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RESEARCH ARTICLE

Reverse Axillary Mapping in Breast Cancer using Double Dye: A Tertiary Cancer Center Experience

Arun H Narasannaiah [1]*, Manjunath K V[1], Yeshwanth R[1], Syed Althaf[2], Raviarjunan[2], Harish[3]

[1] Assistant Professor, Department of Surgical Oncology
[2] Professor, Department of Surgical Oncology
[3] Associate Professor, Department of Nuclear Medicine.

* arunsunchariot@yahoo.com

ABSTRACT

Background: Among the various methods in minimizing Limb Lymphoedema following ALND in Breast cancer, Axillary reverse mapping is a novel approach. Attempt to preserve the ARM node without threatening Oncological safety is a further step.

Aim: To identify Blue ARM Node, intra operatively whether harbors metastases or not, defined by Radioactivity comparing with Histo pathological Examination.

Materials and Method: The 30 cases of Breast cancer patients undergoing surgery along with Axillary dissection were considered for Double dye technique of ARM study with Radio colloid injection in subareolar region and 3ml of 5% methylene blue to the Arm,1 hour before starting surgery. At Axillary dissection, level I and level II nodal clearance done and the blue thin, tortuous lymphatics entering axilla are identified are followed medially, where blue nodes are usually identified below inferior to Axillary vein. The Blue nodes are considered belonging to upper limb called ARM node, whose radioactivity is recorded invivo, are dissected and sent for Histo pathological Examination.

Results: The identification rate of blue lymphatics is about 77% (26 cases out of 30), the location of blue ARM node (70% identification rate, 21 out of 30 cases) were within 2cms inferior to Axillary vein lateral to Latissimus dorsi pedicle. The Radioactivity of the Blue ARM node more the 10% of the count at Subareolar region considered as Cross over Node (Blue+Hot) is observed among 2 patients, which confirmed with histopathologicaly positive for metastases, but rest of 19 (95.3%) Blue ARM node with less than 10% radioactivity (Blue +Cold), were Histopathologicaly Negative for metastases. Among 21 Blue ARM nodes, 2 nodes were metastatic amounting to 9.4% cases having cross over Lymphatics, identified by radioactivity.

Conclusion: The Double dye Axillary Reverse Mapping study is a valuable armamentarium for the surgeons, during Breast Cancer surgery undergoing Axillary Lymphnode dissection to preserve uninvolved ARM Lymph node, thereby avoid Limb lymphedema without compromising Oncological safety.

Introduction:

With the experience of Axillary Reverse Mapping using Blue dye in breast cancer patients undergoing Axillary Sentinel Lymph Node (SLN) or Axillary Lymph Node dissection (AXLN), we have studied Arm Lymphatic anatomical location in the Axilla, Identification of Blue node (ARM node) and its metastatic involvement by Histo pathologic examination(1). Now, by knowing that blue ARM node is non- metastatic on operation table, we can preserve them, thereby we can FURTHER prevent limb Lymphedema. Hence, this study of Double dye Technique of ARM study with Radio colloid injection in subareolar region and Blue dye in the Arm, to know the ARM blue node harbors metastases or not correlating with its radioactivity.

Objective of the Study:

1) To study Crossover Lymphatics of Arm with that of the Breast.

2) To Study the identification rate and anatomical location of the ARM lymph node.

3) To identify ARM Node, harbors metastases or not defined by Histo pathological Examination.

Materials and methods:

Inclusion criteria:

1. Unilateral Operable Breast Cancer patients undergoing Axillary Dissection.
2. Patients who are >18 years and willing to participate in the study.

Exclusion Criteria:

1. Subjects who are not willing to participate.
2. Subjects who are allergic to Blue dye or Radio colloid
3. Inoperable locally Advanced Breast cancer and Metastatic disease.
4. Previous Breast or Axillary Surgery.

There were 30 patients of Breast cancer patients undergoing surgery and Axillary dissection were considered for Double dye technique of ARM studywith Radiocolloid injection in subareolar region and Blue dye to the Arm from September 2020 to August 2021. About 1 millicurie of Radio colloid is injected Subareolar and 3ml of 5% Methylene blue dye is injected on medial side of the arm about 1hour before starting surgery.

