



In The Name of GOD


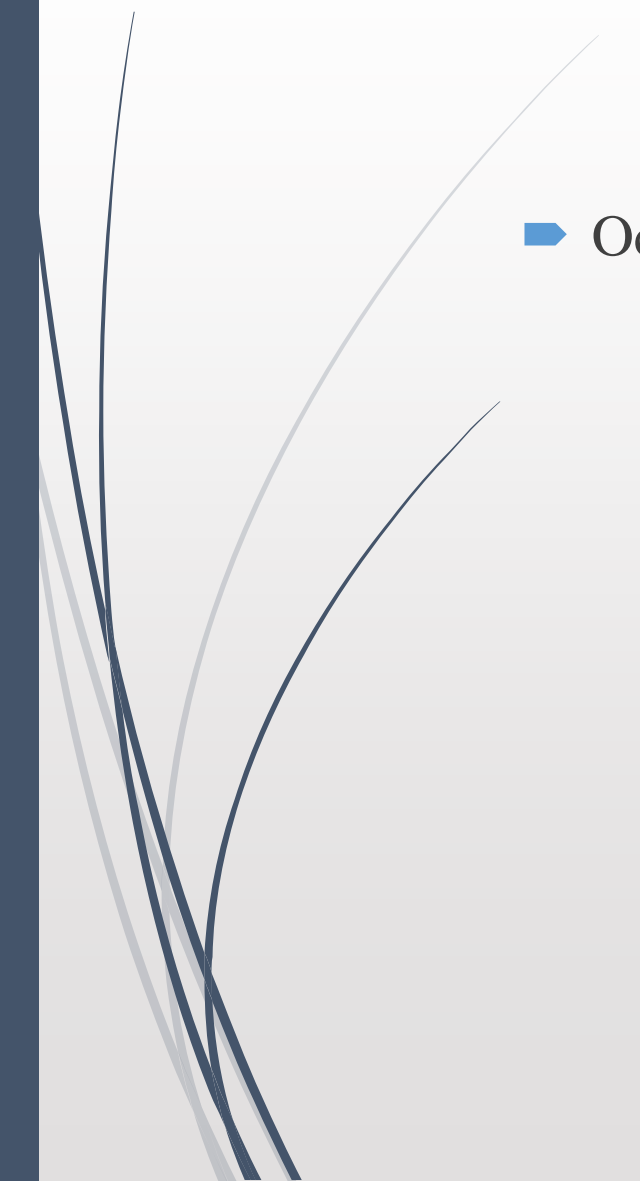
Role of Radiation in local treatment of CUPax

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TUMS

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- ▶ Occult breast cancer (OBC), which generally presents as axillary metastases (adenocarcinoma or poorly differentiated carcinoma) without clinical or radiologic evidence of a primary breast tumor, accounts for less than 1% of all breast cancer cases.

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- ▶ Despite ongoing advances in diagnostic breast imaging,

The management of OBC remains a clinical challenge.


- ▶ Few published guidelines address the treatment of OBC, and

There is **no clear consensus** on the optimal management of these patients.



Mamo, US or MRI

- ▶ In past years, mammography or breast US have been the main diagnostic tools for identifying breast lesions in patients with ALN metastasis with unknown primary.
- ▶ These modalities exhibit low sensitivity for detecting the primary breast lesion.
- ▶ The overall sensitivity of mammography for detecting breast cancer is approximately 77%, which is reduced to 64% in females with dense breast tissue.
- ▶ Supplementing breast MRI to mammography or US elevates the detection sensitivity more than 99 % in screening for breast cancer among high-risk patients.

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- ▶ The **American College of Radiology** recommends the use of MRI for OBC patients that do not have evidence of a breast primary on traditional radiological examination (mammogram and ultrasound) and clinical exam.
 - ▶ Level I evidence has shown MRI significantly more sensitive in detecting a primary lesion than mammography or ultrasound; identifying a primary in 72% of cases that were deemed occult.
 - ▶ **Breast MRI is a crucial modality for defining OBC in current clinical practice.**
 - ▶ Currently, 3.0 T (T) breast MRIs have demonstrated greater spatial resolution and improved signal to noise ratio, compared to earlier 1-1.5T MRIs.



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Review

Occult breast cancer: Where are we at?

