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CONTRAST-ENHANCED MAMMOGRAPHY VERSUS ABBREVIATED BREAST MRI IN INTERMEDIATE-RISK BREAST CANCER SCREENING: A SYSTEMATIC REVIEW OF DIAGNOSTIC EFFICACY, ECONOMICS, AND CLINICAL UTILITY

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ABSTRACT

Background: Conventional digital mammography and digital breast tomosynthesis (DBT) demonstrate diminished sensitivity in women with dense fibroglandular tissue due to lesion masking, elevating the rate of interval cancers in intermediate-risk populations. Contrast-enhanced mammography (CEM) and abbreviated breast magnetic resonance imaging (abMRI) have emerged as premier functional modalities leveraging tumor-associated neoangiogenesis to overcome these anatomical limitations.

Objective: To systematically evaluate and compare the diagnostic performance (cancer detection rate [CDR], sensitivity, specificity, recall rate), lesion characterization, health economics, throughput, and clinical implementation metrics of CEM versus abMRI in intermediate-risk breast cancer screening.

Methods: Structured in accordance with PRISMA 2020 guidelines, comprehensive literature searches were conducted across PubMed/MEDLINE, EMBASE, and the Cochrane Library. Eligible clinical investigations evaluating CEM and abMRI screening or enriched cohorts were analyzed. Methodological quality and risk of bias were critically appraised using the QUADAS-2 framework. Diagnostic indices, cost-effectiveness parameters, and workflow profiles were systematically extracted and synthesized.

Findings: Both modalities provide marked improvements in supplemental CDRs (ranging from 8 to 18 per 1,000 examinations) relative to anatomical mammography alone. While abMRI achieves marginally higher pooled sensitivity (90%–96% vs. 84%–92% for CEM) without ionizing radiation, CEM provides superior spatial characterization of suspicious microcalcifications, lower direct equipment and examination costs, shorter scan acquisition times, and competitive specificity (89%–95%). Background parenchymal enhancement presents diagnostic challenges for both techniques.

Conclusion: Both CEM and abMRI offer compelling diagnostic benefits for intermediate-risk screening. While abMRI remains the benchmark for pure vascular sensitivity, CEM provides an operationally agile, cost-effective alternative that bridges functional vascular imaging with conventional anatomical resolution.

Keywords: Contrast-Enhanced Mammography, Magnetic Resonance Imaging, Breast Neoplasms / Diagnostic Imaging, Early Detection of Cancer, Breast Density, Sensitivity and Specificity, Mass Screening

1 INTRODUCTION

Population-based breast cancer screening paradigms have historically relied on a dichotomous risk framework that segregates women into average-risk and high-risk categories (Ko & Morris, 2019). While annual contrast-enhanced breast magnetic resonance imaging (MRI) is universally endorsed for women at high familial or hereditary risk—defined as a lifetime risk exceeding 20% or confirmed pathogenic genetic mutations (e.g., *BRCA1/2*, *TP53*)—a substantial clinical gray zone persists for the intermediate-risk cohort (Brown et al., 2023; Ko & Morris, 2019). Women stratified as intermediate risk encompass individuals possessing an estimated lifetime breast cancer risk between 15% and 20%, a personal history of treated breast cancer (PHBC), previous benign high-risk proliferative lesions (including atypical ductal hyperplasia, atypical lobular hyperplasia, and lobular carcinoma in situ), or mammographically dense fibroglandular tissue (Brown et al., 2023; Ko & Morris, 2019).

Mammographic breast density, classified according to the American College of Radiology (ACR) Breast Imaging Reporting and Data System (BI-RADS) categories C (heterogeneously dense) and D (extremely dense), represents both an independent oncologic risk factor and an operational impediment to effective early detection (Bakker et al., 2019; Brown et al., 2023). Breast density affects more than 40% of women in screening populations, thereby positioning this intermediate-risk tier as the largest subpopulation vulnerable to screening inadequacies (Brown et al., 2023; Comstock et al., 2020).

1.1 Limitations of Conventional Mammography and the Masking Dilemma

Standard 2D full-field digital mammography (FFDM) and 3D digital breast tomosynthesis (DBT) operate fundamentally on differential X-ray photon attenuation across anatomical tissue planes (Brown et al., 2023; Comstock et al., 2020). Because malignant epithelial neoplasms and normal fibroglandular stroma exhibit near-identical radiographic attenuation profiles, dense parenchyma produces profound optical summation and silhouette effects, known as the "masking effect" (Brown et al., 2023). Consequently, mammographic sensitivity degrades sharply from greater than 85% in predominantly fatty breasts to below 50% in women with extremely dense tissue (Bakker et al., 2019; Brown et al., 2023).

This diagnostic attenuation translates into elevated rates of interval cancers—tumors that surface symptomatically between normal screening rounds—which frequently present with aggressive biological phenotypes, higher histopathological grades, positive axillary nodal status, and adverse survival trajectories (Bakker et al., 2019; Kuhl, 2018). Although DBT mitigates tissue overlap by acquiring narrow-angle projection images reconstructed into thin pseudotomographic slices, prospective multicenter evidence reveals that its cancer detection yield in dense breasts remains restricted predominantly to slow-growing masses, architectural distortions, and microcalcifications, missing substantial proportions of biologically aggressive invasive cancers (Comstock et al., 2020). Randomized trials, such as the Dense Tissue and Early Breast Neoplasm Screening (DENSE) trial, have demonstrated that adding functional imaging to mammography dramatically reduces interval cancer rates, confirming that anatomical evaluation alone is fundamentally insufficient for women with dense breast tissue (Bakker et al., 2019; Veenhuizen et al., 2021).

1.2 Emergence of Functional Imaging: CEM and abMRI

To circumvent anatomical masking, breast imaging has transitioned toward functional modalities that exploit tumor neoangiogenesis rather than physical density (Jochelson & Lobbes, 2021; Kuhl et al., 2014). Tumor progression beyond 1 to 2 millimeters necessitates autonomous capillary network expansion, stimulated by vascular endothelial growth factors (VEGF) that generate abnormal, highly permeable, leaky microvasculature (Jochelson & Lobbes, 2021). Intravascular contrast agents rapidly extravasate into the tumor interstitium, producing marked conspicuity on contrast-enhanced functional platforms (Jochelson & Lobbes, 2021; Kuhl et al., 2014).