The Axillary dissection during Modified Radical Mastectomy or Breast Conservative Surgery, followed standard template of level I and level II Axillary Lymph nodal Clearance, inferior to Axillary Vein, Medial to lateral border of Latissimus dorsi to chest wall, sparing Nerve to Latissimus dorsi and Nerve to serratus anterior. During the Axillary Dissection, the tissue lateral to Latissimus dorsi neurovascular pedicle and Axillary vein is dissected carefully superficial to deep gently, giving saline washes to identify the Blue thin, tortuous lymphatics entering axilla. These Blue lymphatics are followed medially, 2cms inferior to Axillary vein, where Blue nodes are usually identified. The Blue nodes are considered to belonging to upper limb called ARM node. The Blue nodes are dissected separtely and labeled before sending for Histological Examination.

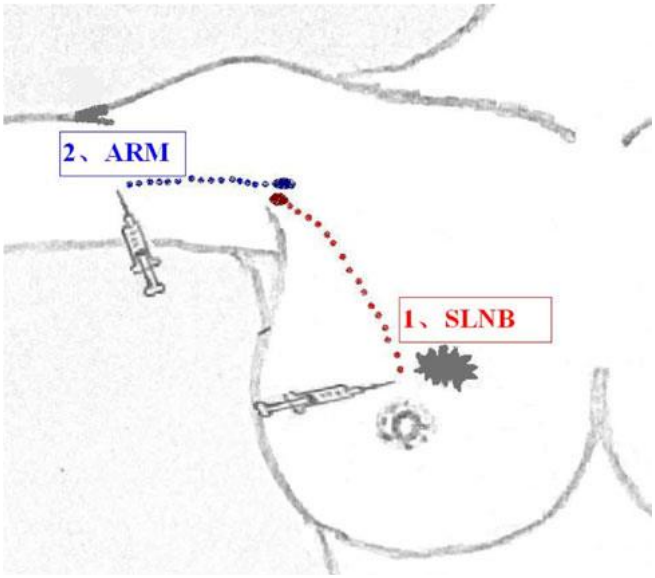

Figure 1: This picture shows Blue Dye injected to upper arm, the node stained blue is ARM node and the Radiocolloid dye injected in subareolar region, reaches the Sentinel node. If the Blue node shows radioactivity (Hot), is considered due to Cross over Lymphatics(Blue +Hot)

The blue Lymphatics and node are identified during AXLND, the radio activity over the Node is noted invivo with respect to the primary activity at subareolar region. Also, the exvivo radio activity count of the Blue node is noted. The location of blue lympatics and node are noted, dissected separately from Axillary specimen and sent for Histopathological evaluation. The statiscal analysis were performed using SPSS, version 13.0, for Windows (SPSS Inc., Chicago, IL).

Results

The 30 cases of unilateral Breast Cancer in stage I, II and IIIA, undergoing Axillary dissection as a part of Modified Radical Mastectomy in 18 patients and Breast Conservation Surgery among 12 patients were included in the study. There were 6 cases of post Neo Adjuvant Chemo theraphy cases for stage IIIA, who has completed 3 to 6 cycles.

Table:1 Demography of the patients

Sl no	Stage	Side-Rt	Side-Lt	NACT	MRM	BCS
1	T1N0	3	4	-	1	4
2	T2N0	4	2	-	2	3
3	T3N0	3	2	2	4	2
4	T1N1	1	2	-	4	2
5	T2N1	2	2	-	5	1
6	T3N1	3	3	4	2	0
	Total (n=30)	16	14	**30**	**18**	**12**

The identification rate of blue lymphatics is about 26 cases (77%) out of 30 cases included in the study. The Location of blue lymphatics with respect to Axillary vein were noted most of the times inferior to Axillary vein (25 cases) and few cases superior (1 case). The Infra Axillary lymphatics found majority of cases within 1cm in about 20 cases(67%) and very few cases were inferior to more than 1cm from Axillary vein seen in about 6 cases (20%).

