Locally Advanced Breast Cancer (LABC) and Response to Neoadjuvant Therapy

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Background information

- Women who undergo routine mammographic screening represent less than 10% of patients with LABC, globally LABC can be seen in up to 60% of diagnosed breast cancers.
- No difference in disease free or overall survival in patients who undergo adjuvant v. neoadjuvant chemotherapy.
- Neoadjuvant chemotherapy is recommended in patients with LABC who would like to consider breast conservation.
- MR has emerged as the most sensitive imaging modality to assess the response of tumor to neoadjuvant chemotherapy.
### Clinical Features of LABC

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<td>Tumor greater than 5 cm in size</td>
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<td>3-5 cm tumors in a small breast</td>
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<td>Any size tumor with associated skin or chest wall involvement</td>
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<td>Matted axillary lymph nodes</td>
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<td>Ipsilateral infra or supra-clavicular lymph nodes</td>
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<td>Absence of distant metastatic disease</td>
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*Patient with clinical presentation of LABC including a 5.0 cm mass in the upper outer quadrant (yellow oval) which has caused nipple retraction (orange arrow).*
97 year old patient with clinical presentation of LABC including skin and nipple involvement by tumor (yellow arrow). Mammogram was limited secondary to patient’s advanced age. Magnification views were not possible. Pleomorphic calcifications and a second mass (circle) were also noted.
Imaging appearance of LABC-size

25 year old patient presenting with triple negative invasive ductal carcinoma nuclear grade 3 measuring 4.5 cm in left upper outer quadrant and relatively small breast size. Kinetic assessment demonstrates rapid initial enhancement followed by washout in the delayed portions of the curve.
Imagining appearance of LABC- pectoralis muscle and chest wall invasion

3.9 cm right upper inner quadrant segmental distribution mixed invasive ductal and lobular carcinoma nuclear grade II/III, pectoralis muscle and chest wall invasion are present (arrow).
Imaging appearance of LABC- skin, chest wall invasion

Patient with invasive breast cancer replacing the entire breast and invading the skin. Patient also has chest wall invasion as manifested by enhancement of the pectoralis and intercostal muscles.
Clinical and imaging appearance of IBC

52 year old presenting with diffuse peau d’orange and enlarged left breast. Baseline DCE-MR demonstrates diffuse non-mass enhancement and skin thickening. Mammographic evaluation shows skin and trabecular thickening.
Comparison of imaging modality

• Mammography, ultrasound and MRI are typically used in conjunction with one another
• Pathologic tumor size correlation coefficient between mammography and pathologic analysis has been reported to be as low as 0.63, even less than that of physical exam at 0.72 and much less than MRI at 0.93
• MRI is superior to ultrasound with a tumor size correlation coefficient of 0.71 for MRI and 0.65 for ultrasound
• DCE-MRI gives us information regarding physiology in addition to morphology

Bhattacharyya 2008
Weatherall 2001
Comparison of imaging modalities

67 yo triple negative breast cancer
Response by modality
Suggested algorithm combining clinical management and imaging assessment

Locally advanced breast cancer diagnosis (mammo, US)

DCE-MR

Initial Chemotherapy

DCE-MR

Response

Additional chemotherapy

DCE-MR

Surgical management

Progress

Change chemo

Response

Additional chemotherapy

DCE-MR

Surgery

Surgery

Continue to progress

 +/- DCE-MR
Goals of imaging in neoadjuvant chemotherapy for management of LABC

• Identifying early markers for response to neoadjuvant chemotherapy could potentially
  – Spare patients for whom chemotherapy is ineffective
    unnecessary toxicity
  – Expedite surgical therapy
  – Predict which patients will achieve pCR
Role of neoadjuvant chemotherapy in the management of LABC

47 yo before and after chemotherapy for LABC demonstrating complete response.
Response Criteria in Solid Tumors (RECIST)

- **pCr**: 30% decrease
- **Partial**
- **Stable**
- **Progression**: 20% increase
Pitfall of DCE-MR
DWI as a biomarker for predicting pathologic response

An increased ADC correlates to decreased tumor burden. Studies have found that the ADC in tumors increases in response to treatment earlier than detectable changes in tumor size or perfusion characteristics with DCE-MRI.
Increase in ADC from $1.0 \times 10^{-3} \text{ mm}^2/\text{s}$ to $1.95 \times 10^{-3} \text{ mm}^2/\text{s}$ represents a favorable response to neoadjuvant chemotherapy. The response to chemotherapy is also noted in the morphology and kinetic assessment.
Restriction Spectrum Imaging (RSI)

- Multiple b-values up to \( b = 4000 \) s/mm\(^2\)
- Multiple directions to characterize the restricted and hindered diffusion
- Distortion correction
Conclusion

- DCE-MR is the most sensitive imaging modality to assess response to neoadjuvant chemotherapy
- RECIST standard for measuring tumor response to therapy
- Assessing early response to chemotherapy may predict tumor changes and allow therapy to be tailored based on response
- Decreased in tumor diameter and tumor volume early during therapy may be the best predictors for pCR
- Patients that undergo preoperative chemotherapy are more likely to undergo lumpectomy if there is shrinkage of tumor
Thank You

UC San Diego
Moores Cancer Center