Growing evidence of diagnostic effectiveness of digital breast tomosynthesis published in *The Lancet Oncology*

HOLOGIC

ToSyMa phase 1 trial studied the innovative diagnostic approach of digital breast tomosynthesis (DBT) plus synthesised 2D mammography (s2D) for the detection of invasive breast cancer.

Tomosynthesis plus Synthesized Mammography trial (ToSyMa) was the largest prospective study of DBT, demonstrating increased detection rates for invasive breast cancer using DBT plus s2D compared to 2D digital mammography (DM) alone.

ToSyMa trial set up and the data pipeline

ToSyMa phase 1

~100,000 Women,
aged **50-69** years underwent screening conducted at **17 screening centres**

Phase 1, multi-centre*, open label, two-stage, adaptive parallel group randomised, controlled, **superiority trial (RCT)** of ~100,000 women in a population-wide German mammography screening programme.

Primary objective: Evaluation of a **clinically relevant increase in the detection rate of invasive breast cancers**, comparing DBT + s2D and DM.

~ 30-month
study in **99,689** women

- DBT plus s2D mammography (n=49 804)
- DM (n=49 830)

ToSyMa phase 2

The study phase 2 is underway; this will use state cancer registry data to evaluate **interval cancer rates at 24 months,** with results expected in early 2025.

Phase 2 will further help to investigate incremental long-term benefits of DBT.

Significant headline results

Significantly higher detection rate for invasive breast cancer with DBT + s2D

	Per 1,000 women DM ↓	Per 1,000 women DBT + s2D ↓
48% Increase in overall detection rate (OR 1.73 [95% CI 1.41-2.0])	4.8	7.1
70% Higher detection rate among those with a tumour size of pT1** (OR 1.73 [95% CI 1.41-2.0])	3.0	5.1
250% Increase in iCDR for very dense breast (cat. D) (OR 1.73 [95% CI 1.41-2.0])	2.3	8.1

Notable secondary findings

No marked differences between the groups in recall rates (RR) or DCIS

- RR - DBT + s2D (2,457/49,756) and 2D (2,515/49,794) (OR 0.98 [0.92-1.03])
- DCIS - DBT + s2D (62/49,756) and 2D (66/49,762) (OR 0.94 [95% CI 0.65-1.35])

40% increase in PPV1 from 12.3% for 2D to 17.2% for DBT + s2D

PPV1 (Positive Predictive Value of recall) increased

Adverse events were rare with six events per group, and no events were classified as serious or related to the device used.

Reading time increased from 48 seconds (2D) to 109 seconds (DBT + s2D).

AI technology could **reduce reading time** and help diagnostic performance.

Promising further analysis

Detailed breast density sub analysis

A subsequent sub analysis of the TOSYMA trial data aimed to compare invasive breast cancer detection rate (iCDR) of DBT + s2D vs DM for different breast densities.

Breast density was assessed using BI-RADS categorisation.

	Per 1,000 women DM	Per 1,000 women DBT + s2D
Category A	3.6	2.7
Category B	4.3	6.9
Category C	6.1	8.3
Category D	2.3	8.1

Pioneering future detection strategies

Commenting on ToSyMa results the study group said:

"Findings from ToSyMa might help to close an important knowledge gap and to develop advanced strategies for an improved systematic early breast cancer detection in population-based settings." - ToSyMa trial group

*Multi-vendor; **Size less than or equal to 20mm in largest dimension

The 'ToSyMa' trial was a randomised, open-label, superiority trial done at 17 screening units in two federal states of Germany. Between 5th July 2018, and 30th December 2020, 99,689 women aged between 50-69 years were randomly assigned to digital breast tomosynthesis plus s2D mammography (n=49 804) or digital mammography (n=49 830). It was conducted by the Tomosynthesis Screening Trial Study Group and funded by Deutsche Forschungsgemeinschaft (German Research Foundation).

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