Adam Ofri ^{a,*}, Katrina Moore ^b



- ▶ Node positive (N1) OBC patients may have a better overall survival (OS) rate to matched patients with T1N1 disease.
- ▶ Theoretically it may be possible to take a more minimalistic approach to management.
- ▶ To date, standard practice for patients with cOBC is to perform an *axillary lymph node dissection* (ALND),
- ▶ but the optimal management of the ipsilateral breast in OBC has been *controversial* and varied.



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Original article

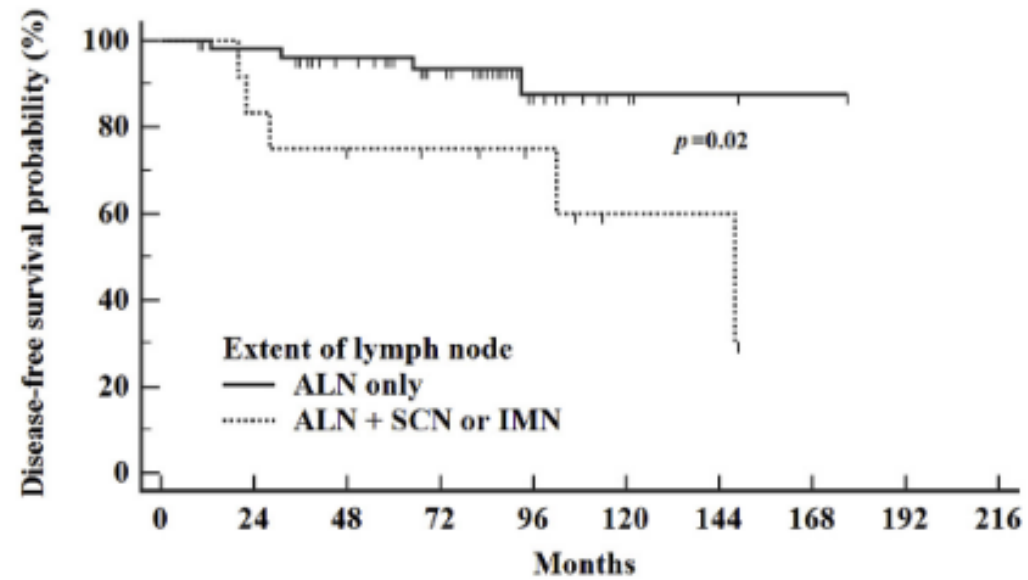
Outcome of breast-conserving treatment for axillary lymph node metastasis from occult breast cancer with negative breast MRI

Haeyoung Kim ^a, Won Park ^{a,*}, Su Ssan Kim ^{b,**}, Sung Ja Ahn ^c, Yong Bae Kim ^d,
Tae Hyun Kim ^e, Jin Hee Kim ^f, Jin-Hwa Choi ^g, Hae Jin Park ^h, Jee Suk Chang ^d,
Doo Ho Choi ^a



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- ▶ Survival rates and failure patterns in 66 patients who received axillary lymph node dissection (ALND) and BCT for MRI-OBC between 2001 and 2013 at seven hospitals were analyzed.
 - ▶ OBC was defined as adenocarcinoma in the axillary lymph node (ALN) +/- supraclavicular (SCN) or internal mammary lymph node (IMN) with a negative breast MRI.
 - ▶ All patients underwent breast MRI in conjunction with mammography to confirm the absence of a breast primary
 - ▶ ALND was performed in all patients; blind upper quadrantectomy was performed in 15 patients.
 - ▶ No patients showed malignant lesion in the quadrantectomy specimen.
 - ▶ 54 patients had only ALN metastasis (ALN only), and 12 patients had ALN metastasis along with SCN or IMN metastasis (ALN +SCN/IMN).

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- ▶ Median follow-up was 82 months.
 - ▶ All patients (except 3) received ipsilateral whole breast irradiation (WBI).
 - ▶ The incidence of breast cancer occurrence was significantly lower among patients who received WBI compared to those who did not (6.3% (4/63) vs. 66.7% (2/3); $p = 0.02$).
 - ▶ The 5-year OS, DFS, and breast cancer-free survival rates were 93.4%, 92.1%, and 96.8%, respectively.
 - ▶ The 8-year DFS for patients with WBI ($n = 63$) was 89.5%.
 - ▶ Five-year disease-free survival was significantly higher in ALN only patients compared to ALN + SCN/IMN patients (96.1% vs. 75.0%; $p = 0.02$).
 - ▶ When prognostic factors were evaluated in a univariate analysis, location of lymph node metastasis and receipt of WBI were significant for predicting DFS.



