

July 16, 2019

Dear Dr. Steindel,

My coauthors and I wish to submit a revision for our manuscript entitled “Ovarian Cancer Detection Using Photoacoustic Flow Cytometry” for consideration by the JoVE. The authors have seen and approved the manuscript, including: Joel F. Lusk, Christopher Miranda, and Barbara S. Smith (corresponding author). We are glad to submit revisions for this invited paper to JoVE.

In this work, we explore a new application in photoacoustic imaging, towards promoting improved diagnostics for ovarian cancer metastasis. This is significant because 85-90% of patients will experience disease recurrence, however, there is no accurate method for detecting ovarian CTCs at the point-of-care. Thus, leading to limitations in clinical applications for the early detection of ovarian cancer metastasis. Photoacoustic detection is widely used for biomedical imaging applications, as presented in the author’s previously published work. Recent studies have shown that folic acid functionalization is an effective strategy for targeting ovarian cancer cells by photoacoustics, however, no study to date has attempted to identify ovarian circulating tumor cells in flow. In this paper, we report on the development and testing of folic acid functionalized copper sulfide nanoparticles (FA CuS NPs) as photoacoustic contrast agents for the identification of ovarian circulating tumor cells in flow. Our results show the detection of ovarian CTCs in flow, down to 1 cell/  $\mu\text{L}$ .

A response to reviewers has been included in the resubmission along with a revised manuscript. Each of the reviewer’s comments were taken into consideration, and updates were made accordingly. The authors believe that these updates have significantly improved the manuscript quality. This manuscript is specifically being sent to JoVE due to the interest of its readership, who are highly in tune with advancements within the field of photoacoustic imaging and advanced diagnostic detection. This paper is relevant to readers in the areas of photacoustics, photacoustic flow cytometry, copper sulfide nanoparticles, circulating tumor cells, ovarian cancer, folic acid, and optoacoustic.

Thank you for your invitation and consideration of our manuscript.

Sincerely,



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