**Opto-Acoustic Imaging of Breast Masses: Correlation with Breast Biopsy Prognostic Indicators**

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### Overview
- **Regulatory Status:** The Imagio® OA/US breast imaging system, a diagnostic opto-acoustic (OA) imaging device bearing the CE Mark, is in the U.S. FDA Premarket Approval process.
- **Principle:** OA/US provides both functional (relative oxygenation/de-oxygenation) and anatomic (angiogenesis) information that is co-registered and temporally interleaved in real time with gray-scale ultrasound improving discrimination between benign and malignant masses. We recently reported correlation studies demonstrating tumor-zone specific OA attributes in histopathologic grade I versus grade III malignancies.
- **Purpose:** To determine the relationship between OA attributes (individual feature scores or summed feature results) and prognostic subtypes of breast cancer (PSBC).

### Materials and Methods
- HIPAA compliant, IRB approved prospective multi-center trial across 16 U.S. clinical sites.
- 1,808 masses in 1,739 subjects assessed as BI-RADS 3, 4 or 5 were imaged with OA/US. Of these, 678 lesions were malignant and the subject of this analysis.
- Each mass was scored by 7 blinded readers on 3 internal zone features of the tumor nidus and 2 external features of the tumor boundary and peripheral zones.
- Pathologic diagnoses were confirmed by an experienced central breast pathologist blinded to the OA assessment. Tumor histologic classification and grading were performed for all subjects.
- Tumor estrogen receptor (ER) and progesterone receptor (PR) were performed at each site by immunohistochemistry (IHC) and reported as positive (+), indeterminate (I), or negative (−). All 2+ results reflexed expression (IHC expressed), 2+ (indeterminate) and 3+ (over-expressed).
- Correlation coefficients were generated for PSBC that were continuous, not categorical. All statistical testing was done at a 5% significance level.
- A total of 678 breast carcinomas (653 invasive and 25 DCIS) were scored for internal (tumor nidus) and external (boundary zone and periphery) OA attributes and compared with PSBC as defined by ER, PR, HER2-neu and Ki-67 expression.
- 292 subjects were not classified and an additional 25 with pure DCIS were excluded.

### Results
- **A** study reports highly significant pre-biopsy, OA differentiation of LUM-A from TNBC with summed internal external OA features:
- **B**- (indeterminate) and **C**- (over-expressed): All 2+ results reflexed expression (IHC expressed), 2+ (indeterminate) and 3+ (over-expressed).
- Both TNBCs and LUM-A cancers have abundant neovascularity and deoxygenation, but the sum of all 5 OA feature scores shows overlap in their 99% confidence intervals and non-significant p-value. It is the difference in distribution of neovascularity and deoxygenation in the tumor zones that distinguishes the OA findings of TNBC and LUM-A breast cancers, as shown by significant p-values and separation of confidence intervals. TNBCs have higher internal OA feature scores, and LUM-A breast cancers have higher external OA feature scores, particularly within the external peripheral zone. P-values and separation of confidence intervals show external OA features to be more significant.