

ARROCase - April 2017

Radiation Indications in the setting of Neoadjuvant chemotherapy for Breast Cancer

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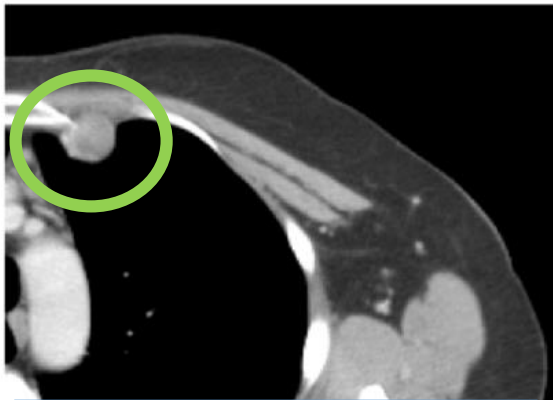
- 37 year old female who presents with self-palpated breast mass.
- History: No past medical history. G1P0A1, previously used OCP's but currently not. Works as a waitress and is a graduate student. Denies drug or alcohol use, never smoker. Family history of cervical cancer (mother) and ovarian cancer (maternal aunt)
- On exam, appreciable fullness of left breast with mild overlying erythema. Multiple palpable, mobile lymph nodes in left axilla

- Ultrasound reveals mass corresponds to 5.1 x 3.2 x 4.0 cm heterogeneous hypoechoic mass with punctate hyperechogenicity.
- Mammogram demonstrates high density, irregular mass with associated pleomorphic calcifications and palpable finding in the left breast upper hemisphere at 12 o'clock. The central nidus is located approximately 2 cm from the nipple. The **calcifications extend to the nipple base** and to within 0.4 cm of the anterosuperior skin.
- US-guided core biopsy reveals high grade invasive ductal carcinoma, ER 94.8% positive, PR 96%; Her2/neu 3+, Ki-6 53.6%. FISH amplified (Her2/CEP17 ratio >11.8).
- US of left nodal basins demonstrates **>10 left axillary nodes in level 1, 2-3 level 2 nodes**. The index level 1 node was biopsied and clip was placed, and positive for malignancy.
- Next steps?
- Clinical Stage?

Careful Pre-Treatment Evaluation

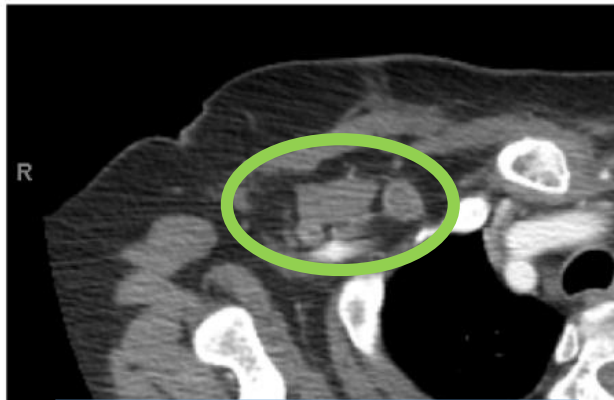
- Imaging:
 - Mammogram
 - Ultrasound with careful assessment of all lymph node basins (Infraclavicular, supraclavicular, internal mammary nodes)
 - If node positive, then cross-sectional imaging (CT Chest/ neck, PET/CT)