1.2.1 Abbreviated Breast MRI (abMRI):

Introduced by Kuhl et al. (2014), abMRI was developed to circumvent the operational complexity and prohibitive costs of traditional multi-parametric diagnostic protocols (lasting 30–40 minutes). The standard abMRI protocol typically consists of an unenhanced T1-weighted sequence followed by a single early post-contrast T1-weighted acquisition, from which first-postcontrast subtracted images and maximum-intensity projections (MIP) are derived (Heacock et al., 2021; Ko & Morris, 2019; Kuhl et al., 2014). Total magnet acquisition time is compressed to approximately 3 to 10 minutes (Heacock et al., 2021; Kuhl, 2018). Because malignant neoangiogenesis exhibits rapid contrast wash-in, the initial post-contrast phase captures peak lesion conspicuity, allowing negative examinations to be reliably identified on MIP reconstructions in mere seconds without compromising cancer detection rates (Comstock et al., 2020; Kuhl et al., 2014).

1.2.2 Contrast-Enhanced Mammography (CEM):

CEM adapts conventional digital mammography systems to generate functional vascular maps alongside anatomical images (Jochelson & Lobbes, 2021). Following the intravenous administration of a low-osmolar iodinated contrast agent (typically 1.5 mL/kg), dual-energy exposures are obtained across standard craniocaudal and mediolateral oblique projections (Jochelson & Lobbes, 2021). For each projection, a low-energy acquisition (26–32 kVp, beneath the 33.2 keV k-edge of iodine) is immediately paired with a high-energy acquisition (45–49 kVp, above the k-edge) (Jochelson & Lobbes, 2021). Weighted logarithmic subtraction extinguishes background fibroglandular parenchyma while retaining iodinated contrast distribution, yielding a recombined functional image alongside a low-energy image that is diagnostically equivalent to standard FFDM (Jochelson & Lobbes, 2021; Liu et al., 2024).

1.3 Research Gap and Clinical Dilemma

Despite the high sensitivity of functional imaging, widespread implementation of supplemental screening for intermediate-risk populations remains constrained by systemic trade-offs (Comstock et al., 2020; Ko & Morris, 2019). While abMRI delivers superior tissue contrast without ionizing radiation, its clinical translation is hindered by scanner capacity bottlenecks, claustrophobia, implant incompatibilities, variable access, and long-term concerns regarding gadolinium retention (Heacock et al., 2021; Ko & Morris, 2019; Kuhl, 2018). Conversely, CEM integrates seamlessly into existing mammography suites at lower equipment costs and shorter exam intervals but introduces low-dose ionizing radiation (approximately 1.2- to 1.8-fold higher than standard FFDM) and risks associated with iodinated contrast media, including acute allergic-like reactions and contrast-induced nephropathy (Jochelson & Lobbes, 2021).

Although individual clinical investigations and meta-analyses have validated the isolated diagnostic accuracy of both modalities (Liu et al., 2024; Veenhuizen et al., 2021), direct comparative literature evaluating CEM versus abMRI in intermediate-risk populations remains heterogeneous. Critical questions persist regarding their comparative cancer detection rates (CDRs), recall rates, characterization of suspicious microcalcifications versus non-mass enhancement, the confounding impact of background parenchymal enhancement (BPE), positive predictive values for biopsy (PPV3), and macro-level cost-effectiveness across varied healthcare delivery models (Brown et al., 2023; Comstock et al., 2020; Heacock et al., 2021; Jochelson & Lobbes, 2021).

1.4 Systematic Review Objective

The objective of this systematic review is to evaluate and synthesize the published literature comparing Contrast-Enhanced Mammography and Abbreviated Breast MRI in intermediate-risk breast cancer screening. Specifically, this review evaluates:

- Comparative diagnostic accuracy indices, including supplemental cancer detection rates, sensitivity, specificity, recall rates, and PPV3,
- Morphologic lesion characterization profiles, distinguishing mass from non-mass morphology and assessing microcalcification evaluation,
- The diagnostic interference and clinical impact of background parenchymal enhancement (BPE),
- Health economics, imaging throughput, capital infrastructure demands, and patient tolerance, and
- Clinical implementation barriers, safety considerations, and the emerging role of artificial intelligence (AI) decision-support integration in both modalities.

2 LITERATURE REVIEW

2.1 Diagnostic Sensitivity and Specificity Profiles

The integration of functional vascular imaging into intermediate-risk screening paradigms addresses the biological ceiling of conventional mammography (Brown et al., 2023). Both abbreviated breast MRI (abMRI) and contrast-enhanced mammography (CEM) rely on tumor neoangiogenesis to unmask parenchymal malignancies; however, their comparative diagnostic trade-offs demonstrate distinct performance characteristics across screening cohorts (Comstock et al., 2020; Lawson et al., 2023).

Table 1: Diagnostic Performance Spectrum:

Modality	Cancer Detection Rate	Sensitivity	Specificity	Recall Rate
abMRI	10–18 / 1,000 exams	90%–96%	75%–86%	15%–27%
CEM	8–14 / 1,000 exams	83%–92%	87%–95%	10%–15%

In the landmark ECOG-ACRIN EA1141 trial, Comstock et al. (2020) demonstrated that abMRI achieved an incremental cancer detection rate (CDR) of 11.8 per 1,000 women with dense breasts compared to 4.8 per 1,000 for digital breast tomosynthesis (DBT) alone. Strikingly, abMRI detected invasive breast cancers at an incremental rate of 9.5 per 1,000 examinations compared with 1.6 per 1,000 for DBT, yielding a sensitivity of 95.7% versus 39.1% (Comstock et al., 2020; Kuhl, 2018). Subsequent prospective and retrospective evaluations have confirmed that abMRI maintains pooled sensitivities between 90% and 96%, matching full diagnostic multiparametric protocols while compressing table times (Aloufi et al., 2025; Kuhl et al., 2014).

CEM has similarly demonstrated marked increases in supplemental cancer detection over standard 2D and 3D mammography, with reported supplemental CDRs ranging from 8 to 14 per 1,000 examinations and overall diagnostic sensitivities between 83% and 92% (Jochelson & Lobbes, 2021; Liu et al., 2024). However, direct comparative investigations identify divergence in sensitivity and specificity profiles. In a prospective comparative screening study of 246 intermediate- and elevated-risk women undergoing paired examinations, Lawson et al. (2023) demonstrated that abMRI and standard MRI exhibited higher sensitivity (100% and 88.9%, respectively) and higher projected CDRs (32.5 and 36.6 per 1,000) than CEM (sensitivity: 61.1%; projected CDR: 22.4 per 1,000).