Number at risk


Group: ALN only

54 50 43 31 12 4 2 1 0

Group: ALN + SCN or IMN

12 10 8 7 5 2 2 0 0

Fig. 1. Disease-free survival according to initial disease extent in patients with occult breast cancer.

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- Wu et al. (2017), also retrospectively reviewed outcomes of 980 pts from the SEER database.
 - ALND +
 - Observation (n=219)
 - Surgery (n = 263)
 - RT (n = 252)
 - Surgery + RT (n = 246)
 - The 10-year cause specific survival rate and OS was significantly better in the ipsilateral breast treatment arm, 71.5, 81% versus 57.2% ($p < 0.001$) and 67, 69.5% Vs 46% ($p < 0.001$).
 - No significant difference in OS between the three treatment arms.
 - ALND with either surgery or RT had equivalent outcomes.

Oncologic Outcomes After Treatment for MRI Occult Breast Cancer (pToN+)

[Damian P. McCartan MD](#), [Emily C. Zabor MS](#), [Monica Morrow MD](#), [Kimberly J. Van Zee MS, MD](#) & [Mahmoud B. El-Tamer MD](#) 

- ▶ OBC patients comparing mastectomy to WBRT has been performed at MSKCC
- ▶ 38 Pts
 - ▶ ALND and WBRT (n = 25)
 - ▶ ALND and mastectomy (n = 13)
- ▶ All patients had an MRI and all patients received chemotherapy
- ▶ At a median follow up of 7 years, there was no local or regional recurrence in either arms.
- ▶ Ten-year DFS
 - ▶ The ALND and mastectomy group was 77%
 - ▶ The ALND and WBRT group of 67%
- ▶ No statistical significance.
- ▶ Suggest that ALND + ipsilateral breast RT ± regional nodes is a reasonable option.

Optimal Surgical Management for Occult Breast Carcinoma: A Meta-analysis

**Francisco Igor B. Macedo, MD¹, Joseph J. Eid, MD¹, Jeff Flynn, PhD², Michael J. Jacobs, MD¹, and
Vijay K. Mittal, MD¹**

¹Department of Surgery, Providence Hospital and Medical Centers, Michigan State University, Southfield, MI;

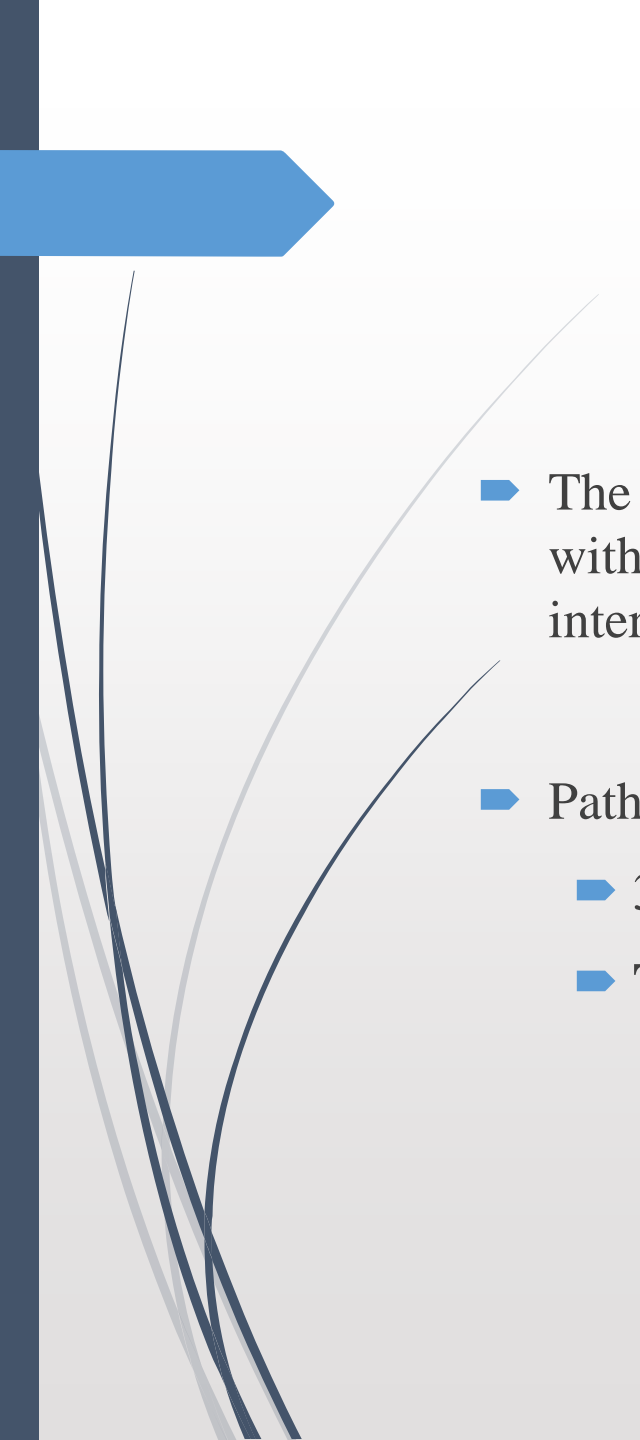
²Department of Biostatistics, Providence Hospital and Medical Centers, Michigan State University, Southfield, MI

