Can optoacoustic imaging combined with ultrasound non-invasively offer prognosis for breast cancer molecular subtypes?

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Overview

- To investigate the role of optoacoustic imaging combined with gray-scale ultrasound (OA/US) to better differentiate between breast cancer molecular subtypes.

Materials and Methods

- This prospective 5-center study was performed in the Netherlands between March 2015 and February 2016. Only masses considered suspicious at conventional diagnostic breast ultrasound (US) were included.
- The study was approved by the institutional ethical boards of the participating hospitals and written informed consent was obtained from all patients.
- Dedicated breast radiologists evaluated the included masses using OA/US and scored the internal and external OA/US features accordingly.
- Spearman Correlation was used to analyze the relationship between OA/US features and percentages of ER, PR and Ki67.
- Wilcoxon-Mann-Whitney tests were used to analyze the relationship between OA/US features and molecular subtypes of breast cancer (Luminal A - LUMA, Luminal B - LUMB, Triple Negative - TNBC and HER2-enriched - HER2-E breast cancers).

Results

- Overall, 209 patients with 215 breast lesions were included in this study. Sixty-seven masses were considered malignant and the 59 masses classified as invasive breast cancers were included in the final analyses.
- Significant correlations were found between OA/US Total Internal Features and ER (p = 0.0033) and Ki-67 (p = 0.0092) percentages.
- Regarding molecular subtypes, Internal Vessels (p = 0.0257), Total Internal Features (p = 0.0196) and combined Total Internal and External Features (p = 0.0289) helped to differentiate between LUMA and LUMB cancers. Internal Vessels (p = 0.0030), Internal Blush (p = 0.0044), Total Internal Hemoglobin (p = 0.0053), Total Internal Features (p = 0.0010), Total Internal divided by Total External Features (p = 0.0068) and combined Total Internal and External Features (p = 0.0108) helped to differentiate between LUMA and TNBC.
- Total Internal Features showed a borderline result (p = 0.0490) regarding the differentiation between TNBC and HER2-E.

Conclusions

- The use of OA/US features to non-invasively differentiate between breast cancer molecular subtypes may help to establish an earlier prognosis and treatment planning, potentially decreasing costs and facilitating larger scale diagnosis. Future research with larger sample sizes may confirm these preliminary results.

Figure 1. TNBC IDC (grade III) showing predominantly internal findings at OA/US (A). The aqua-color, purple and green rectangles (A and B) show the areas of high vascularization seen on both OA/US (A) and histopathological specimen (B). The orange rectangle (A and B) shows an area of low vascularization. TNBCs show predominantly internal findings and have poor external findings compared to LUMA breast cancers (p = 0.0030 for Internal Vessels, p = 0.0044 for Internal Blush, p = 0.0053 for Internal Hemoglobin, p = 0.0010 for Total Internal Features, p = 0.0068 Total Internal Features Divided by Total External Features and p = 0.0108 Combined Internal and External Findings).

Figure 2. An example of a LUMA IDC (grade II). Figure A shows the central nodule of the lesion (white ROI) and the boundary zone of the same lesion (aqua-color ROI) on the Total Hemoglobin OA/US map. Part B shows the histopathological specimen. Notice the remarkable difference between LUMA and TNBC. TNBC are usually more well-circumscribed (round/lobular) and have mostly internal findings at OA/US (see Figure 1). LUMA cancers usually show abundant external peripheral zone radiating vessels (colored rectangles in Figures A and B), but a relative paucity of internal OA/US findings (dark central nidus in figure A). The paucity of internal findings and robust external findings help to differentiate between LUMA and TNBC (compare Figures 1 and 2).

Figure 3. LUMA IDC (grade II). These tumors are characterized by abundant internal and external OA/US findings simultaneously. Figure A shows the central nodule of the lesion (white ROI) and the boundary zone (aqua-color ROI). Aqua-color, orange and yellow rectangles in Figures A and B show the corresponding areas of internal and external blush. Dark blue rectangles (A and B) show the peripheral radiating vessels. The correspondent areas in the pathological specimen can be seen in Figure B (colored rectangles). Spiculations are seen around the mass (Figure B).

Figure 4. HER2-E IDC (grade III) showing important peripheral findings at both OA/US and histopathological specimen (areas highlighted by colored rectangles in A and B). The radiating vessels usually course parallel to spiculations (aqua-color rectangles in A and B) and/or to Cooper's ligaments (yellow rectangles in A and B). HER2-E have similar OA/US findings to LUMAs with important external/ peripheral findings and poor internal findings. Total Internal Features showed a borderline result (p = 0.0490) regarding the differentiation between TNBC and HER2-E.