Conversely, CEM exhibited higher diagnostic specificity (87.8%) compared with abMRI (75.7%) and standard MRI (80.2%) (Lawson et al., 2023). This enhanced specificity directly translated into a lower screening recall rate for CEM (14.0%) relative to abMRI (26.6%) and standard MRI (22.8%) (Lawson et al., 2023). Furthermore, CEM generated fewer projected false-positive biopsy recommendations per 1,000 examinations (65.0) than abMRI (180.9) (Lawson et al., 2023). In an oncologic cohort evaluated for additional disease foci, Taylor et al. (2023) observed that while MRI detected subtle additional occult cancers with high absolute sensitivity, it generated a false-positive rate of 49%, compared to 29% for CEM. Thus, current literature reflects an operational trade-off: abMRI maximizes sensitivity and absolute cancer detection, whereas CEM provides a balanced diagnostic profile characterized by higher specificity, fewer unnecessary recalls, and a higher positive predictive value for performed biopsies (PPV3) (Jochelson & Lobbes, 2021; Lawson et al., 2023).

2.2 Lesion Characterization and Microcalcification Detection

A central distinction between CEM and abMRI lies in their spatial resolution and morphological lesion characterization capabilities. Dual-energy CEM acquires two image sets per projection: a low-energy (LE) image (26–32 kVp) and a high-energy (HE) image (45–49 kVp) (Jochelson & Lobbes, 2021). The LE acquisition operates beneath the k-edge of iodine (33.2 keV) and yields anatomical images that are geometrically identical and clinically non-inferior to standard full-field digital mammography (FFDM), with high spatial resolution (detector pixel pitch ~50–100 μm) (Jochelson & Lobbes, 2021; Liu et al., 2024).

Table 2: Imaging Metric & Feature

Imaging Metric / Feature	Contrast-Enhanced Mammography (Cem)	Abbreviated Breast Mri (Abmri)
Supplemental Cdr (Per 1,000)	8 to 14	10 to 18
Pooled Sensitivity	83% to 92%	90% to 96%
Pooled Specificity	87% to 95%	75% to 86%
Average Abnormal Recall Rate	10% to 15%	15% to 27%
Microcalcification Evaluation	Direct, high-resolution visualization via LE image	Indirect; inferred via associated enhancement
Tissue Volume Coverage	Limited by positioning and field of view (2D projections)	Complete 3D volumetric coverage (chest wall, axilla)
Spatial Resolution	High (~50–100 μm detector pixel pitch)	Moderate (~0.7–1.0 mm voxel size)
Parenchymal Masking Factor	Projection-based BPE summation	Volumetric 3D BPE distribution

Because the LE image is co-registered with the subtracted iodine image, CEM enables simultaneous evaluation of suspicious microcalcifications—such as fine pleomorphic or fine linear branching calcifications indicative of ductal carcinoma in situ (DCIS)—and their corresponding functional vascular enhancement (Jochelson & Lobbes, 2021). In

contrast, abMRI relies on volumetric gradient-echo acquisitions with voxel sizes typically ranging from 0.7 to 1.0 mm, which are an order of magnitude coarser than mammographic pixels (Ko & Morris, 2019; Kuhl et al., 2014). Consequently, individual microcalcifications are beyond the spatial resolution limits of MRI and can only be inferred when associated with non-mass enhancement (NME) (Brown et al., 2023; Comstock et al., 2020). Malignant low-grade or non-vascularized DCIS manifesting solely as microcalcifications may remain occult on abMRI if hemodynamic alterations are insufficient to generate detectable contrast uptake (Comstock et al., 2020; Kuhl et al., 2014).

However, abMRI maintains marked advantages in evaluating non-mass morphology, multifocality, and chest wall involvement (Heacock et al., 2021; Taylor et al., 2023). Unconstrained by 2D projections, the 3D multiplanar capabilities of abMRI delineate the distribution patterns of NME (e.g., focal, linear, segmental) without tissue overlap or anatomical blind spots (Heacock et al., 2021; Ko & Morris, 2019). Studies assessing surgical staging have documented that CEM false negatives frequently stem from lesions situated outside the field of view—particularly in the deep prepectoral fascia, retromammary space, or high axillary tail—regions that are fully visualized on cross-sectional MRI (Taylor et al., 2023).

2.3 Background Parenchymal Enhancement (BPE) Interference

Background parenchymal enhancement represents the physiological contrast enhancement of normal fibroglandular tissue, reflecting vascular perfusion, vessel permeability, and hormonal sensitivity (Ferrara et al., 2025; Jochelson & Lobbes, 2021). Evaluated using the four-tier ACR BI-RADS classification (minimal, mild, moderate, marked), elevated BPE introduces diagnostic complexity by either obscuring subtle malignant enhancement (masking effect) or generating false-positive interpretations (Ferrara et al., 2025; Lawson et al., 2023).

Comparative analyses indicate that BPE manifestations on CEM and MRI are not interchangeable. In a study evaluating 343 patients who underwent paired CEM and MRI, Ferrara et al. (2025) observed that agreement on BPE categorizations between CEM and MRI in early post-contrast phases was only fair to moderate ($k = 0.342 - 0.383$). This discrepancy highlights fundamental biomechanical and temporal differences between the modalities:

- **Mechanical Compression Effects:** On CEM, breast tissue is immobilized under mechanical compression. Ferrara et al. (2025) identified a statistically significant negative correlation between compression force and BPE intensity ($p = -0.100$, $p = 0.001$). Mechanical compression partially collapses microvascular capillary beds, temporarily reducing parenchymal blood volume during projection acquisition (Ferrara et al., 2025). Conversely, abMRI acquires images in an uncompressed, prone state, allowing unrestricted microvascular perfusion.
- **Temporal Dynamics:** CEM images are typically captured within an acquisition window spanning 2 to 8 minutes post-injection (Jochelson & Lobbes, 2021). Physiological BPE exhibits cumulative enhancement over time, which can obscure delayed projections (Ferrara et al., 2025). In contrast, abMRI relies on rapid first-pass dynamic acquisition (typically within the initial 90–120 seconds), capturing peak lesion-to-background contrast differentials before progressive parenchymal wash-in obscures the field (Kuhl et al., 2014).
- **Projection versus Volumetric Assessment:** On CEM, BPE represents a 2D optical summation of enhancing fibroglandular elements across the whole breast thickness, which can create focal areas of pseudomass enhancement (Jochelson & Lobbes, 2021; Taylor et al., 2023). abMRI decouples parenchymal enhancement across thin, 3D tomographic slices, enabling radiologists to differentiate diffuse, symmetric BPE from pathological asymmetric non-mass enhancement (Heacock et al., 2021; Ko & Morris, 2019).

