to say in the Abstract Results, Abstract Conclusions, and in the middle of page 13 Discussion that PPIX-PDD positivity increased without increasing Gleason score without qualifying this statement. The p value is .11 for correlation with Gleason score, so it should be stated that either "no change occurred with Gleason score" or that "a non-significant trend (p =0.11) was noted." It is misleading to say PPIX-PDD positivity increased without increasing Gleason score without qualifying this statement. The p-value should be added wherever this is mentioned to emphasize this.

We revised the abstract.

- The incidence of PPIX–PDD positivity did not increase with increasing total PSA levels, tumor stage or Gleason score. (page 2, line 4)
- (The incidence of PPIX–PDD positivity increased with increasing Gleason score.) → This sentence was omitted. (page 2, line 8)

We added "a non-significant trend (p =0.11) was noted." in every part about relation between PPIX-PDD positivity and GS.

2. It is misleading to say in the middle of page 13, "These results indicated that PCa detection...identified more clinically significant PCa...." Clinically significant is based on tumor volume in prostatectomy < 0.5 cc, tumor extent in prostate needle biopsy cores being < 50% of 2 or fewer cores, and on Gleason score being 3+3. Not only is (1.) above misleading, but to say PPIX-PDD identifies
more clinically significant cancer based on a NON-significant trend with Gleason score is not consistent with the definition of clinically significant (Epstein JI et al. J Urology Volume 160, Issue 6, Part 2, December 1998, Pages 2407–2411). Can the authors get the number and percent of core involvement and then determine whether PPIX-PPD really does, or does not, predict insignificant tumor?

We evaluated whether PPIX-PPD really does, or does not, predict insignificant tumor by this criteria. 16 patients had insignificant tumors using this criteria. PPIX-PPD didn’t predict insignificant tumor using chi-square test.

Page 3 first line don’t capitalize Prostate → done
Page 3 second line from bottom, say instead: Of the 138 patients, PCa was detected on needle biopsy in 81 (58.7%). → done
Page 9 top Palo Alta --> Palo Alto
Page 10 was the mean PSA of patients with prostate cancer really 50? In my experience the mean is 10 to 20 but not as high as 50. How many patients had PSA over 100? → Nine patients (range 101-690)
What if PSA was not measurable, how was that handled? In this situation it is more meaningful to give the Median PSA instead of the mean PSA because a few outliers are driving the mean very high. Also true for Table 3 for the free PSA and % free. → We changed the mean to the median of all parameter. We change Table 1.

Page 12 first line. Insert a space before Furthermore...Page 12 line 5 Capitalize Table 3. → capitalized
Page 14 bad sentence "...had to auto fluorescence." → We changed to autofluorescence
Page 15 put prostate cancer: PCa on new line → done
Figure 1. add spaces ALA (1 mM) exposure → done
Level of interest: An article of outstanding merit and interest 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.
Reviewer's report
Title: Photodynamic diagnosis of shed prostate cancer cells in voided urine treated with 5-aminolevulinic acid
Version: 1 Date: 28 May 2014
Reviewer: Yasutoshi Murayama
Reviewer's report:
PPIX-PDD is a new diagnosis of prostate cancer, and interesting for me. However, there are some questions.
1. You must show a comparison of the results of PDD and RT-PCR.

   We didn’t performed RT-PCR for every patients. We demonstrated RT-PCR in the first twenty patients. Then we evaluated the expression of PSA. We could confirmed the existence of cells from prostate by that. So I cannot show a comparison of the results of PDD and RT-PCR.

   We will add the limitation in the discussion section. (Page 14, line 9)

2. How many cases were the positive cases by other diagnostic methods that negative by the result of the PDD? And please show how many cases were PDD is positive, and other diagnostic methods are negative.

   Of 60 prostate cancer patients positive by PDD, 34 patients was negative by DRE, 38 patients by TRUS, 52 patients by PSAD and 38 patients by %fPSA. Of 21 prostate cancer negative by PDD, 10 patients was positive by DRE, 6 patients by TRUS 20 patients by PSAD, and 16 patients by %fPSA.

3. Please indicate as far as you understand the results of the surveillance about the false positive cases.

   We added "Only 4 patients of the false positive had got prostate needle biopsies after this study. 2 patients of them were diagnosed as prostate cancer. These false positive patients may need strict PSA follow-up or a saturation biopsy. " in discussion session. (Page 14, line 7)

Level of interest: An article of importance in its field
Quality of written English: Acceptable
Statistical review: Yes, and I have assessed the statistics in my report.
Declaration of competing interests:
I declare that I have no competing interests