

Smaller, faster, brighter

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Impact Paragraph

Role of very small tissue samples in the diagnosis of breast cancer

Breast cancer is the most frequent cancer in women worldwide, and too many women still die of the disease. Thanks to mammography screening and better treatment, the disease has become less threatening for women in western countries such as Europe, Australia or the United States. In other areas around the world, however, breast cancer is actually becoming more frequent.[1]

Once a patient notices a lump herself or her physician by physical exam, or there are abnormalities in a screening exam she will be referred to a breast center and encounters a whole team of breast specialists. This is quite distressing for the patient, and every woman looks for a fast and reliable way to get this problem sorted out. Is it benign, or is it cancer? Is surgery needed, or can this be left alone? The work presented here describes studies based on the author's own practice as a pathologist in the hospital. The goal was to show that breast cancer can be diagnosed with very small tissue samples that are not very painful to obtain and barely leave a trace.

Studies presented in this thesis are of interest for all of these specialist colleagues in the multidisciplinary breast teams. We examine how very small tissue samples can be used to diagnose the nature of a breast lesion. The sampling can consist of a very fine needle (so thin it does barely leave a trace), or slightly thicker needles which remove a small cylinder of tissue. A tissue sample is necessary for diagnosis but the goal is to obtain just enough cells to make a diagnosis, and allow extra studies on the tissue to determine the individual treatment plan for the patients. Even advanced molecular testing is now possible on small tissue samples as one of the papers presented here show.[2]

First, other physicians will be informed about the research progress with those small tissue samples. The author of this thesis is a pathologist, and communicates the findings with the other breast specialists that testing with those fine needle biopsies is very reliable by ways of writing a paper that is made accessible on medical databases. Our group presented at several conferences as posters and talks internationally, for example the presentation *Breast Cytology Continues to be Relevant in a Large Academic Medical Center* as a platform presentation (selected abstract) at the 31st International Academy of Pathology and 28th European Society of Pathology Congress, Cologne, Germany, 2016. Papers published about this work can be retrieved through publicly available databases.

Medical practitioners in various parts of the world, also in areas where access to specialized medical care is not readily available, can use the findings of this study and improve their practice. For example, people in many countries in Asia or Africa do not have access to breast cancer screening by mammography or radiographically targeted biopsies as in Europe or the US. Access to the internet helps disperse knowledge and articles to update practice. A women with a breast lump can find out through a fast and affordable procedure at the clinic if this lump is nothing to worry about or cancerous. Her health care provider can receive actionable guidance through freely accessible publications.[3]

Several international studies were reported alone in the past year about the utility of the Yokohama Breast Cytology classification system.[4-9]

New techniques in breast images to guide the hands of pathologists and surgeons

New forms of *in vivo* imaging allow pictures of breast tissue right in the operating room or surgical bench for the pathologist to see what is in the tissue, and for the surgeon to possibly adjust the procedure right away during the operation.

Some decades ago, only a growing lump in the breast led to surgery, which then consisted mostly of a radical operation with removal of the axillary lymph nodes if the mass was found to be

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malignant. Now those cancers are often caught earlier and can be removed with smaller operations, where only as much breast tissue as necessary is excised to allow for complete removal of the tumor with a safe rim of normal tissue.

Research findings of those novel methods were first presented at meetings with other physicians, for example those about *MicroCT of Breast Specimens* that were presented at the Deutsche Gesellschaft für Pathologie Annual Meeting, Berlin, Germany, in June 2012, or at the American Society of Breast Surgeons (ASBS) 14th Annual Meeting, in Chicago, IL in May 2013. A recent meta-analysis comparing breast imaging techniques including micro-CT for margin evaluation was published recently.[11]

Detection of residual breast cancer in breast excisions by the LUM imaging system was presented as a poster the 107th Annual Meeting of the United States and Canadian Academy of Pathology (USCAP), Vancouver, BC, Canada, March 2018.

The novel fluorescent imaging system was not only shown to be feasible but also with good performance for better intraoperative margin evaluation in breast cancer. [12,13] The method has recently completed enrollment in the Investigation of Novel Surgical Imaging for Tumor Excision (INSITE) Pivotal Trial NCT03686215.[14] Those studies will help obtain further knowledge about the usefulness and of this novel technique for the future.

Conclusion

In this thesis diagnostic methods of breast cancer take center stage. Tissue core biopsy is standard of care for initial diagnosis in well-resourced medical settings. We showed that even smaller tissue biopsies and specifically breast cytology is suitable for this purpose. Contemporary pathology practice integrates all tissue specimens to maximize information also from minimal samples.

Breast excision is the standard of care for breast-conserving surgical treatment, but positive margins still provide a risk for local recurrence. We evaluated several novel imaging modalities to immediately visualize tumor in breast excision specimens that may help guide tissue evaluation and tested an imaging system for intraoperative margin evaluation.

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