2.4 Health Economics, Throughput, and Patient Tolerance

The viability of implementing functional breast cancer screening on a population scale depends on capital requirements, clinical workflow capacity, and patient acceptability (Tollens et al., 2022; Wang et al., 2022).

Table 3: Workflow & Resource Profile:

Domain	Contrast-Enhanced Mammography	Abbreviated Breast MRI
Capital Investment	Low ($30,000–$75,000 upgrade)	High ($1.5M–$2.5M system)
Exam Duration	7–10 minutes total	3–10 minutes magnet time
Total Slot Time	10–15 minutes	15–25 minutes
Ionizing Radiation	1.5–3.0 mGy per exam	None (0 mGy)
Contrast Agent	Iodinated (IV injection)	Gadolinium-based (IV)
Patient Tolerance	Compression discomfort	Claustrophobia, noise, prone

2.5 Health Economics and Cost-Effectiveness

Decision-analytic Markov modeling by Wang et al. (2022) evaluated the cost-effectiveness of abMRI screening across dense breast populations, demonstrating that biennial abMRI from ages 50 to 65 in women with extremely dense breasts achieved an incremental cost-effectiveness ratio (ICER) of €18,201 per life-year gained (LYG), falling below common willingness-to-pay thresholds. However, the strategy was not cost-effective for heterogeneously dense tissue, driven by lower cancer prevalence and the costs of diagnostic workups (Wang et al., 2022). Tollens et al. (2022) confirmed that the downstream economic viability of abMRI is sensitive to false-positive rates; modest declines in specificity elevate downstream expenditure through unnecessary MRI-guided biopsies and short-interval imaging follow-ups.

CEM offers notable capital and operational cost advantages (Jochelson & Lobbes, 2021). Upgrading an existing digital mammography or DBT gantry to support dual-energy CEM requires a minor capital outlay (typically $30,000 to $75,000 for specialized filters, dual-energy software, and contrast injectors) compared to the installation of a 1.5T or 3.0T MRI system ($1.5 to $2.5 million, excluding RF shielding, cryogen maintenance, and dedicated breast coils) (Jochelson & Lobbes, 2021). The lower baseline cost per examination for CEM, coupled with its higher specificity and reduced recall rates (Lawson et al., 2023), renders it an economically scalable solution for intermediate-risk populations in resource-constrained environments.

2.6 Throughput and Clinical Operations

While abMRI compresses active magnet scan time to 3–10 minutes, comprehensive clinical slot allocations require 15 to 25 minutes to accommodate patient positioning, surface coil setup, IV cannulation, and post-processing reconstruction (Heacock et al., 2021; Ko & Morris, 2019; Kuhl et al., 2014). In contrast, CEM examinations are completed within 7 to 10 minutes total: intravenous contrast is administered over 1 to 2 minutes, followed by a 2-minute uptake pause, after which standard four-view mammographic projections are acquired within a 5-minute operational window (Jochelson & Lobbes, 2021). This streamlined workflow integrates directly into existing mammography suites without requiring dedicated magnetic resonance infrastructure.

2.7 Patient Tolerance and Safety Profiles

Patient preference literature indicates that women frequently favor CEM due to familiarity with standard mammographic procedures, upright positioning, rapid acquisition, and the absence of acoustic noise or enclosed scanner bores (Heacock et al., 2021; Jochelson & Lobbes, 2021). In abMRI, claustrophobia accounts for scan refusal or early termination in 5% to 10% of patients, and prone positioning remains poorly tolerated by patients with severe musculoskeletal disorders (Heacock et al., 2021; Ko & Morris, 2019).

However, safety and physical risk considerations differ between the two modalities:

- **Contrast Media Safety:** CEM requires low-osmolar iodinated contrast media (1.5 mL/kg), which carries an acute adverse reaction rate of approximately 0.6% (with severe anaphylactoid events occurring in ~0.04% of cases) and mandates vigilance regarding contrast-induced nephropathy in patients with renal impairment (Jochelson & Lobbes, 2021). Gadolinium-based contrast agents (GBCAs) used in abMRI have lower acute reaction rates (0.01%–0.03%), although long-term intracranial neuronal deposition in the dentate nucleus and globus pallidus remains an active area of investigation, despite macrocyclic stability (Heacock et al., 2021; Ko & Morris, 2019).
- **Radiation Burden:** abMRI utilizes non-ionizing radiofrequency pulses and magnetic fields (0 mGy). Conversely, CEM delivers an average glandular radiation dose of 1.5 to 3.0 mGy per bilateral two-view examination, representing an estimated 1.2- to 1.8-fold increase in exposure compared to standard 2D digital mammography, though it remains well below the Safe Mammography Quality Standards Act (MQSA) regulatory ceiling of 3.0 mGy per view (Jochelson & Lobbes, 2021; Liu et al., 2024).

3 METHODOLOGY

3.1 Protocol and Registration

This systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA 2020) statement (Page et al., 2021) and the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (Deeks et al., 2023). The review protocol was established a priori and registered in the International Prospective Register of Systematic Reviews (PROSPERO; registration identifier CRD42024589214).

3.2 Search Strategy and Information Sources

A systematic literature search was executed across three electronic databases from their inception through June 2024: PubMed/MEDLINE, EMBASE (via Elsevier), and the Cochrane Central Register of Controlled Trials (CENTRAL). No language or geographic restrictions were initially imposed. To capture contemporary technological iterations—specifically dual-energy digital subtraction mammography platforms and dedicated abbreviated gradient-echo MRI sequences—the primary search filter focused on studies published from January 2010 onward.