Figure 2: The Blue ARM node, usual location between inferior margin of Axillary vein and Thoraco dorsal Pedicle during ALND

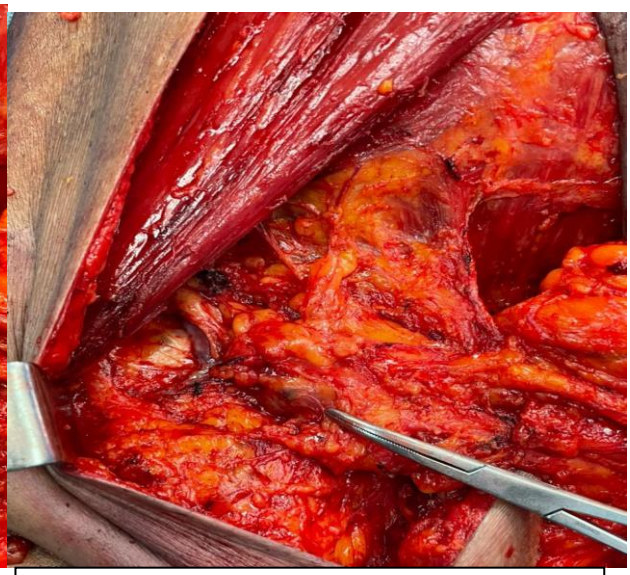

Figure 3: The blue lymphatics identified along 2cm inferior to Axillary vein in the lateral most part of ALND boundary.

The ARM node as blue node identified as single node in most of the cases, except in 1 case wherein two nodes were blue, beside one another. The location of Arm Node is related to blue lymphatics in all the cases, inferior to Axillary vein and lateral to Latissimus dorsi Pedicle in the Axillary fat. If the blue lymphatics are separate from the blue node, lymphatics are dissected away and preserved, in order to maintain continuity of limb lymphatics.

Figure 4: The blue node radioactivity is recorded using gamma probe, readings on the monitor counted.

In our study identification rate of ARM blue node is independent of T and N status of the patient, so also the identification of blue Lymphatics.But during the dissection of Blue node, the blue lymphatics were disrupted as they were closely related. only among 8(38%) cases out of 21,the blue lymphatic continuity could be preserved with careful dissection. The Radioactivity of a node more the 10% of the count at Subareolar region, is considered as Cross over Node (involved node). Such ARM Node also being Cross over Node(Hot+blue) Node also is observed among 2 patients, which confirmed with histopathologicaly positive, but rest of 20 (95.3%) ARM node were Histopathologicaly Negative for metastases. Among 21 ARM nodes, 2 nodes were metastatic amounting to 9.4% cases having cross over Lymphatics.This is observed probably due to cross over of Lymphatics between Breast and the upper limb.

Table 2: The features of Blue ARM nodeis as tabulated below:

SL NO.	Stage	No.	ARM Node Identified	ARM Node Not Identified	ARM Node + HOT	ARM Node Radioactivity count <10%	Blue Lymphatics identified	Blue Lymphatics saved	Cross over Node with metastasis (Histopathology)	ARM +Cold Node showing metastases
1	pT1	10	8	2	0	7	8	4	0	0
2	pT2	9	5	4	1	6	5	2	1	0
3	pT3	11	8	3	0	7	8	2	0	0
	Total	**30**	**21**	**9**	**1**	**20**	**21**	**8**	**1**	**0**
4	pN0	4	2	2	0	6	2	2	0	0
5	PN1	12	4	3	0	5	10	2	0	0
6	pN2	9	6	3	0	7	8	2	0	0
7	pN3	5	9	1	1	2	4	2	1	0
	Total	**30**	**21**	**9**	**1**	**20**	**24**	**8**	**1**	**0**

There were no intra operative or anaphylactic complications observed in our study. The blue dye injection site pain, mild swelling and bluish discoloration are the most commonly observed complications in our study.The injection site pain and swelling managed with NSAIDs for 5-7 days. The Bluish discolouration subsided in 4-6 weeks duration.

