Reviewer's report

Title: Confocal Microscopy of Unfixed Breast Needle Core Biopsies: A Comparison to Fixed and Stained Sections

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Reviewer: Rebecca Richards-Kortum

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This paper provides a first study to compare reflectance confocal images of unfixed breast needle core biopsies to fixed and stained sections. The authors use two simple contrast agents: citric acid to enhance nuclear reflectivity and glycerol to reduce stromal reflectance. The paper demonstrates that reflectance confocal microscopy can provide real time images of pathologic features of interest with a similar level of morphologic detail as available in fixed and H&E stained sections. This is an important advance as confocal images can be obtained rapidly and without the need for extensive sample preparation. As high quality reflectance confocal microscopes are now available clinically, this is a technique which should be considered for wider adoption. The paper is an important advance and will be of general interest to the readers of BMC.

However, this reviewer feels that the paper would be improved if the authors considered a number of additional issues.

1. The authors collect data from 49 patients, but present images from a subset of 7 cases. Even in these cases, a single small image is presented which represents only a fraction of the data collected. The paper would be strengthened if a pathologist reviewed the confocal images to provide a diagnosis and these diagnoses were then compared to that obtained from the H&E sections.

2. Is there a more effective way to summarize the data of Table 2? This reviewer feels it would be sufficient to report the fraction of samples in which the staining impacted subsequent histologic processing.

3. The nuclear detail that is present in the images does not appear as sharp as that which has been reported in previous work with cervical and oral biopsies treated with acetic acid (for example see Academic Radiology, 9:504-512, 2002 or Clinical Cancer Research, 9(13):4714-4721, 2003.) Do the authors attribute this to differences in the contrast agents used, lower spatial resolution or differences in the tissue? Since visualization of nuclear morphology is crucial for diagnosis, this is an important point.