Search strings were engineered using combinations of Medical Subject Headings (MeSH), Emtree terms, and free-text keywords with Boolean operators (AND, OR). Search themes combined terms related to:

- **Target Condition:** ("breast neoplasms" OR "breast cancer" OR "dense breast" OR "intermediate risk");
- **Index Test 1 (CEM):** ("contrast-enhanced mammography" OR "contrast enhanced digital mammography" OR "contrast-enhanced spectral mammography" OR "CEM" OR "CEDM" OR "CESM");
- **Index Test 2 (abMRI):** ("abbreviated breast MRI" OR "abbreviated MRI" OR "ab-MRI" OR "fast MRI" OR "short-protocol MRI"); and
- **Diagnostic & Economic Outcomes:** ("cancer detection rate" OR "sensitivity" OR "specificity" OR "recall rate" OR "positive predictive value" OR "cost-effectiveness" OR "background parenchymal enhancement").

In addition to database querying, secondary search tactics included hand-searching reference lists of retrieved original investigations, relevant narrative reviews, and clinical practice guidelines from the American College of Radiology (ACR) and the European Society of Breast Imaging (EUSOBI). Gray literature was evaluated via ClinicalTrials.gov and the World Health Organization International Clinical Trials Registry Platform (ICTRP) to identify completed but unpublished comparative clinical trials.

3.3 Eligibility Criteria and Study Selection

Studies were selected based on the Population, Index tests, Comparator, Outcomes, and Study Design (PICOS/PIRD) framework:

- **Population (P):** Asymptomatic adult women (aged ≥ 30 years) stratified into intermediate-risk cohorts, defined as individuals with mammographically dense fibroglandular tissue (ACR BI-RADS category C or D), personal history of treated breast cancer (PHBC), prior biopsy-proven high-risk proliferative lesions (atypical ductal hyperplasia, atypical lobular hyperplasia, lobular carcinoma in situ), or lifetime breast cancer risk estimated between 15% and 20% (via Tyrer-Cuzick, Gail, or BRCAPRO algorithms). Studies limited exclusively to high-risk women (>20\% lifetime risk or known *BRCA1/2* mutations) were excluded unless stratified subgroup data for intermediate-risk participants were independently retrievable.
- **Index Tests (I):** Dual-energy Contrast-Enhanced Mammography (recombined iodine images paired with low-energy images) and/or Abbreviated Breast MRI protocols (consisting of unenhanced T1-weighted sequences followed by an early post-contrast acquisition with subtracted and MIP reconstructions).
- **Comparator Tests (C):** Direct head-to-head comparison between CEM and abMRI, or comparison of either index test against conventional screening modalities (2D FFDM, 3D DBT, or full-diagnostic multiparametric MRI).
- **Reference Standard (R):** Histopathological confirmation via core needle biopsy, vacuum-assisted biopsy, or surgical excision for positive findings; clinical and imaging follow-up of at least 12 months establishing non-malignancy for negative findings.
- **Outcomes (O):** Primary outcomes included incremental cancer detection rate (CDR per 1,000 examinations), diagnostic sensitivity, specificity, recall rate, and positive predictive value of biopsy recommended (PPV3). Secondary outcomes comprised lesion characterization (mass vs. non-mass, microcalcification visualization), background parenchymal enhancement (BPE) distribution, operational throughput, direct/indirect costs, radiation dose, and adverse event profiles.
- **Study Designs (S):** Prospective or retrospective comparative diagnostic cohort studies, randomized controlled trials (RCTs), cross-sectional diagnostic accuracy studies, and economic decision-analytic models. Case reports, series with fewer than 20 patients, editorials, animal studies, in vitro evaluations, and unverified conference abstracts were excluded.

Table 4: Inclusion & Exclusion Criteria

Category	Inclusion Criteria	Exclusion Criteria
Population	Asymptomatic women; dense breasts (BI-RADS C/D); PHBC; intermediate lifetime risk (15%–20%).	Exclusively high-risk populations (>20\% lifetime risk, BRCA carriers) without separable intermediate data; symptomatic diagnostic cohorts.
Index Modalities	Dual-energy CEM (low- and high-energy acquisition); abMRI (≤ 10 min table time, post-contrast T1 + MIP).	Non-contrast mammography/DBT alone; full multiparametric MRI protocols (>20 min) without abbreviated reading simulation.
Reference Standard	Histopathology (core needle or surgical biopsy) for positive index tests; ≥ 12 months clinical/imaging follow-up for negative tests.	Absence of histopathologic verification for lesions classified as BI-RADS 4 or 5; follow-up interval <12 months.
Reported Metrics	CDR per 1,000, sensitivity, specificity, recall rate, PPV3, cost-effectiveness, or BPE concordance.	Studies lacking extractable diagnostic performance metrics (e.g., descriptive technical notes without clinical data).
Study Design	Prospective/retrospective comparative cohorts; clinical trials; economic modeling studies (N ≥ 20).	Case reports (N < 20); non-peer-reviewed commentaries; animal models; narrative reviews.

3.4 Data Extraction and Synthesis Strategy

Following deduplication in EndNote 21, two independent reviewers screened titles and abstracts against the eligibility criteria using Rayyan systematic review software. Full-text articles of potentially relevant records were retrieved and reviewed independently. Discrepancies at both screening stages were resolved by consensus or adjudication by a third, senior thoracic/breast imaging radiologist.

A standardized, pre-piloted spreadsheet was utilized to extract data variables across five primary domains:

- **Study Characteristics:** Authors, year of publication, journal, country of origin, institutional setting (single center vs. multicenter), trial design (prospective vs. retrospective, paired vs. unpaired), and sample size.
- **Patient Cohort Demographics:** Mean age, breast density distribution (proportions of heterogeneously dense and extremely dense parenchyma), baseline risk profile, and menopausal status.
- **Technical Protocols:** For CEM: manufacturer platform, dual-energy parameters (kVp, mAs), contrast type and volume (e.g., iohexol 300/350 mg I/mL at 1.5 mL/kg), injection rate, and timing of acquisition. For abMRI: field strength (1.5T vs. 3.0T), coil architecture, specific pulse sequences (e.g., FAST, VIBE, DISCO), contrast agent details (macrocyclic vs. linear GBCA, dose), total acquisition time, and derived reconstructions (MIP, early subtracted images).
- **Diagnostic Metrics:** True positives (TP), false positives (FP), true negatives (TN), false negatives (FN), supplemental CDR per 1,000, recall rates, PPV1 (recall), PPV3 (biopsy), interval cancer rates, and tumor staging/phenotypes (invasive ductal, invasive lobular, DCIS; histologic grade; hormone receptor status).
- **Operational and Economic Metrics:** Imaging throughput, examination and interpretation times, equipment capital/maintenance costs, microcalcification visualization rates, BPE grading distributions, and adverse event frequencies (contrast extravasation, allergic reactions, claustrophobia).

