Tissue classification during a stereotactic breast biopsy procedure using diffuse reflectance spectroscopy

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Ethical review	Approved WMO
Status	Pending
Health condition type	Breast therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON51435

Source
ToetsingOnline

Brief title
Optimizing stereotactic breast biopsies

Condition

- Breast therapeutic procedures

Synonym
Breast cancer, Suspected Breast Lesions

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: KWF grant

Intervention

Keyword: Breast leasions, Diffuse reflectance spectroscopy, Stereotactic breast biopsy

Outcome measures

Primary outcome

The primary objective of this study is to determine the performance of DRS measurements for malignant (invasive carcinoma and DCIS) tissue type discrimination during a stereotactic breast biopsy. The main study endpoint is to achieve a sensitivity higher than 90% of our previous developed tissue classification algorithm in the detection of malignant (invasive carcinoma and DCIS) tissue types during a biopsy procedure.

Secondary outcome

The secondary objective of this study is to evaluate the added value of DRS measurements during a stereotactic biopsy procedure i.e. predict which biopsies are the most important for correct diagnosis (based on the results of the tissue sensing device). If we can predict which biopsies are the most important then in the future we can reduce the number of biopsies during the stereotactic biopsy procedure.

Study description

Background summary

Stereotactic Vacuum Assisted Breast Biopsy (VABB) is a minimal invasive percutaneous biopsy technique for non-palpable breast lesions that appear as microcalcifications on mammograms but are invisible on US. Microcalcifications play a crucial role in early breast cancer diagnosis, the second leading cause of cancer death among women. Approximately 50% of non-palpable breast cancers are detected by mammography, exclusively by microcalcifications patterns.

Moreover, 80-90% of ductal carcinoma in situ (DCIS) lesions present with microcalcifications only, without any accompanying mass lesions. Therefore, non-palpable lesions with microcalcifications found in mammography should be urgently evaluated.

Stereotactic VABB is a safe and accurate method for the evaluation of suspicious microcalcifications and diagnosis of early breast cancer with a 71-100% sensitivity and 85-100% specificity range. VABB devices enable to obtain multiple larger specimens under vacuum suction using a single insertion. For cases where the microcalcification is spread over a large area, the needle can be withdrawn and reinserted to perform biopsy retrieval in different areas. Complications from VABB may include bleeding or pain during the procedure, as well as postoperative pain, hemorrhaging, hematomas and infection. Scar formation following VABB is observed in 16.1% of the procedures. While much progress has been made over the past decade, there is still room for improvement through the development of new technologies that increase accuracy, safety, and cost-effectiveness of the procedure.

The accuracy of the stereotactic VABB depends, besides accurate positioning and quality assurance during the procedure, on the number and volume (and thereby needle thickness) of the specimens taken. The main disadvantage of stereotactic VABB is the underestimation of invasive cancer diagnosis from biopsy specimens. An overall underestimation rate from 8% till 88% for have been reported. Atypical ductal hyperplasia (ADH) is generally considered a direct precursor of low-grade DCIS and thus low-grade invasive ductal cancer. The histological features of biopsy specimens containing ADH show many similarities of those involving DCIS. Therefore, there would be a chance that a small sample of a DCIS lesion may be interpreted as ADH by the pathologist [9]. The histological underestimation in such cases may simply result from sampling error and are inversely correlated with the amount of tissue excised. Not only is it psychologically distressing for patients when breast cancer is underestimated, but it also implies a delay in establishing a definitive diagnosis, hence, appropriate treatment.

During the stereotactic VABB, the retrieval of calcification might suggest that sufficient and representative tissue has been sampled from the targeted lesion. Recently, new biopsy devices are introduced (Brevera® HOLOGIC) which make direct specimen radiography during the procedure possible. However, if radiologists decide to end the procedure as soon as calcifications are retrieved, a false negative result may arise since a definite diagnosis is not only based on specimens with calcifications. Zagouri et al. studied the diagnostic value of specimens with and without calcifications and found that VABB cores with microcalcifications are superior in DCIS and ADH diagnosis but cores without microcalcifications may be more valuable for the diagnosis of the invasive component. So during the procedure, the radiologist will have to consider how many biopsies are needed to make the correct diagnosis which can lead to under- of oversampling of breast tissue. Current developed techniques

for quality control during the procedure are not efficiently contributing to this trade off so, improvement is needed to optimize the retrieval of the invasive component.

