Standardized Safety Protocol and Structured Informed Consent Framework for Contrast-Enhanced Mammography (CEM)

This supplementary material provides a proposed structured framework, as referenced in the main text, aligned with the Italian regulatory context (Law 24/2017 and Civil Code Articles 1176/2236) and with the safety recommendations of leading scientific societies (SIRM and SIAARTI). It is intended to support institution-specific adaptation rather than direct unmodified implementation.

Standardized Clinical and Safety Protocol for CEM

1. Pre-Examination Screening & Patient Selection

● Renal Function Assessment: eGFR should be evaluated within 30 days prior to the examination in patients with relevant risk factors (age > 65 years, diabetes mellitus, hypertension, or known renal disease). CEM should be considered contraindicated in case of eGFR < 30 mL/min/1.73 m², unless clinically justified after multidisciplinary evaluation.

● Hypersensitivity History: Careful assessment of previous reactions to iodinated contrast media (ICM) is mandatory. In patients with prior mild-to-moderate reactions, premedication may be considered according to institutional protocols and current SIRM/ESUR recommendations.

● Comorbidity Evaluation: Assessment should include thyroid dysfunction, severe cardiovascular disease, and ongoing metformin therapy, managed in accordance with ESUR/SIRM guidance.

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2. Injection and Acquisition Protocol

● Contrast Agent: Low-osmolar non-ionic iodinated contrast media (e.g., Iomeprol, Iopromide, Iohexol), selected according to institutional availability and established safety profiles.

● Dosage: Standard dose of approximately 1.5 mL/kg body weight, administered via power injector.

● Flow Rate: 2.0–3.0 mL/s followed by a saline flush (20–30 mL), adaptable according to patient condition and technical setup.

● Timing: Dual-energy acquisition typically begins approximately 120 seconds

after contrast injection, with minor adjustments permitted based on equipment specifications.

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3. Post-Procedural Monitoring & Emergency Preparedness

● Observation Period: Patients should remain under observation for at least 30 minutes after contrast administration to detect potential acute hypersensitivity reactions.

● Emergency Preparedness: Immediate availability of an emergency cart equipped with oxygen, epinephrine (1:1000), bronchodilators, and intravenous fluids is required within the imaging unit.

● Staff Training: All personnel should hold updated certification in Basic Life Support (BLS/BLSD) and receive specific training in the management of ICM-related adverse reactions in accordance with SIRM and SIAARTI recommendations.

Structured Patient Informed Consent Framework

Patient Name: _____ DOB: _____

ID/Fiscal Code: _____ Date: _____

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1. Nature and Purpose of the Procedure

You have been scheduled for a Contrast-Enhanced Mammography (CEM). This examination combines conventional digital mammography with intravenous administration of an iodinated contrast medium (ICM). It allows visualization of areas of increased vascularity (neo-angiogenesis), which may be associated with breast lesions, and provides diagnostic performance comparable to breast MRI.

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2. Information Regarding "Off-Label" Use

By signing this form, you acknowledge that while international guidelines and scientific evidence support the clinical use of CEM, the iodinated contrast media used are authorized by regulatory agencies (e.g., AIFA and EMA) for computed tomography and other radiological applications, but do not have a specific marketing authorization for mammographic use.

Therefore, their use in CEM is considered off-label within the applicable regulatory framework.
In accordance with Italian Law (Law 24/2017 and Articles 1176/2236 of the Civil Code), this use is supported by current scientific evidence and clinical necessity, within established medico-legal principles.

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3. Potential Risks and Adverse Reactions

The safety profile of iodinated contrast media in CEM is consistent with their use in CT examinations. Evidence from clinical studies, including the TOCEM trial, indicates that adverse reactions are generally uncommon.

● Common/Mild: transient warmth, metallic taste, nausea, or injection-site discomfort.

● Uncommon/Moderate: urticaria, rash, pruritus, mild bronchospasm.

● Rare/Severe: anaphylactic reactions, significant renal impairment, or severe cardiovascular events.

Appropriate emergency measures are available on site for immediate management of adverse reactions.

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4. Alternative Imaging Modalities

An alternative functional imaging modality is Breast Magnetic Resonance Imaging (MRI). Compared to MRI, CEM offers shorter acquisition times, improved accessibility, and may be suitable for patients with contraindications to MRI.

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5. Patient Statement & Consent

I confirm that I have read and understood this document, including the off-label nature of iodinated contrast media for this application, and that I have had the opportunity to ask questions.

[ ] I CONSENT to undergo Contrast-Enhanced Mammography (CEM) and administration of iodinated contrast media.

Patient Signature: _____

Physician Signature: _____