- 42 publications (7 studies met the inclusion criteria) (241 Pts)
 - 94 (39 %) ALND with XRT
 - 112 (46.5 %) ALND with mastectomy
 - 35 (14.5 %) ALND alone
- Mean follow-up was 61.8 ± 16.2 months (range 5–396 months).
- Locoregional recurrence, distant metastasis, and mortality rates were similar between ALND with XRT and mastectomy.
- ALND with XRT was superior to ALND alone regarding locoregional recurrence (12.7 vs. 34.3 %, $p = 0.01$)
- Radiotherapy improves locoregional recurrence and possibly mortality rates in patients undergoing ALND

ORIGINAL ARTICLE – BREAST ONCOLOGY

Factors Influencing Management and Outcome in Patients with Occult Breast Cancer with Axillary Lymph Node Involvement: Analysis of the National Cancer Database

- ▶ Female patients with cT0 N1/2 M0 BC were selected from the National Cancer Database (2004–2013) and categorized into four treatment groups
- ▶ Among 2.03 million BC cases, 1853 females (0.09%) with cT0 N1/2 M0 disease were identified and 1231 patients were categorized into a treatment group:
 - ▶ MAST + ALND = 592 (323 (56.6%) receiving RT)
 - ▶ RT + ALND = 342
 - ▶ ALND alone = 106
 - ▶ OBS = 191

