

Super-Resolution Ultrasound Microvascular Mapping for Non-Invasive Breast Cancer Molecular Subtyping: A Validated Nomogram

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1. Background

Breast cancer is the most common malignancy in women worldwide. Accurate preoperative assessment of molecular subtypes, particularly distinguishing Luminal from Non-luminal types, is crucial for determining neoadjuvant chemotherapy strategies and predicting prognosis. Current standard imaging (Conventional Ultrasound, DCE-MRI) primarily reflects anatomical morphology and has limitations in characterizing microvascular hemodynamics. This study aims to investigate the value of Super-Resolution Ultrasound (SRUS) in non-invasively differentiating breast cancer molecular subtypes by visualizing microvascular architecture.

2. Objective

To evaluate the diagnostic performance of SRUS-based microvascular features in distinguishing Luminal (A/B) from Non-luminal (HER2-enriched and Triple-Negative) breast cancer subtypes.

3. Study Design

Type: Prospective, Single-Center, Observational Study.

Setting: Department of Medical Ultrasound, Anhui Provincial Cancer Hospital, Hefei, China.

Duration: Anticipated enrollment period: [2025.05] to [2026.01].

4. Participants

Sample Size: 94 patients (calculated based on expected effect size and power analysis).

Inclusion Criteria:

Patients with breast lesions scheduled for surgical resection.

Age more than 18 years.

Eastern Cooperative Oncology Group (ECOG) performance status 0-1.

Written informed consent obtained.

Exclusion Criteria:

History of breast surgery or radiotherapy.

Severe coagulation dysfunction.

Allergy to ultrasound contrast agents (Sulfur Hexafluoride microbubbles).

Pregnancy or lactation.

5. Interventions and Procedures

Conventional Ultrasound (US): Standard B-mode and Doppler imaging will be performed.

Super-Resolution Ultrasound (SRUS):

Patients will receive an intravenous bolus injection of sulfur hexafluoride microbubbles.

Long-duration (5-10 minutes) raw data acquisition will be performed using a high-end ultrasound scanner with a high-frequency linear array transducer.

Offline microbubble localization and tracking algorithms will be applied to generate super-resolved microvascular maps.

Histopathology: The gold standard will be obtained from postoperative pathological reports, including ER, PR, HER2, and Ki-67 status.

6. Outcome Measures

Primary Outcome: Diagnostic accuracy (AUC, Sensitivity, Specificity) of SRUS vascular density and vessel diameter metrics in differentiating Luminal vs. Non-luminal subtypes.

Secondary Outcomes:

Correlation between SRUS parameters and microvessel density (MVD) on pathology.

Inter-observer reproducibility of SRUS measurements.

7. Data Analysis

Statistical analysis will be performed using R or SPSS software. Continuous variables will be compared using Student's t-test or Mann-Whitney U test. ROC curves will be constructed to determine optimal cut-off values.

8. Ethics and Dissemination

Ethics Approval: Approved by the Institutional Review Board (IRB) of Anhui Provincial Cancer Hospital(Approval No:2026-LLYJ-WZ-0012).

Consent: Written informed consent will be obtained from all participants.

Data Sharing: De-identified data will be made available upon reasonable request after study completion.