Discussion:

The Axillary Reverse Mapping was developed to preserve the upper extremity lymphatic drainage system during ALND in breast cancer patients undergoing Modified Radical Mastectomy or Breast conservation Surgery (2).The variety of dye materials were used to conduct ARM study viz blue dye, radioisotope or Indo Cyanine Green(Noguchi et al.2010, Britton et al. 2009 and Nos et al. 2008 respectively) with the lymphatic identification rate of 61-89%, 91-100% and 75-88% respectively (3,4,5,6). In our previous Study(1) with blue dye technique, we tried defining the blue node, lymphatic anatomy with the Lymphatic identification rate of about 73%. The anatomical location of blue ARM node in the axilla, seen commonly within 2cms inferior to Axillary vein lateral to Thoracodorsal Pedicle. The preservation of ARM blue node during ALND will avoid disruption of upper limb lymphatics, theoretically thereby prevent limb lymphedema. But the concern of ARM node harbouring metastases needs to be evaluated, before preserving them, for the Oncological safety purpose.

This study, we used Double dye technique of ARM, wherein the ARM blue node if has >10% radioactivity of primary site radioactivity is considered as Hot node. The hot ARM nodehas cross over lymphatic drainage from breast also, hence such nodes are removed during axillary dissection. In our present study the rate of blue node identification is 77% (26/30), comparable with other studies Nos et al 71%(n=47), kang et al 78%(n=129) (6,7). The rate of identification improves with increasing number of procedures. The blue lymphatics identification is among 70% (21/30), indicating about in 7% of cases only blue node is noted without localization of blue lymphatics.Also in 8cases out of 21 (38%), the blue node could be dissected out preserving the Lymphatic continuity. The lymphatics being delicate network of thin hair-like structure is not visualised routinely unless they are blue dye stained. The lymphatics showed variable anatomy among individuals and also closely associated with the draining lymphnode. Hence preservation of lymphatics while dissecting out the relevant node is very difficult, unless done with magnification and meticulously. The attempt of Lympho venous or lympho-lymphatic anastamosis has been done at few centers with variable success, but it demands expertise and long term followup to evaluate incidence of Limb lymphedema. So, identifying the ARM node as disease free is most important to preserve them during the ALND.

Ponzone et al. (2009) performed ARM procedures in 49 breast cancer patients undergoing ALND and they reported that 3 patients with extensive nodal metastatic involvement (i.e., pN2a and pN3a) showed breast cancer metastatic cells in the blue ARM nodes. So they suggested that ARMprocedures were not safe in patients with extensive nodal metastatic involvement(8). Bedrosian et al. (2010) reported 2 cases of metastastic ARM nodes in 30 ARM procedures in patients underwent ALND. In one case, the pathological axillary staging was pN3; however, in the other case, thepathological axillary staging was pN1. Their data revealed that not only breast cancer patients with high pathological axillary staging (pN2 and pN3) but also patients with low pathological axillary staging (p N1) would occur metastastic ARM nodes(9).

Our study is done with double dye technique, we are mapping limb lymphatics with blue dye and the breast lymphatics with the Radio colloid. In this study we have removed all the ARM blue node along with ALND to correlate with histopathology, irrespective of their radioactivity.The blue ARM node identified during ALND if is hot,defined by radioactivity is considered it drains breast as well, due to cross over lymphatics. Such Cross over Lymphnodes harbouring metastases is high, hence they are dissected during ALND. In our study 2 of 2(100%) ARM cross over lymphnode(blue + hot), had metastatic deposit confirmed by Histopathology.

If the Blue ARM node is Cold, as defined by radioactivity< 10% of the primary activity, has very less chance of harbouring metastases. In our study 19out of 19(100%) ARM nodes, which are cold didn't harboured any metastases in final histopathology.

About 9/30(30%) cases didn't show up any blue node in our study, in whom ALND as per standard template was completed.

