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Quantitative Transmission Imaging Evaluation (QTIE Study)  
Compared With MRI As Supplemental Screening In Patients With  
High Lifetime Risk Of Breast Cancer

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## Mayo Clinic Protocol Template for Minimal Risk Research

### General Study Information

Principal Investigator: Dr. Tiffany Sae-Kho

Study Title: Quantitative Transmission Imaging Evaluation (QTIE Study) compared with MRI as supplemental screening in patients with high lifetime risk of breast cancer.

Current Protocol Version Number: 1

Current Date: 6/26/2024

### Research Question and Aims

#### Hypothesis:

- Quantitative transmission imaging (QTI) is as effective as magnetic resonance imaging (MRI) for use as a supplemental screening tool in high-risk patients.

#### Aims, purpose, and/or objectives (primary, secondary, and exploratory):

- Our objective is to perform a prospective feasibility study with a goal of n=25 to compare the screening performance of QTI to MRI and other standard of care imaging in patients with high lifetime risk of developing breast cancer.
- Our primary endpoint will be to compare the detectability of positive exam findings identified on MRI and QTI.
  - This will include the description of number of positive findings, characteristics, size, and location.
  - BIRADS classification of the screening exam and potential diagnostic work up may allow for calculation of PPV1 and PPV3
    - Calculation of PPV1:
      - BIRADS 1 and 2 will be considered negative exams
    - Calculation of PPV3:
      - BIRADS 3, 4, and 5 exams will be considered positive exams.
  - If biopsies are obtained, then findings will be compared to histopathologic diagnosis
    - Perform stratification of biopsies as malignant, elevated risk, or benign.
- Our secondary endpoint will be determining if QTI is a reasonable tool for assessment of lymphadenopathy
  - Axillary, intramammary, and mediastinal lymphadenopathy can be included with correlation to histopathologic results if available.

#### Background:

- Historically, supplemental screening ultrasound is known to increase cancer detection rate in breast cancer but has also been associated with increased false positives, lower specificity, and decreased positive predictive value of biopsy. Cancer detection rate with supplemental ultrasound has been shown



to be lower than with supplemental MRI screening (Kuhl et al and ACRIN 6666). Screening ultrasound also has not been shown to identify additional cancers in high-risk patients with prior mammography and MRI, but it can serve as an alternative in patients who are unable to undergo MRI.

- QTI is FDA-approved and intended to be used as an initial evaluation method for asymptomatic women identified with above-average risk for developing breast cancer based upon genetic testing and/or other established criteria, and who have not reached the age of mammography screening for their risk level in applicable breast cancer screening guidelines.
- Current ACR guidelines recommend that high risk patients who are unable to undergo MRI should consider supplemental screening with ultrasound but are counseled that the cancer detection rate of ultrasound is inferior to MRI.
- Currently, screening mammography and MRI are the dominant imaging modalities for women with an elevated lifetime risk of breast cancer (Monticciolo et al, 2023).

## Study Design and Methods

### Methods:

- To test our hypothesis, we plan to perform a prospective feasibility study identifying patients who are already undergoing clinically ordered contrast enhanced breast magnetic resonance imaging (MRI) and have a high lifetime risk of breast cancer >20% (as calculated by a risk assessment model such as Tyrer-Cuzick). 25 to 30 patients will be enrolled with the intent to compare traditional supplemental screening methods with quantitative transmission imaging (QTI). Our intended patient population will focus on women over the age of 18 years of age with a high risk of breast cancer. Details of the study will be discussed with the patient by a study coordinator and patients will sign a consent form. Patients will then be scheduled for a QT examination within 30 days of their clinical MRI. No additional follow-up appointments will be required after the QTI is obtained and interpreted. Radiologists trained to read QTI from Mayo Clinic will interpret the QTI and compare findings to those seen on MRI and mammogram if available. Positive exam findings will then be compared to histopathological diagnosis if available. Findings from QTI imaging will be compared to MRI findings to determine performance and feasibility of QTI as a potential supplemental screening tool. We have external collaborators for this study who have provided the QTI imaging system and have assisted in the development of the IRB. A common research question was developed with subsequent development of a research protocol as a collaborative effort.
- For QTI, the subject will be asked by the female technician in the imaging suite to remove shirt/blouse and bra. An adhesive retention pad will be gently placed near the peri-areolar, most pendent portion of the breast to minimize motion of the breast inside the water bath by attaching the retention pad to the magnetic breast retention rod. The subject will then be asked to lie prone on the scanner bed with one breast in the water bath. The complete volumetric ultrasound tomography scan takes approximately 15 minutes, during which time the subject is asked to be as still as possible. No breath hold is required. The procedure is then repeated for contra-lateral breast. Upon completion of imaging, a towel is supplied to the subject to dry the skin, an alcohol-based wipe can be used to remove any residual adhesive.



