EVALUATING THE DIAGNOSTIC BURDEN OF TUMOR LOCALIZATION STRATEGIES FOR MULTI-CANCER EARLY DETECTION TESTS

OBJECTIVES
- To evaluate the diagnostic burden of tumor localization strategies for multi-cancer early detection (MCED) tests.
- To compare the diagnostic burden of imaging- and molecular-based tumor localization strategies.
- To assess the impact of test performance characteristics on diagnostic burden.

METHODS
- In the context of a multi-cancer diagnostic process, the predictive value of single-tissue imaging tests was evaluated.
- Diagnostic outcomes were categorized into true positives, false positives, false negatives, and correctly-localized true positives.
- An expression for diagnostic burden was derived as a function of test PPV and TOO accuracy to quantify the relative diagnostic burden of each strategy.
- Probabilistic sensitivity analyses were performed to assess the robustness of the approach and alternative assumptions.

RESULTS
- Molecular TOO strategies were determined to be more burdensome than imaging TOO strategies across 95.5% of all possible PPV and TOO accuracy values.
- At 90% molecular TOO accuracy, a PPV of 79% is necessary for molecular TOO to have the same diagnostic burden as imaging TOO.
- Figure 2 plots the breakeven curve, which illustrates the threshold PPV at which a molecular TOO strategy becomes less burdensome than an imaging TOO strategy.

CONCLUSIONS
- We developed a method to evaluate the diagnostic burden of MCED TOO localization strategies.
- An imaging-based TOO localization strategy shows better efficiency than a molecular TOO strategy across 95.5% of all possible PPV and TOO accuracies.
- Molecular TOO strategies are likely to require very high PPV or localization accuracy to be more efficient than an imaging TOO strategy.
- A nuanced molecular TOO strategy that incorporates cancer-specific risks and likelihoods may represent a more efficient approach than blanket molecular TOO.