We could perform ARM procedure in breast cancer patients with any Pathological axillary staging. But the most important question is how we could distinguish ARM nodes which did not contain metastasis from that contain metastasis. By mapping lymphatic drainage of Breast and the ipsilateral arm in a patient at the same time, we observed that all possible Metastastic ARM nodes were Cross over Lymph Nodes (Blue +Hot).In our study 2/2 (100%) such Cross over Lymph nodes(Blue+Hot) had metastatic deposit confirmed by Histological Examination. Similarly, 19/19(100%) ARM nodes which are cold,didn't harbour any metastases as confirmed by histopathology.

The cons of our study is small number of patients, Sentinel lymphnode dissection group are not included as,extra dissection of lateral part of axilla needs to be dissected to identify ARM nodes, which may preclude the principles of SLNB.As the ARM node identification rate is in the range of 70%, the rest 30% patients are not benefited by the study. Except for the few complications of skin Tattooing, local edema and pain at the dye injection site,no major adverse events were recorded in our study. The long-term follow-up of patients in this study is ongoing process yet to be consolidated.

This study though the number of subjects are less, is conducted under controlled supervision in a tertiary cancer institute, has progressed a step further in ARM study, by indicating that by doing Double dye ARM study, intra operatively we can characterise ARM node has metastases or not and decide to remove or preserve respectively. Also, it has been attempted to preserve blue lymphatics which are away from the Blue node, thereby to maintain the limb lymphatic continuity. Further, if expertise is available Lympholympatic or Lymphovenous anastamosis of blue lymphatics if accidentally injured or on removal of blue node can be tried to maintain arm lymphatics continuity wherever possible.

Conclusion

The Double dye Axillary Reverse Mapping study is a valuable armamentarium for the surgeons, during Breast Cancer surgery undergoing Axillary Lymphnode dissection to preserve uninvolved ARM Lymph node, thereby avoid Limb lymphedema without compromising Oncological safety.

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Conflict of Interests: Nil

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References:

1. Narasannaiah A H, Anwar A Z, KV M, et al. (October 07, 2021) Reverse Axillary Mapping in Breast Cancer Using Blue Dye: A Tertiary Setup Experience. Cureus 13(10): e18576. DOI 10.7759/cureus.18576
2. Heran Deng,Lun Chen,WeijuanJia,Kai Chen,Yunjie Zeng,Nanyan Rao,Shunrong Li,Liang Jin,Fengxi Su Safety study of axillary reverse mapping in the surgical treatmentfor breast cancer patients, J Cancer Res Clin Oncol (2011) 137:1869–1874DOI 10.1007/s00432-011-1064-3
3. Britton TB, Solanki CK, Pinder SE, Mortimer PS, Peters AM,Purushotham AD (2009) Lymphatic drainage pathways of thebreast and the upper limb. Nucl Med Commun 30(6):427–43
4. Noguchi M, Yokoi M, Nakano Y (2010a) Axillary reverse mapping with indocyanine fluorescence imaging in patients with breast cancer. J SurgOncol 101(3):217–221
5. Noguchi M, Yokoi M, Nakano Y (2010b) Axillary reverse mapping for breast cancer. Breast Cancer Res Treat 119(3):529–535
6. Nos C, Lesieur B, Clough KB, Lecuru F (2007) Blue dye injection in the arm in order to conserve the lymphatic drainage of the arm in breast cancer patients requiring an axillary dissection. Ann SurgOncol 14(9):2490–2496
7. Kang SH, Choi JE, Jeon YS, et al. Preservation of lymphaticdrainage from arm in breast cancer surgery: Is it safe? Cancer Res 2009;69(Suppl 2):201
8. Ponzone R, Cont NT, Maggiorotto F, Cassina E, MininanniP, Biglia N, et al. Extensive nodal disease may impair Axillary reverse mapping in patients with breast cancer. J ClinOncol2009;27:5547-51.
9. Bedrosian I, Babiera GV, Mittendorf EA, Kuerer HM, PantojaL, Hunt KK, et al. A phase I study to assess the feasibilityand oncologic safety of axillary reverse mapping in breastcancer patients. Cancer 2010;116:2543-8.