



TMIST: Frequently Asked Questions

Key Topics for Site Investigators and Staff

This document answers frequently asked questions about the Tomosynthesis Mammographic Imaging Screening Trial (TMIST/EA1151); it is not meant to substitute for the protocol. It is divided into five sections: Protocol, Recruitment, Imaging, Screening, and Funding FAQs. The information in this document is current through protocol version 12/12/18.

Protocol FAQs

Q1: What does the TMIST trial examine?

A1: TMIST examines two mammography screening technologies, digital mammography (DM) and tomosynthesis (TM), and compares their ability to reduce advanced breast cancer in the screened population.

Q2: What are the screening arms, and how many women will be enrolled?

A2: TMIST will randomize women to either the DM or TM arm. Each woman will get screened either annually or biennially, depending on certain breast cancer risk factors. The accrual goal is 164,946 women in approximately 130 sites.

Q3: What is the population for this trial?

A3: The TMIST population is women 45 to 74 years old who present for screening mammography at participating centers. This is a study of screening for breast cancer, intended for asymptomatic women, not a study of a treatment for women who have breast cancer.

Q4: Who is eligible to participate in the annual screening cohort of TMIST?

A4: Most women in the trial will get annual screening. To be eligible for annual screening in the trial, a woman must be premenopausal *or* must be postmenopausal and age 45 to 69 with any of the following risk factors: dense breasts (BIRADS category c–heterogeneously dense, or d–extremely dense), be a known breast cancer deleterious mutation carrier, have a first-degree relative with breast cancer or whose family history of breast cancer is unknown, or currently on hormone replacement therapy *or* must be postmenopausal and age 70 to 74 and have dense breasts (BIRADS category c or d), or currently taking hormone replacement therapy. Additionally, postmenopausal women age 45 to 74 are eligible for annual screening if they have

had at least one benign breast biopsy with a diagnosis of LCIS or atypia of any kind (atypical ductal hyperplasia, atypical lobular hyperplasia, atypical hyperplasia NOS, or intraductal papilloma with atypia).

Q5: How does the trial define “postmenopausal”?

A5: The trial defines postmenopausal women as those who had their last menstrual period more than 12 months before study entry or who no longer have menses due to bilateral oophorectomy with either hysterectomy or endometrial ablation. Women who had either hysterectomy or endometrial ablation who have at least one ovary will be considered premenopausal until age 52, and postmenopausal thereafter.

Q6: Who is eligible to participate in the biennial screening cohort of TMIST?

A6: All postmenopausal women not meeting eligibility for the annual screening cohort are eligible for the biennial screening.

Q7: Who is not eligible to participate in TMIST?

A7: Women may not participate if they are symptomatic for breast disease, have new breast complaints (ie, lump or nipple discharge), had a screening mammogram within the last 11 months, previously had breast cancer, have breast enhancements, or are pregnant or lactating. Women with mild breast pain are eligible to participate.

Q8: What is the duration of follow-up for this trial?

A8: The screening examinations that are part of the screening period in TMIST occur within the first 5 years after randomization. The site trial team will collect clinical and imaging data regarding the screening, diagnosis, and treatment of breast cancer during this period. After the study-specific screening mammograms are completed, there is a long-term follow-up period to monitor women for the diagnosis of breast cancer. The study will follow women for up to 8 years in total or until the end of the study in 2025. The site trial team will conduct surveys to determine breast cancer status, either when the participant returns to the clinic for standard-of-care follow-up and routine breast cancer screening, or through telephone surveys, chart reviews, and/or death and tumor registries.

Q9: How can my site join the TMIST trial?

A9: Your institution must be either a part of a National Community Oncology Research Program (NCORP) site or hold membership in a National Clinical Trials Network (NCTN) Research Group. Contact tmist@ecog-acrin.org for help in identifying status. There are five qualification steps to complete: IRB approval, credentialing phantom image submission, online trial training, physics/it survey completion, sample mammography reports submission.

Q10: Whom should I contact with questions?

A10: Please direct general questions about the TMIST trial to TMIST@ecog-acrin.org.

Recruitment FAQs

Q11: How can we recruit women into TMIST?

A11: Sites can educate women by providing informational material describing the trial by mail or email after they have scheduled a screening mammography visit, during visits to the mammography clinic, or through phone calls. Many of these recruitment materials are also available in Spanish. PI or co-investigator radiologists can present or share materials about the trial with primary care physicians, who in turn can inform women about the trial. In addition, your recruitment efforts may be helped by clinical trial volunteer portals, where a description of the study can be posted along with local site contact information for individuals interested in participating.

Q12: What type of person can do the recruitment?

A12: Personnel at participating mammography clinics can recruit women to the trial.