N2b



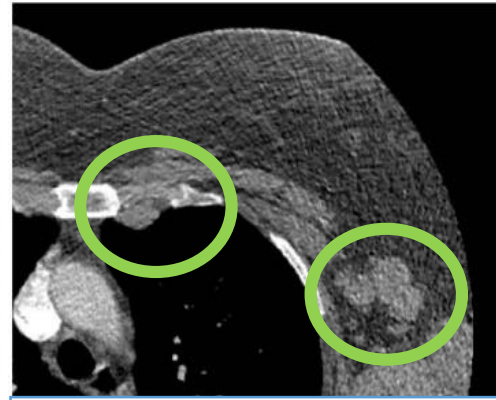
IM Node in the absence of Axillary Node

N3a



Ipsilateral Infraclavicular nodes

N3b



Ipsilateral IM node + Axillary Nodes

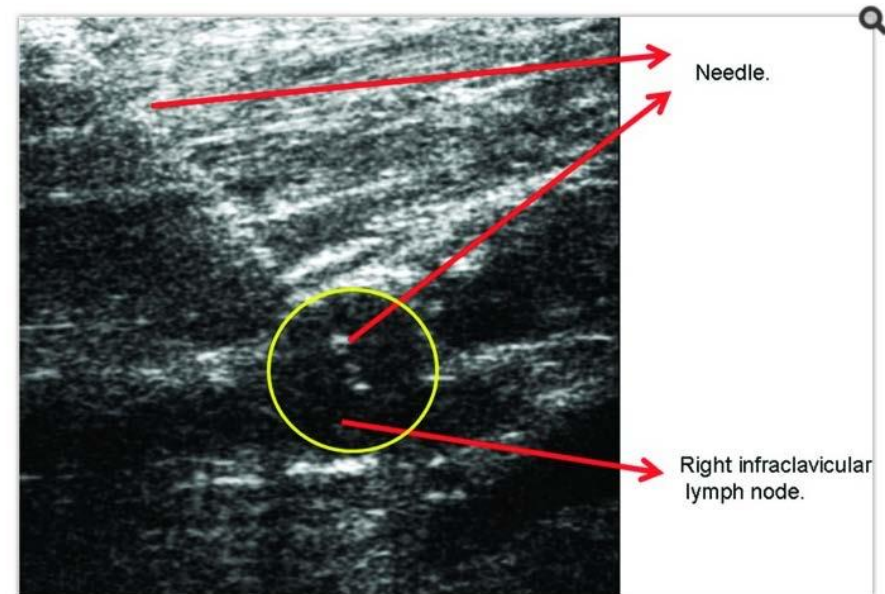
N3c



Ipsilateral SCV

Courtesy of B. Smith

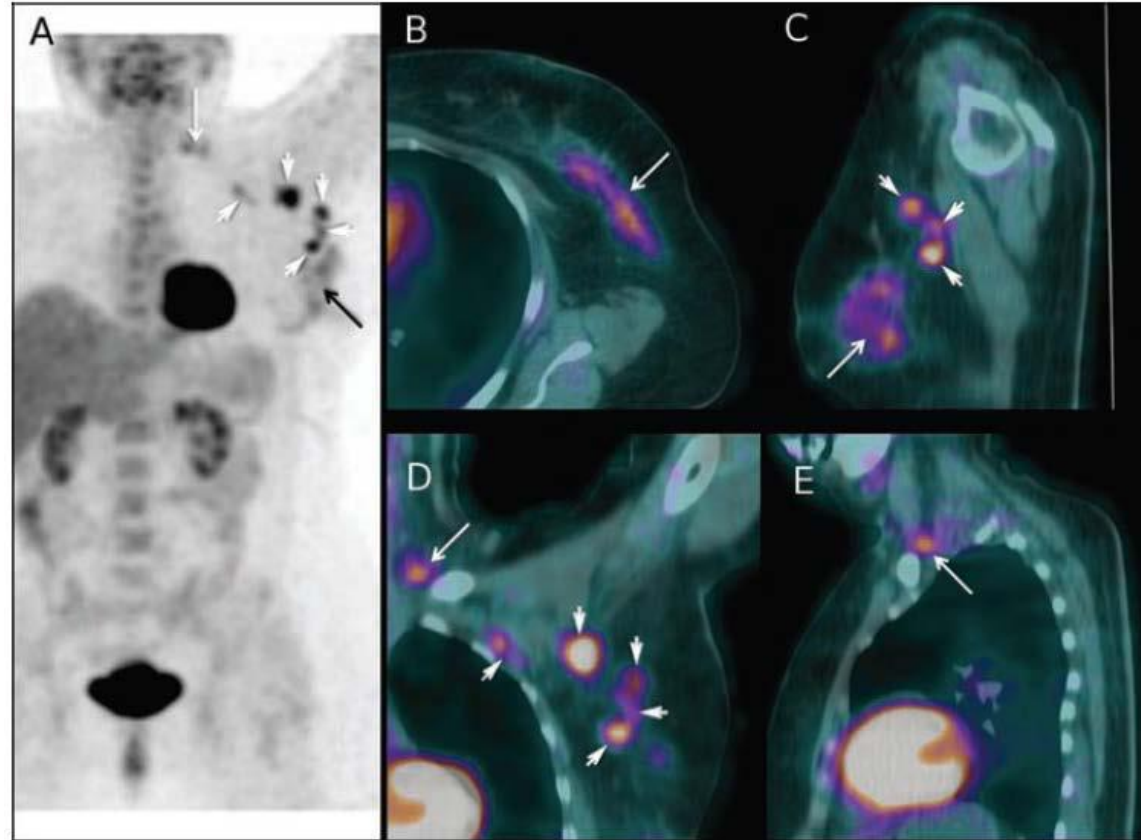
- In clinical Stage III, ultrasound identified N2b/N3 nodal disease in 37% (325/865) of patients, leading to change in radiation field design and/or dosing
 - 32% infraclavicular
 - 16% supraclavicular
 - 11% internal mammary