In addition, stereotactic VABB procedures can be technically demanding due to the nature of lesions and patient factors, which occasionally leads to failure in retrieving the targeted lesion. The causes of retrieval failure include significant bleeding, perception factors, targeting factors, unfavorable calcification location, patient movement and technical factors. The failure rate varies from up to 21%. In those cases, the procedure must be repeated several times which leads to unnecessary tissue removal. Especially scattered microcalcification locations or small clusters of microcalcifications within the breast are difficult to target, as it is technically challenging to identify the same calcification focus on the stereotactic images. In those cases, sometimes up to 25 biopsies are collected to achieve calcification retrieval. Not taking more specimens than necessary is essential to prevent complications, maintain cost-effectiveness and to keep patient burden to a minimum.

To summarize, quality control during the stereotactic VABB procedure is needed to improve current limitations such as the underestimation of invasive carcinoma in biopsy samples, the under- and oversampling of breast tissue and to optimize microcalcification retrieval for challenging locations. This can be possible by using an optical technology for real-time tissue sensing during the stereotactic VABB procedure. To this end, we developed a tissue sensing introducer with integrated optical fibers that enable diffuse reflectance spectroscopy (DRS) measurements. The developed tissue sensing introducer can be used in conjunction with a standard vacuum-assisted stereotactic biopsy (VAB) device. DRS is a light-based technology that enables the discrimination of tissue types based on their optical characteristics. The DRS measurements reflect functional, biochemical and morphologic information of measured tissue and in that way are able to discriminate tumorous tissue from healthy tissue. The advantages of DRS are that it is non-destructive, does not require exogenous contrast with dyes, and has the potential to be performed in real-time. DRS technology has already been successfully evaluated in multiple oncological domains for discriminating tumor tissue from healthy tissue with classification accuracies of 0.86-1.00.

In our previous studies, we show that fiber-optic DRS is able to detect invasive carcinoma (IC) and Ductal Carcinoma In Situ (DCIS) ex-vivo with high accuracies (93-100%) without the substantial influence of patient factors such as menopausal status. Our result mainly relies on the Near Infrared (NIR) wavelength range, which eliminates the influence of blood on the measurements, which is of great benefit for in-vivo measurements during stereotactic biopsy procedures. With DRS measurements derived from ex-vivo breast specimens, a real-time tissue classification algorithm was developed for the discrimination of invasive carcinoma and DCIS from healthy breast tissue using the optical

introducer. Compared to this previous study, the current study is a step towards the use case of optical spectroscopy during stereotactic biopsy procedures. In this way, we will be able to predict tissue types during the stereotactic biopsy procedure and assess whether the biopsy sample needs to be collected before retrieval. With improved biopsy site selection during the procedure the diagnostic yield will increase, the number of biopsies will be reduced and the overall accuracy of the procedure will improve which results in reduced complications for the patient.

Study objective

This study is designed as a single-center diagnostic accuracy study. The duration of the study is 2 years. To introduce tissue sensing during the stereotactic VABB, we developed an optical introducer with DRS fibers that can be integrated with the HOLOGIC eviva system, capable of rotating to align the gap on the introducer with the needle aperture. This way, DRS measurements can be performed for each clockwise position of the VAB needle. The optical introducer makes it possible to determine the correct position of the VAB device (in tumor or normal breast tissue) and to measure the retrieved tissue within the biopsy cavity of the VAB needle before it is definitely sucked away by VAB system. In this way, optimal real-time tissue feedback can be obtained from the position of the VAB needle as well as of the actual biopsy tissue that is taken. Since the DRS measurements will be acquired in a new configuration (designed for Hologic eviva needles) and a different setup,, the algorithm for tissue classification has to be further evaluated during the stereotactic vacuum-assisted biopsy.

This study is therefore dedicated to validate the sensing VAB device and the algorithm developed in the previous study in an existing clinical workflow during vacuum-assisted biopsy under stereotactic guidance. In this study, we will be able to test the optical introducer in a controlled manner by histopathological confirmation of the optically measured locations. In addition, we will collect a new dataset for DRS measurements in vivo with a reliable histopathological gold standard. This will also provide us with the opportunity to fine-tune the classification algorithm if there are differences between the previously collected dataset based on ex-vivo measurements. The goal is to achieve a real-time tissue classification algorithm for the discrimination of tumor tissue (invasive carcinoma and DCIS) from healthy breast tissue using the optical introducer with a sensitivity of at least 90%.