Q13: What type of personnel are needed to support this trial at the site?

A13: To support TMIST, sites need a credentialed breast imaging radiologist to serve as the lead radiologist investigator (study-specific PI or Co-PI), and at least one research associate (capable of performing recruitment, consent/enrollment, and data entry tasks) for the first year. The addition of research associates to the study team may be needed in years 2 and 3, based on total enrollment volume. The lead radiologist has to maintain CTEP investigator credentials during the trial.

Imaging FAQs

Q14: Where are the study activities expected to take place?

A14: Imaging must take place in a mammography clinic that routinely performs both TM and DM. The participating mammography facility must be able and willing to randomize women to undergo either TM or DM for screening. The scanners must be accredited under US ACR MQSA or equivalent for non-US sites.

Q15: How many radiologist readers are needed per site?

A15: You need at least one. However, you should base the number of radiologists that you will need to read screening mammograms in support of this trial on your expected site screening volume for the trial. All interpreting radiologists who are participating at each site should read imaging exams in both conditions (TM and DM) over the course of the study.

Q16: Does the same radiologist have to review all the TMIST exams?

A16: No, any MQSA or equivalent qualified breast imaging radiologist within the mammography clinic where the imaging examination will take place can interpret TMIST subject mammograms. However, one breast imaging radiologist at a site must be designated as lead radiologist for TMIST; that person must have a CTEP investigator ID.

Q17: Does the PI have to be a radiologist?

A17: No, but it is recommended that a radiologist be at least a study specific Co-PI at the site. Any PI or Co-PIs for this study should obtain CTEP investigator ID credentials and complete training as appropriate to serve in these types of roles at their institution.

Q18: Do the radiologist readers need to complete the CTEP IAM registration process?

A18: Radiologists serving as lead radiologist (PI or Co-PI) for TMIST at a site need to complete the CTEP IAM registration process. Other radiologists serving solely as readers do not.

Q19: Do the radiologists have to enter data directly into Medidata Rave?

A19: No, radiologists do not have to enter their interpretations directly in the electronic case report forms. Research associates with the appropriate CTEP IAM credentials and CTSU user role of “Rave CRA” at the site can perform the data entry task if the mammography clinic reports include all required reporting elements and the research associates understand how to extract the information from the radiology and other clinical reports.

Q20: How are the images submitted to ECOG-ACRIN?

A20: Image submission will be completed with TRIAD, the American College of Radiology’s (ACR) proprietary image exchange application. This is the sole method of data transfer to the ACR Clinical Research Institute Imaging Core Laboratory. Site-designated staff who will submit images through TRIAD should be registered with CTEP and have a valid and active CTEP IAM account. To submit images using TRIAD, the site-designated image submitter should be on the site’s affiliate rosters and be assigned the “TRIAD site user” role on the CTSU roster.

Q21: Can we run this study at multiple radiology facilities?

A21: Yes. You can run the study at multiple radiology facilities. A facility receives enrollment credit if they have a unique CTEP ID number and have completed the site activation process. Each mammography unit that is planned to be used in the trial, whether at one facility or across multiple radiology facilities, will need to be credentialed as part of the site qualification process.

Q22: How do you effectively screen and obtain consent from participants?

A22: Obtain a list of women scheduled for screening mammograms. Contact them by mail, email, or phone to tell them about the study and determine their interest in participating. If they are interested in participating, you can ask them to come in 30 minutes before their scheduled mammogram or on a separate day before the scheduled mammogram, depending on mammography clinic workflow, to perform the consent and enrollment process. Contact women consecutively until you reach your site's maximum accrual for that day, an average of 3-5 daily.

Screening FAQs

Q23: What happens if a woman has a positive screen?

A23: She will undergo the usual standard-of-care diagnostic workup, which may include additional imaging and/or biopsy. She remains in the trial, but the results of the downstream exams and/or procedures will dictate whether she remains in the screening population and continues with study screening rounds. For women who are clinically recommended for short-term follow-up or biopsy, we will follow clinical care as it is performed for the duration of the trial.

Q24: What happens if a woman is diagnosed with breast cancer?

A24: She will cease protocol screening and continue clinical follow-up for up to 8 years following randomization or through the end of the study in 2025. This includes the collection of all procedures and treatments (eg, imaging, biopsy, surgery, chemotherapy, and radiation therapy). These women will be followed by the site trial team for progression, recurrence, and vital status, either when they return to the clinic for standard-of-care follow-up or through telephone surveys, chart reviews, and/or death and tumor registries.

Funding FAQ

Q25: How is the trial being funded?

A25: This trial is being funded by the National Cancer Institute through the National Community Oncology Research Program or National Clinical Trials Network funding mechanisms based on your institution's NCI affiliation.