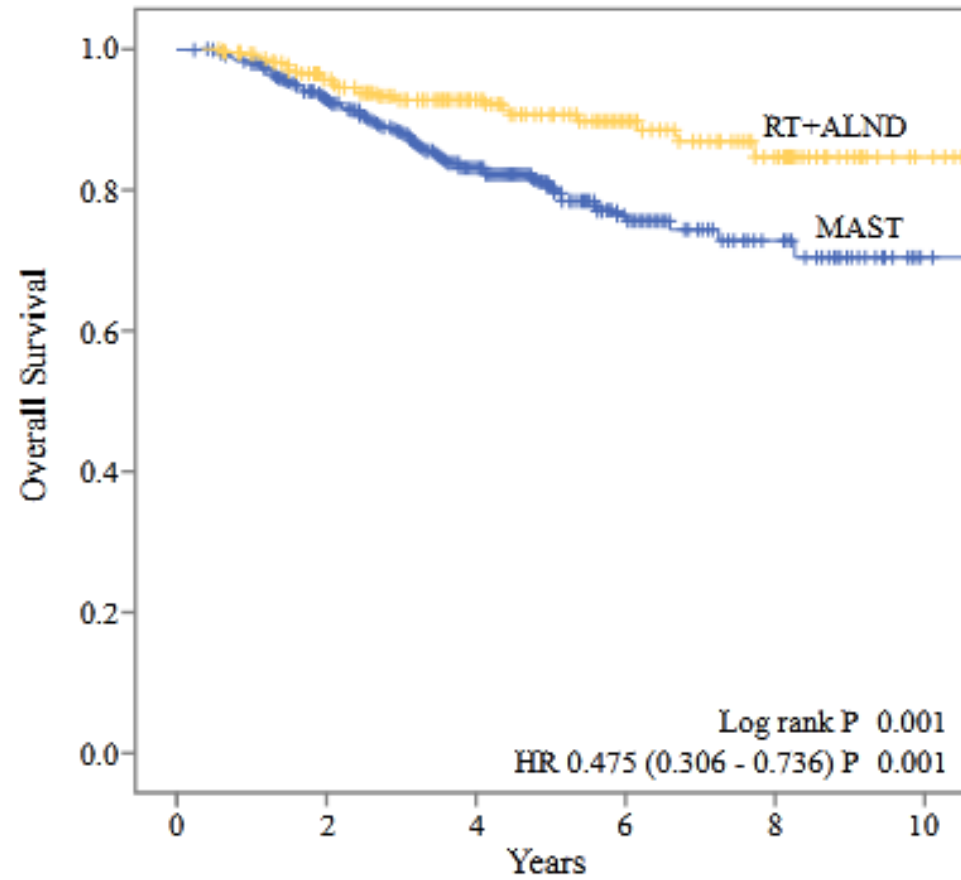
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- ▶ The only factor associated with type of **treatment was care at an academic center**, with a higher likelihood of treatment with RT + ALND (odds ratio 2.03, 95% confidence interval; 1.50–2.74, $p < 0.001$)
 - ▶ Pathologic Findings on Mastectomy Of the 592 MAST patients,
 - ▶ 397 (67%) had primary tumors that were classified as T0 or TX on final pathology.
 - ▶ **Tumors were identified in the breast after mastectomy in 195 patients (33%).**
 - ▶ The majority of these were in situ or T1 tumors ($n = 124$, 63.6%),
 - ▶ while 71 patients (36.4%) had tumors that were T2 or greater.

- ▶ Treatment with MAST + ALND versus RT + ALND Univariate survival analysis showed that patients treated with ***RT + ALND had a significantly better OS*** compared with patients treated with MAST (Hazard ratio, 0.475, 95% CI 0.306–0.736, p = 0.001)

Table 2
Treatment groups and OS [9].


Groups	n	5-year OS %	8-year OS (%)
Observation alone	191	56.5 ± 4.8	49.0 ± 5.9
ALND alone	106	76.2 ± 5.0	65.1 ± 6.7
ALND + RT	342	90.8 ± 1.9	84.7 ± 3.6
ALND + Mastectomy ± RT	592	80.0 ± 2.2	72.8 ± 3.2

OS Overall Survival, ALND Axillary lymph node dissection, RT Radiotherapy.





No. at risk	0	2	4	6	8	10
MAST	506	408	230	96	35	4
RT+ALND	296	251	149	76	33	4

FIG. 1 Kaplan–Meier curve illustrating overall survival for patients

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- Masinghe et al. (2010) reported upon 53 patients who all had surgery to their axilla (biopsy, sampling or clearance) and either
 - Regional node RT (n = 12) or
 - Ipsilateral breast RT ± regional node RT (n = 41)
 - LRR
 - 54% in those treated with regional node RX alone
 - 28% in those that had both regional nodes and breast radiation.
 - Conclude that those that received treated to the breast did better

Masinghe SP, et al. Breast radiotherapy for occult breast cancer with axillary nodal metastases—does it reduce the local recurrence rate and increase overall survival. Clin Oncol 2011;23(2):95-100.

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- ▶ The management of OBC remains a clinical challenge
 - ▶ There is **no clear consensus** on the optimal management of these patients



صلوات خاصة حضرت امام رضا عليه السلام

اللَّهُمَّ صَلِّ عَلَى عَلِيِّ بْنِ مُوسَى الرِّضَا المُرْتَضَى
الْإِمَامِ النُّقِيِّ النُّقَى وَجَجَّتِكَ عَلَى مَنْ فَوْقِ الْأَرْضِ
وَمَنْ تَحْتَ الثَّرَى الصِّدِّيقِ الشَّهِيدِ صَلَاةً كَثِيرًا
بِأَمَّةٍ زَاكِيَةٍ مُتَوَاصِلَةٍ مُتَوَاتِرَةٍ مُتَرَادِفَةٍ كَأَفْضَلِ مَا
صَلَّيْتَ عَلَى أَحَدٍ مِنْ أَوْلِيَائِكَ

