

Smaller, faster, brighter

Citation for published version (APA):

Brachtel, E. F. (2022). *Smaller, faster, brighter: new concepts in the tissue diagnosis of breast cancer*. [Doctoral Thesis, Maastricht University]. Maastricht University. <https://doi.org/10.26481/dis.20220516eb>

Document status and date:

Published: 01/01/2022

DOI:

[10.26481/dis.20220516eb](https://doi.org/10.26481/dis.20220516eb)

Document Version:

Publisher's PDF, also known as Version of record

Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

www.umlib.nl/taverne-license

Take down policy

If you believe that this document breaches copyright please contact us at:

repository@maastrichtuniversity.nl

providing details and we will investigate your claim.

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 pathol-

ogist, 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

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.

References

1. Heer, E., et al., *Global burden and trends in premenopausal and postmenopausal breast cancer: a popula-*

- tion-based study.* Lancet Glob Health, 2020. **8**(8): p. e1027-e1037.
2. Dong, J., et al., *Breast fine needle aspiration continues to be relevant in a large academic medical center: experience from Massachusetts General Hospital.* Breast Cancer Res Treat, 2016. **158**(2): p. 297-305.
3. Field, A.S., et al., *The International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Biopsy Cytopathology.* Acta Cytol, 2019. **63**(4): p. 257-273.
4. Agrawal, N., et al., *Fine-Needle aspiration biopsy cytopathology of breast lesions using the International Academy of Cytology Yokohama System and rapid On-Site Evaluation: A Single-Institute Experience.* Acta Cytol, 2021;**65**(6): p. 463-477.
5. Dixit, N., et al., *A retrospective analysis of 512 cases of breast fine needle aspiration cytology utilizing the recently proposed IAC Yokohama system for reporting breast cytopathology.* Diagn Cytopathol, 2021. **49**(9): p. 1022-1031.
6. Marabi, M., et al., *The International Academy of Cytology Yokohama System for Reporting Breast Cytopathology showed improved diagnostic accuracy.* Cancer Cytopathol, 2021. **129**(11): p. 852-864.
7. Nigam, J.S., et al., *The International Academy of Cytology standardized reporting of breast fine-needle aspiration biopsy cytology: A 2 year's retrospective study with application of categories and their assessment of risk of malignancy.* Cytojournal, 2021. **18**: p. 27.
8. de Rosa, F., et al., *The continuing role of breast fine-needle aspiration biopsy after the introduction of the IAC Yokohama System for Reporting Breast Fine Needle Aspiration Biopsy Cytopathology.* Diagn Cytopathol, 2020. **48**(12): p. 1244-1253.
9. Sarangi, S., et al., *Risk stratification of breast fine-needle aspiration biopsy specimens performed without radiologic guidance by application of the International Academy of Cytology Yokohama System for Reporting Breast Fine-Needle Aspiration Cytopathology.* Acta Cytol, 2021. **65**(6): p. 483-493.
10. Tang, R., et al., *Intraoperative micro-computed tomography (micro-CT): a novel method for determination of primary tumour dimensions in breast cancer specimens.* Br J Radiol, 2016. **89**(1058): p. 20150581.
11. Manhoobi, I.P., et al., *Diagnostic accuracy of radiography, digital breast tomosynthesis, micro-CT and ultrasound for margin assessment during breast surgery: A systematic review and meta-analysis.* Acad Radiol, 2022. **S1076-6332**(21): p. 00571-7.
12. Smith, B.L., et al., *Feasibility study of a novel protease-activated fluorescent imaging system for real-time, intraoperative detection of residual breast cancer in breast conserving surgery.* Ann Surg Oncol, 2020. **27**(6): p. 1854-1861.
13. Lanahan, C.R., et al., *Performance of a novel protease-activated fluorescent imaging system for real-time, intraoperative detection of residual breast cancer in breast conserving surgery.* Breast Cancer Res Treat, 2021. **187**(1): p. 145-153.
14. <http://www.lumicell.com/news/news-press-releases-2021-09-30.php> (accessed 21 January, 2022).