With this, we will be able to predict tissue types during the stereotactic biopsy procedure and assess whether the biopsy sample needs to be collected before retrieval. With improved biopsy selection during the procedure, the number of biopsies can be reduced as well as the complications for the patient. Most important, the diagnostic yield of the procedure will increase.

Study design

Single-center diagnostic accuracy study. The duration of the study is 2 years.

Intervention

The procedure will take place under standard conditions in the department of Radiology using the stereotactic guided HOLOGIC Affirm® Prone biopsy system and HOLOGIC Suros vacuum console. The biopsy will be performed by experienced radiologists familiar with VAB. We will use the HOLOGIC eviva Stereotactic Guided Breast Biopsy Device 9Ga in combination with the tissue sensing introducer [D2: IMDD - Tissue Sensing Introducer - Design]. The optical fibers of the tissue sensing introducer will be connected to the DRS console [D2: IMDD - DRS console], as described earlier. The DRS measurements will be performed over a wavelength range of 400-1600 nm.

At the start of the procedure, a 3D mammography image (Tomosynthesis) will be acquired, and the area of interest is targeted. Once the targeting is completed, coordinates of the lesion within the breast are available, and the needle position is determined. In cases with mainly microcalcifications, no tumor lesion may be present. In those cases where no tumor lesion can be recognized, the device will be moved through the most suspicious area, e.g. the tissue with microcalcifications.

Next, the automatic targeting system will be activated, and the HOLOGIC eviva breast biopsy device will be partly moved to the identified coordinates so that the needle tip is just before the skin surface of the breast to ensure accurate anesthetic placement. Thereafter, the needle will be manually advanced as usual into the breast until the firing position has been reached. During the insertion of the needle, DRS measurements will be acquired continuously at the tip of the sensing VAB biopsy system (Figure 1 (a-c)). The measurements will be obtained along the entire needle trajectory and will provide spectral information from normal breast tissue and in larger lesions also from the transition zone of the normal tissue to the lesion. The positioning of the VAB needle with consecutive DRS measurements will end at the edge of the tumor lesion, or in those cases with no clear tumor lesion, until the most suspicious area.

A pair of pre-fire stereo images will be taken to determine that the area of interest is correctly targeted. The device is then fired using the remote firing mechanism advancing the needle 23 mm toward the target.

Once the needle is positioned in the lesion, DRS measurements will be made from the tissue in the biopsy aperture/cavity (biopsy location) on different locations of the aperture by sliding the optical introducer over the needle as illustrated in Figure 1 (d-f). After the DRS measurements, the biopsy procedure

will be continued by pulling the optically measured tissue further into the aperture with vacuum suction and subsequently advancing the tissue cutter. The biopsied core will be transported into a tissue collection chamber at the back of the biopsy device. Since we want a direct correlation between the sample and the measured DRS signal, we take only a single core each time. To keep track of the order of biopsy samples, the tissue filter basket will be replaced with a new one after each biopsy retrieval. The procedure will be repeated for at least 6 clock positions for every patient, or more if clinically indicated. For each obtained core specimen, the developed classification algorithm will be validated against histopathological examination.

It should be noticed that the whole stereotactic biopsy procedure is thus performed according to the standard procedure, except for the DRS measurements and biopsy samples handling.

Study burden and risks

The light used in the measurements is visual light and near infrared light. This light, to the extent that we use it, has no negative side effects. No adverse reactions have occurred for patient who participated in previous studies with similar instruments. We do not expect any side effects or complications when using this new instrument. The procedure time will increase by 5 minutes.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Woman (and trans man without mastectomy), >= 18 years old
Patients with a suspected breast lesion on imaging that requires stereotactic diagnostic biopsy
Written informed consent

Exclusion criteria

Patients with breast implants
History of breast-related radiotherapy treatment
Previous breast surgery
Suspected oversensitivity to light; e.g. patient who has had photodynamic therapy
Pregnant and nursing patients

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending

Start date (anticipated):	01-01-2022
Enrollment:	120
Type:	Anticipated

Medical products/devices used

Generic name:	Optical Introducer
Registration:	No

Ethics review

Approved WMO Date:	07-07-2022
Application type:	First submission
Review commission:	METC NedMec

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL79255.031.21