Right infraclavicular lymph node ultrasound with fine-needle aspiration.

Highlighted in the yellow circle is the location of the right infraclavicular lymph node and demonstration of adequate targeting of the fine-needle aspiration attempt to the specific node by ultrasound.

- In clinical Stage II-III, PET/CT identified N2b/N3 nodal disease in 16% (40/255) of patients.

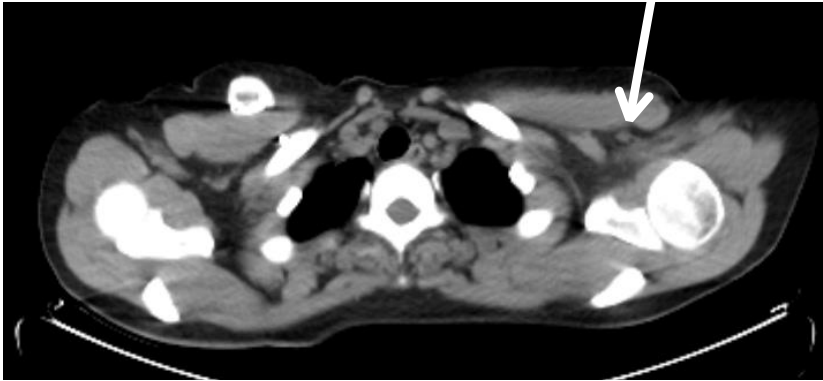


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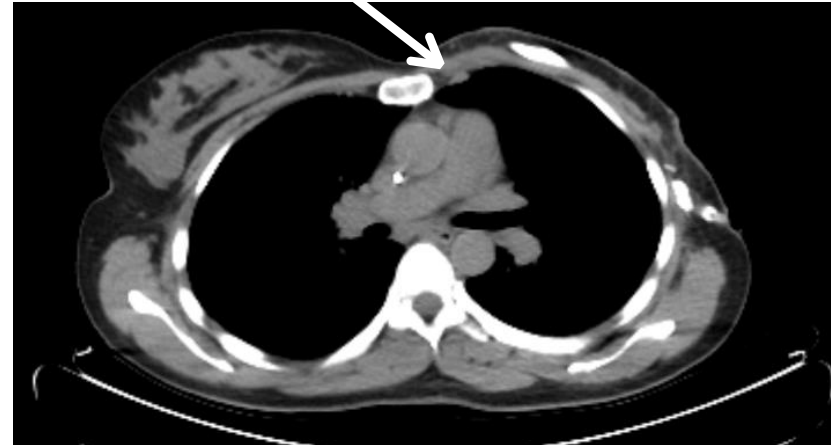
- Groheux et al, J Natl Cancer Inst, 104:1879-87, 2012

Review Images Carefully

Biopsy-proven axillary disease



Suspicious IM node



Report: "Postoperative changes. No evidence of distant metastasis".

For our patient...

