

optically image label-free inside the tumor cavity and across the resection bed addresses the critical need for improved intraoperative detection of residual disease to ensure local control, and to potentially eliminate reintervention due to postoperative margin findings. Future work will involve OCT imaging of the *in vivo* resection bed during other surgical procedures such as for melanoma and pancreatic, gastrointestinal, and thyroid cancers.

Disclosure of Potential Conflicts of Interest

D. Darga is an employee and has ownership interest (including patents) in Diagnostic Photonics, Inc. A. Cittadine is a CEO and has ownership interest (including patents) in Diagnostic Photonics, Inc. A.M. Zysk has ownership interest in and patents from Diagnostic Photonics, Inc. A.M. Zysk also has patents from the University of Illinois. S.A. Boppart has ownership interest (including patents) and is a consultant/advisory board member for Diagnostic Photonics, Inc. S.A. Boppart also has patents from the University of Illinois. No potential conflicts of interest were disclosed by the other authors.

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Acknowledgments

The authors thank Darold Spillman for his operations and information technology support for this research and Doug Simpson for his helpful input on the statistical analysis of these results. They also thank Christine Canfield and the clinical research and surgical nursing staff at Carle Foundation Hospital for their contributions.

Grant Support

This research was supported in part by grants from the National Institutes of Health (1 R01 EB012479 and 1 R01 CA166309; S.A. Boppart). S.J. Erickson-Bhatt was supported by a Beckman Institute Fellowship.

Received February 13, 2015; revised June 17, 2015; accepted June 19, 2015; published online September 15, 2015.

References

1. Singletary SE. Surgical margins in patients with early-stage breast cancer treated with breast conservation therapy. *Am J Surg* 2002;184:383-93.
2. Jorns JM, Visscher D, Sabel M, Breslin T, Healy P, Daignaut S, et al. Intraoperative frozen section analysis of margins in breast conserving surgery significantly decreases reoperative rates: one-year experience at an ambulatory surgical center. *Am J Clin Pathol* 2012;138:657-69.
3. D'Halluin F, Tas P, Rouquette S, Bendavid C, Foucher F, Meshba H, et al. Intra-operative touch preparation cytology following lumpectomy for breast cancer: a series of 400 procedures. *Breast* 2009;18:248-53.
4. Emmadi R, Wiley EL. Evaluation of resection margins in breast conservation therapy: the pathology perspective-past, present, and future. *Int J Surg Oncol* 2012;2012:180259.
5. Molina MA, Snell S, Franceschi D, Jorda M, Gomez C, Moffat FL, et al. Breast specimen orientation. *Ann Surg Oncol* 2009;16:285-8.
6. Boppart SA, Luo W, Marks DL, Singletary KW. Optical coherence tomography: feasibility for basic research and image-guided surgery of breast cancer. *Breast Cancer Res Treat* 2004;84:85-97.
7. Hsiung PL, Phatak DR, Chen Y, Aguirre AD, Fujimoto JG, Connolly JL. Benign and malignant lesions in the human breast depicted with ultrahigh resolution and three-dimensional optical coherence tomography. *Radiology* 2007;244:865-74.
8. Nguyen FT, Zysk AM, Chaney EJ, Kotynek JG, Oliphant UJ, Bellafiore FJ, et al. Intraoperative evaluation of breast tumor margins with optical coherence tomography. *Cancer Res* 2009;69:8790-6.
9. Nguyen FT, Zysk AM, Chaney EJ, Adie SG, Kotynek JG, Oliphant UJ, et al. Optical coherence tomography: the intraoperative assessment of lymph nodes in breast cancer. *IEEE Eng Med Biol Mag* 2010;29:63-70.
10. Zysk AM, Chen K, Gabrielson E, Tafta L, May Gonzalez EA, Canner JK, et al. Intraoperative assessment of final margins with a handheld optical imaging probe during breast-conserving surgery may reduce the reoperation rate: Results of a multicenter study. *Ann Surg Oncol* 2015 (in press).
11. Kuo WC, Kim J, Shemonski ND, Chaney EJ, Spillman DR Jr, Boppart SA. Real-time three-dimensional optical coherence tomography image-guided core-needle biopsy system. *Biomed Opt Express* 2012;3:1149-61.
12. McLaughlin AG, Quirk BC, Curatolo A, Kirk RW, Scolaro L, Lorensen D, et al. Imaging of breast cancer with optical coherence tomography needle probes: feasibility and initial results. *IEEE J Sel Top Quantum Electron* 2012;18:1184-91.
13. John R, Adie SG, Chaney EJ, Marjanovic M, Tangella KV, Boppart SA. Three-dimensional optical coherence tomography for optical biopsy of lymph nodes and assessment of metastatic disease. *Ann Surg Oncol* 2013;20:3685-93.
14. Assayag O, Antoine M, Sigal-Zafrani B, Riben M, Harms F, Burcheri A, et al. Large field, high resolution full-field optical coherence tomography: a pre-clinical study of human breast tissue and cancer assessment. *Technol Cancer Res Treat* 2014;13:455-68.
15. Schnabel F, Boolbol SK, Gittleman M, Karni T, Tafta L, Feldman S, et al. Randomized prospective study of lumpectomy margin assessment with use of MarginProbe in patients with nonpalpable breast malignancies. *Ann Surg Oncol* 2014;21:1589-95.
16. Brown JQ, Bydlon TM, Kennedy SA, Caldwell ML, Gallagher JE, Junker M, et al. Optical spectral surveillance of breast tissue landscapes for detection of residual disease in breast tumor margins. *PLoS ONE* 2013;8:e69906.
17. Abeytunge S, Li Y, Larson B, Peterson G, Seltzer E, Toledo-Crow R, et al. Confocal microscopy with strip mosaicing for rapid imaging over large areas of excised tissue. *J Biomed Opt* 2013;18:61227.
18. Moran MS, Schnitt SJ, Giuliano AE, Harris JR, Khan SA, Horton J, et al. Society of Surgical Oncology-American Society for Radiation Oncology consensus guideline on margins for breast-conserving surgery with whole-breast irradiation in stages I and II invasive breast cancer. *Ann Surg Oncol* 2014;21:704-16.
19. Tummers QR, Verbeek FP, Schaafsma BE, Boonstra MC, van der Vorst JR, Liefers GJ, et al. Real-time intraoperative detection of breast cancer using near-infrared fluorescence imaging and Methylene Blue. *Eur J Surg Oncol* 2014;40:850-8.
20. Urano Y, Sakabe M, Kosaka N, Ogawa M, Mitsunaga M, Asanuma D, et al. Rapid cancer detection by topically spraying a γ -glutamyltranspeptidase-activated fluorescent probe. *Sci Transl Med* 2011;3:110ra119.
21. Ahmad A, Shemonski ND, Adie SG, Kim HS, Hwu WM, Carney PS, et al. Real-time *in vivo* computed optical interferometric tomography. *Nat Photonics* 2013;7:444-8.
22. Ralston TS, Marks DL, Carney PS, Boppart SA. Interferometric synthetic aperture microscopy. *Nat Phys* 2007;3:129-34.