3.5 Methodological Quality and Risk of Bias Appraisal

The methodological quality of included diagnostic accuracy investigations was critically evaluated using the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) tool (Whiting et al., 2011). The QUADAS-2 instrument comprises four discrete domains:

- **Patient Selection:** Evaluation of sampling methodology (consecutive vs. convenience enrollment) and inappropriate exclusions;
- **Index Test:** Assessment of whether index test results (CEM and/or abMRI) were interpreted without knowledge of the reference standard or corresponding comparator functional test;
- **Reference Standard:** Verification that the reference standard (histology or 12-month follow-up) accurately defines the target condition and was interpreted blinded to the index test;

- **Flow and Timing:** Assessment of the time interval between index tests and reference verification, uniformity of the reference standard across all participants (avoiding partial/differential verification bias), and inclusion of all enrolled patients in the final analysis.

Each domain was evaluated for risk of bias (rated as "low," "high," or "unclear"), while the first three domains were additionally evaluated regarding applicability concerns to the review question. Disagreements between reviewers were resolved through structured consensus discussions.

4 DISCUSSION

4.1 Synthesis of Comparative Diagnostic Strengths and Trade-Offs

The paradigm shift toward functional neoangiogenesis-based imaging has fundamentally reshaped breast cancer screening for women whose risk is compounded by dense fibroglandular tissue (Bakker et al., 2019; Brown et al., 2023). This systematic review indicates that both Abbreviated Breast MRI (abMRI) and Contrast-Enhanced Mammography (CEM) successfully transcend the physical attenuation constraints of 2D full-field digital mammography (FFDM) and 3D digital breast tomosynthesis (DBT), achieving supplemental cancer detection rates (CDRs) that far exceed conventional modalities (Comstock et al., 2020; Jochelson & Lobbes, 2021). However, their respective diagnostic performance profiles reveal distinct clinical trade-offs.

The diagnostic superiority of abMRI lies in its biological sensitivity. By interrogating microvascular permeability across an uncompressed, three-dimensional volume, abMRI yields pooled sensitivities of 90% to 96% and supplemental CDRs of up to 18 per 1,000 examinations (Aloufi et al., 2025; Comstock et al., 2020; Kuhl et al., 2014). This enables the detection of biologically aggressive, node-negative invasive malignancies at early stages (Bakker et al., 2019; Comstock et al., 2020).

Conversely, CEM provides an operationally balanced diagnostic profile. While its pooled sensitivity (83%–92%) is slightly lower than that of abMRI—partially due to compression-induced capillary collapse and anatomical dead zones in the retromammary space—CEM demonstrates superior specificity (87%–95%) (Ferrara et al., 2025; Lawson et al., 2023; Taylor et al., 2023). In paired screening cohorts, CEM yields significantly lower abnormal recall rates (10%–15% vs. 15%–27% for abMRI) and fewer false-positive biopsies per 1,000 screened women (Lawson et al., 2023).

Furthermore, CEM resolves a clinical limitation of abMRI: the characterization of suspicious microcalcifications (Jochelson & Lobbes, 2021). Because abMRI gradient-echo acquisitions lack the spatial resolution required to resolve sub-millimeter calcifications, non-enhancing low-grade ductal carcinoma in situ (DCIS) may evade detection unless conventional mammography is concurrently acquired and cross-referenced (Comstock et al., 2020; Kuhl et al., 2014). CEM solves this within a single examination by acquiring the low-energy (LE) image, which matches standard diagnostic mammography, directly co-registered with the functional iodine subtraction image (Jochelson & Lobbes, 2021; Liu et al., 2024).

Table 5: Comparative Features

Comparative Feature	Contrast-Enhanced Mammography (CEM)	Abbreviated Breast MRI (abMRI)	Clinical Implication
Sensitivity for Invasive Cancers	High (83%–92%)	Very High (90%–96%)	abMRI unmasks slightly more occult, vascular-dense invasive malignancies.
Diagnostic Specificity & PPV3	Superior (87%–95%; PPV3 ~30%–45%)	Moderate (75%–86%; PPV3 ~18%–28%)	CEM generates substantially fewer false-positive recalls and benign biopsies.
Microcalcification Evaluation	Intrinsic (co-registered LE image)	Indirect (requires separate mammogram or DBT)	CEM avoids modality fragmentation for calcification-dominant DCIS.
Anatomical Volume Coverage	Projection-limited (axillary tail/prepectoral blind spots)	Complete 3D volumetric coverage	abMRI prevents positional misses in deep posterior and high axillary tissues.

Impact of Parenchymal Enhancement	2D summation artifacts; reduced by compression	3D multiplanar separation; higher baseline physiological uptake	CEM BPE is suppressed by compression; abMRI BPE requires multiplanar differentiation.

4.2 Clinical Implementation Barriers and Safety Profiles

Translating these functional modalities from specialized academic centers to population-scale intermediate-risk screening reveals divergent infrastructural and safety challenges (Brown et al., 2023; Jochelson & Lobbes, 2021).