- Clinical Stage T3N1
- Multidisciplinary evaluation with breast medical oncology, surgical oncology, radiation oncology, oncofertility service and cancer genetics
- **Does patient have inflammatory breast cancer?** No – based on timeline of symptom onset and skin findings.
- Dispositioned to neoadjuvant chemotherapy with ddAC x4, followed by THP x4 and trastuzumab to complete one year.

Post-chemotherapy Evaluation

- Repeat imaging
- Carefully evaluate pathology – Treatment response may help predict locoregional recurrence risk
 - Study design
 - N=701
 - cT1-3, N1-2 breast cancer
 - Pathologically confirmed nodal involvement -> Neoadjuv chemo -> Surgery
 - Radiation standard after BCS, at discretion of MD after mastectomy
 - Residual Cancer Burden strongly correlated with LRR risk
 - RCB 0 HR 1 (referent)
 - RCB 1 HR 1.38 (0.15-12.4)
 - RCB 2 HR 2.25 (0.66-7.7)
 - RCB 3 HR 4.65 (1.53-14.1)

Z1071
(Haffty et al,
ASTRO 2016)

Making Treatment Decisions

Indications for PMRT/RNI after NCT

Don't Treat

Treat

15% LRR risk

Risk of
LRR

- Clinical Characteristics
- Pathologic Characteristics
- Response to neoadjuvant therapy

Estimating Locoregional Recurrence Risk

Clinical Stage	Pathologic Stage	LRR Risk WITHOUT RT	General Recommendation for PMRT/ RNI
T1/T2, N0	ypT0-2 N0	6% at 10 years (NSABP B-18/27)	-
T1/T2, N1	ypT0-2, N0	0%-11% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)	= (NRG B-51)
T3, N+	ypT0-3, N0	0%-9% at 10 years (NSABP B18/27)	= (NRG B-51)
T1/2, N1	ypT0-2, N+	13% to 40% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)	+
T3, N+	ypT0-3, N+	22% at 10 years (NSABP B18/27)	+
T4 or N2/N3	Any	33% to 52%	+

Our patient

Is this pathologic CR? Yes. pCR is defined as no residual invasive cancer

- Pathology: **ypTisN0** (21 nodes), negative margins
- Locoregional Recurrence Risk: 0% to 9% at ten years
- Candidate for NRG B-51 trial, treated with PMRT/ RNI

NSABP B-51

- Clinical T1-T3 N1 M0 breast cancer → Axillary nodal involvement (FNA or core needle biopsy) → Neoadjuvant chemotherapy → Definitive surgery with negative axillary nodes (axillary dissection or SLNB +/- ALND) → Stratified by type of surgery, ER status, Her2 status, pCR status → Randomize to:

No Regional Nodal XRT

Breast XRT if breast-conserving surgery, but no chest wall XRT if mastectomy

Regional Nodal XRT

With breast XRT if breast-conserving surgery or chest wall XRT if mastectomy

What if there was residual disease in nodes?

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T3, N+	ypT0-3, N0	0%-9% at 10 years (NSABP B18/27)	= (NRG B-51)
T1/2, N1	ypT0-2, N+	13% to 40% at 10 years (NSABP B18/27, ACOSOG Z1071, MDA)	+
T3, N+	ypT0-3, N+	22% at 10 years (NSABP B18/27)	+
T4 or N2/N3	Any	33% to 52%	+

LRR is much higher with residual nodal disease

- Recurrence Free Survival with residual axillary disease (60%) vs with axillary pCR (87%) (Hennessy et al, 2005)
- Z1071/ Alliance: Mamounas et al, J Clin Oncol 30:3960-66, 2012
- Haffty et al, PROC ASTRO 2016
- Huang et al, J Clin Oncol 22:4691-4699, 2004

Summary

- In the setting of neoadjuvant chemotherapy for breast cancer, pre-treatment evaluation is very important
- Pay attention to residual cancer burden at surgery (nodal or primary)
- Current standard of care for T1-T3, N1 patients with nodal CR is NSABP B-51
- Treatment decisions regarding nodal irradiation/ PMRT should be made with the goal of balancing LRR with risks of treatment.