- Patients will be de-identified. The complete image study set for each subject will consist of QT Ultrasound Breast Scanner images will be stored on a dedicated Mayo clinic research computer or laptop.

### Subject Information

#### Target enrollment (if prospective):

- Women over the age of 18 with a high risk of breast cancer (>20% lifetime risk as based on an assessment model such as Tyrer-Cuzick). Enrollment will favor patients who are between the ages of 18-40 years old.

#### Target accrual:

- Enrollment will favor patients who are between the ages of 18-40 years old. We are hoping to include 25-30 patients in our study.

#### Inclusion Criteria:

- Women 18+ years of age
- High lifetime risk of breast cancer as determined by a risk assessment tool such a Tyrer-Cuzick model.
- Clinical ordered screening MRI.
  - MRI and QTI performed within 30 days of each other
- Breasts that will fit in the QT Ultrasound Breast Scanner (e.g. bra cup size less than DDD)

#### Exclusion Criteria:

- Pregnant patients
- Lactating patients
- Patients with open wounds or discharge
- Patients < 18 years of age
- Patients who are > 350 lbs.
- Patients who are unable to lay prone for >15 minutes.

### Study Procedures

#### Screening visit:

- Discussion of QTI with the patient via a study coordinator.
- Consent

#### Visit 1:

- QTI will be performed at this visit and subsequently interpreted by a Radiologist trained to read QTI.

### Biospecimens



- No biospecimens will be acquired for the study.

### Review of medical records, images, specimens

☐ Only retrospective data that exists before the IRB submission date will be collected.

#### Date Range for Specimens and/or Review of Medical Records:

Examples: 01/01/1999 through 12/31/2015, or all records through mm/dd/yyyy.

☒ The study involves data that exist at the time of IRB submission **and** data that will be generated after IRB submission. Include this activity in the Methods section.

Examples

- The study plans to conduct a retrospective chart review and ask subjects to prospectively complete a questionnaire.
- The study plans to include subjects previously diagnosed with a specific disease and prospectively add newly diagnosed subjects in the future.

☐ The study will use data that have been collected under another IRB protocol. Include this activity in the Methods section and enter the IRB number from which the research material will be obtained.

Enter one IRB number per line, indicate for each line whether data only, specimens only, or data and specimens will be used from each IRB protocol. Add more lines as needed. If specimens will be obtained under another IRBe application, attach a letter of support within the IRBe application.

☐ Data ☐ Specimens ☐ Data & Specimens: \_\_\_\_\_

☐ Data ☐ Specimens ☐ Data & Specimens: \_\_\_\_\_

☐ Data ☐ Specimens ☐ Data & Specimens: \_\_\_\_\_

### Data Analysis

Power Statement: Descriptive statistics will be the plan for our study as this is a prospective feasibility study.

Data Analysis Plan:

Endpoints for this feasibility study:

- Our primary endpoint will be to determine if positive findings potentially identified on MRI were well visualized on QTI. This will include number of positive findings, characteristics, size, and location. Calculation of PPV1 and PPV3 may also be performed with analysis of histopathologic diagnosis if available.



- Our secondary endpoint will be determining if QTI is a reasonable tool for assessment of lymphadenopathy. Axillary, intramammary, and mediastinal lymphadenopathy can be included with correlation to histopathologic results if available

Indicate which of the following methods will be utilized for analysis of the data

☒ Descriptive statistics will be utilized to broadly analyze the sample. No power calculation is needed.

**Describe:** Given that this is a prospective feasibility study with lower enrollment our statistics will be descriptive and will look at PPV1, PPV3, as well as cancer detection rate.

☐ Statistical modeling including multivariable modeling will be utilized and power calculations will be utilized when appropriate.

**Describe:**

☐ Formal modeling with unique data sets within the entire data group will be compared.

**Describe:**

Protocol Versions (optional)\*\*

*(delete table if study team will not be updating)*

Protocol version	Date	Summary of Changes
1.0	8/6/2024	Original Protocol
2.0	9/23/2024	

**\*\*The study team is responsible to keep the Protocol Versions section up to date. The IRB will not review this table for accuracy.**