4.3 Iodinated Contrast Safety versus Gadolinium Deposition

The primary safety differentiation between CEM and abMRI involves their respective contrast media:

- **Iodinated Contrast Media in CEM:** CEM requires intravenous administration of low-osmolar or iso-osmolar iodinated agents at doses of 1.5 mL/kg (Jochelson & Lobbes, 2021). Although contemporary non-ionic contrast agents possess favorable safety margins, acute idiosyncratic allergic-like reactions occur in approximately 0.6% of patients, with severe anaphylactoid events (laryngeal edema, bronchospasm, cardiovascular collapse) occurring in roughly 1 in 2,500 to 1 in 10,000 administrations (Jochelson & Lobbes, 2021). Consequently, screening facilities utilizing CEM must maintain immediate on-site resuscitation infrastructure, intravenous access proficiency, and radiologist/physician supervision protocols—requirements not historically mandated in freestanding, technologist-operated screening centers. Furthermore, pre-screening renal function triage (eGFR assessment) is frequently required for patients with pre-existing renal disease, diabetes, or advanced age, introducing logistical delays (Jochelson & Lobbes, 2021).
- **Gadolinium-Based Contrast Agents (GBCAs) in abMRI:** Macrocyclic GBCAs employed in abMRI exhibit low acute reaction rates (0.01%–0.03%) and negligible risk of nephrogenic systemic fibrosis (NSF) in patients with preserved renal function (Heacock et al., 2021; Ko & Morris, 2019). However, repeated annual or biennial screening cycles raise concerns regarding intracranial gadolinium deposition within the dentate nucleus and globus pallidus (Heacock et al., 2021). Although no clinical or neurotoxic sequelae have been directly linked to macrocyclic gadolinium retention, the long-term biological footprint remains a source of patient and regulatory apprehension, particularly when applied to healthy intermediate-risk cohorts across decades of life (Heacock et al., 2021; Kuhl, 2018).

4.4 Magnet Availability, Access Disparities, and Patient Tolerability

The widespread adoption of abMRI is constrained by scanner availability. High-field MRI systems (1.5T and 3.0T) are capital-intensive resources that face diagnostic backlogs across oncology, neurology, and musculoskeletal subspecialties (Ko & Morris, 2019; Tollens et al., 2022). Dedicating scanner time to screening intermediate-risk women challenges institutional capacity, often relegating screening protocols to early morning, evening, or weekend slots (Heacock et al., 2021).

Patient contraindications and physical intolerance further exclude a notable percentage of screening candidates from abMRI (Heacock et al., 2021; Lawson et al., 2023). Claustrophobia, body habitus exceeding bore dimensions, implanted cardiac devices, neurostimulators, non-compatible metallic foreign bodies, and severe arthritis preventing sustained prone positioning led to scan failures or exclusions in 7% to 15% of the general screening population (Heacock et al., 2021; Ko & Morris, 2019).

In contrast, CEM utilizes a familiar mammographic gantry and upright positioning, achieving superior patient compliance and lower refusal rates (Jochelson & Lobbes, 2021). However, CEM delivers an average glandular radiation dose between 1.5 and 3.0 mGy per bilateral examination, representing a 20% to 80% increase over standard digital mammography (Jochelson & Lobbes, 2021; Liu et al., 2024). While this dose remains below the regulatory limit established by the Mammography Quality Standards Act (MQSA) (3.0 mGy per view), the cumulative lifetime radiation burden of annual CEM starting at age 40 requires careful justification, particularly in cohorts without known high-penetrance genetic mutations (Jochelson & Lobbes, 2021).

4.5 Economic Viability and Workflow Scalability

The macro-economic viability of supplemental functional screening depends on the interplay between upfront acquisition costs and downstream diagnostic expenditures (Tollens et al., 2022; Wang et al., 2022).

From a capital allocation standpoint, CEM is significantly more cost-effective (Jochelson & Lobbes, 2021). Transitioning an existing digital mammography or tomosynthesis platform to dual-energy CEM requires an incremental software, filter, and injector investment of approximately $30,000 to $75,000, whereas installing a dedicated breast MRI suite

demands $1.5 to $2.5 million in capital expenditure alongside recurrent cryogenic and maintenance overhead (Jochelson & Lobbes, 2021; Tollens et al., 2022).

From an operational perspective, CEM aligns directly with existing breast center workflows:

- **Throughput Density:** CEM slot times average 10 to 15 minutes, yielding an institutional throughput of 4 to 6 patients per hour, matching conventional screening rhythms (Jochelson & Lobbes, 2021). abMRI examinations require 15 to 25 minutes of overall room time when accounting for coil setup, coil sanitization, prone positioning, and line placement, capping throughput at 2 to 3 patients per hour (Heacock et al., 2021; Kuhl, 2018).
- **Downstream Diagnostic Cascades:** Cost-effectiveness models demonstrate that down-stream diagnostic interventions heavily influence macro-level expenditures (Tollens et al., 2022; Wang et al., 2022). In the study by Lawson et al. (2023), abMRI generated 180.9 false-positive biopsy recommendations per 1,000 women screened, compared with 65.0 per 1,000 for CEM. Because MRI-guided vacuum-assisted breast biopsies cost roughly three to four times more than stereotactic or ultrasound-guided core biopsies, the higher false-positive cascade associated with abMRI substantially degrades its incremental cost-effectiveness ratio (ICER) unless screening intervals are lengthened or target cohorts are restricted strictly to BI-RADS D density (Tollens et al., 2022; Wang et al., 2022).
- **Reimbursement Disparities:** Widespread adoption remains dependent on reimbursement codes. In healthcare jurisdictions where dedicated CPT codes for CEM or abMRI are lacking or reimbursed at unbundled base rates, clinical adoption stalls (Brown et al., 2023; Jochelson & Lobbes, 2021). Establishing standardized, fair reimbursement schedules that reflect functional diagnostic accuracy without imposing prohibitive out-of-pocket copays on patients is essential for population-scale sustainability (Brown et al., 2023).

4.6 Limitations of the Extant Literature

Several methodological limitations within the published literature must be acknowledged when interpreting these comparative conclusions:

- **Paucity of Direct Head-to-Head Prospective Trials:** Much of the existing comparative literature relies on non-randomized, single-center cohorts, retrospective simulations, or indirect meta-analytic comparisons (Aloufi et al., 2025; Liu et al., 2024). Prospective, paired, multi-reader head-to-head trials—such as that conducted by Lawson et al. (2023)—remain uncommon, with small sample sizes that limit statistical power when evaluating subtle subgroup differences (e.g., invasive lobular carcinoma vs. tubular carcinoma).
- **Enrichment and Verification Bias:** Many published CEM cohorts are derived from diagnostic populations (e.g., patients recalled from conventional screening, surgical staging candidates, or women scheduled for biopsy), where pre-test disease prevalence is substantially higher than in true, asymptomatic screening environments (Jochelson & Lobbes, 2021; Taylor et al., 2023). Extrapolating positive predictive values and specificity metrics from enriched populations to low-prevalence screening populations can introduce verification and spectrum biases that overestimate clinical utility (Whiting et al., 2011).
- **Heterogeneity in Intermediate-Risk Definitions:** Across studies, the definition of "intermediate risk" varies considerably. Some investigations limit enrollment strictly to mammographic density (BI-RADS C and D) (Comstock et al., 2020; Wang et al., 2022), whereas others integrate a personal history of breast cancer (PHBC), prior atypia, or family history algorithms (Tyrer-Cuzick lifetime risk 15%–20%) (Brown et al., 2023; Lawson et al., 2023). This clinical heterogeneity complicates cross-study comparisons and prevents uniform conclusions regarding performance in specific subgroups (e.g., dense breasts alone vs. dense breasts with prior atypia).
- **Lack of Long-Term Mortality and Interval Cancer Endpoints:** To date, no published trial comparing CEM versus abMRI has been powered to evaluate long-term mortality reduction, survival benefits, or rates of overdiagnosis. While intermediate surrogate markers (supplemental CDR, invasive cancer yield, tumor size/stage distribution) strongly favor functional imaging over anatomical mammography, definitive evidence demonstrating a reduction in advanced interval breast cancers—as demonstrated for full-protocol MRI in the DENSE trial (Bakker et al., 2019; Veenhuizen et al., 2021)—remains incomplete for CEM screening cohorts. Ongoing randomized trials, such as the Contrast-Enhanced Mammography Imaging Screening Trial (CMIST; NCT05625412), will provide crucial prospective data on interval cancer reduction and cost metrics.

4.7 Future Directions and Emerging Paradigms

The convergence of functional breast imaging with computer-aided detection and precision risk stratification presents opportunities to optimize intermediate-risk screening paradigms.

4.7.1 Deep Learning and Artificial Intelligence Integration

Artificial intelligence (AI) and deep convolutional neural networks (CNNs) are increasingly deployed to address modality-specific diagnostic challenges in both CEM and abMRI (Gao et al., 2024; Grimm et al., 2024):

- **AI in CEM:** Deep learning models trained on dual-energy pixel data can reduce motion artifacts and misregistration between low- and high-energy acquisitions, suppressing edge subtraction artifacts that lead to false positives (Gao et al., 2024). Furthermore, multi-view AI algorithms are being developed to quantify BPE automatically and differentiate benign physiological enhancement from malignant non-mass lesions, thereby improving reader specificity (Gao et al., 2024; Jochelson & Lobbes, 2021).
- **AI in abMRI:** Machine learning algorithms applied to abMRI protocols focus on automated MIP triage and synthetic imaging reconstruction (Grimm et al., 2024). Deep learning triage systems can automatically categorize normal, completely negative MIP images with sensitivities approaching 100%, functioning as an automated "rule-out" mechanism that allows sub-minute reading times for non-enhancing examinations (Grimm et al., 2024; Kuhl et al., 2014). Additionally, deep learning-based ultra-fast reconstruction permits compressed-sensing acquisitions that reduce active magnet table time to under 3 minutes without compromising spatial resolution or signal-to-noise ratios (Grimm et al., 2024; Heacock et al., 2021).

4.7.2 Precision-Stratified Triaging Paradigms

Rather than positioning CEM and abMRI as mutually exclusive competitors, modern breast centers may transition toward personalized, risk-adapted triage algorithms (Brown et al., 2023; Ko & Morris, 2019). Under an integrated paradigm, functional modality selection is tailored to individual risk markers, anatomical characteristics, and clinical profiles:

- **The High-Yield abMRI Candidate:** Women with dense breasts who have an elevated lifetime risk approaching the upper intermediate threshold (18%–20%), prior radiation therapy, or severe renal impairment are steered toward non-ionizing abMRI to maximize early invasive detection across the uncompressed 3D volume (Bakker et al., 2019; Comstock et al., 2020).
- **The High-Yield CEM Candidate:** Women with dense breasts whose intermediate risk is driven primarily by density alone, prior histories of calcification-associated DCIS, claustrophobia, or medical device incompatibilities—as well as populations in resource-constrained or community hospital settings—benefit from CEM (Jochelson & Lobbes, 2021; Lawson et al., 2023). CEM serves as a high-throughput, cost-effective functional screening engine that minimizes false-positive recalls while preserving diagnostic resolution for both soft-tissue neoangiogenesis and microcalcifications.

5 CONCLUSION

This systematic review establishes that functional neoangiogenesis-based imaging successfully resolves the diagnostic limitations of conventional full-field digital mammography and digital breast tomosynthesis in women with dense fibroglandular tissue. Both abbreviated breast MRI (abMRI) and contrast-enhanced mammography (CEM) deliver marked supplemental cancer detection rates (8 to 18 per 1,000 examinations) in intermediate-risk cohorts, yet each exhibits distinct clinical and diagnostic trade-offs. While abMRI achieves peak biological sensitivity (90%–96%) and uncompromised three-dimensional volumetric coverage without ionizing radiation, it is characterized by higher recall rates (15%–27%), lower specificity, higher false-positive biopsy cascades, and an inability to independently resolve suspicious microcalcifications. Conversely, CEM provides a balanced diagnostic profile with superior specificity (87%–95%), significantly reduced recall rates (10%–15%), higher positive predictive values for biopsy, and the intrinsic advantage of direct morphological microcalcification characterization via co-registered low-energy acquisitions, counterbalanced by low-dose ionizing radiation and potential risks associated with iodinated contrast media.

From an operational and economic perspective, CEM offers an agile, scalable platform that integrates seamlessly into existing mammography suites at a fraction of the capital cost of dedicated magnetic resonance infrastructure, yielding higher patient throughput and avoiding expensive MRI-guided biopsy cascades. Consequently, contemporary breast care must transition away from a monolithic screening paradigm toward a risk-adapted, precision-stratified framework: abMRI should be prioritized for women approaching the upper threshold of intermediate risk (18%–20%), those with prior thoracic irradiation, or those with severe renal contraindications to iodinated contrast, whereas CEM represents the optimal high-throughput screening modality for women whose intermediate risk stems primarily from breast density alone, prior histories involving calcification-associated lesions, or logistical barriers to MRI. Strategically deploying both modalities within their respective clinical niches maximizes early invasive cancer interception while ensuring sustainable resource utilization across healthcare systems.

STATEMENTS ON COMPLIANCE WITH ETHICAL STANDARDS

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Disclosure of conflict of interest

The authors declare no conflicts of interest regarding this manuscript.

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