

# Guidelines for locoregional therapy in primary breast cancer in developing countries: The results of an expert panel at the 8<sup>th</sup> Annual Women's Cancer Initiative – Tata Memorial Hospital (WCI-TMH) Conference

Anusheel Munshi, Sudeep Gupta<sup>1</sup>, Benjamin Anderson<sup>2</sup>, John Yarnold<sup>3</sup>, Vani Parmar<sup>4</sup>, Rakesh Jalali, Suresh Chander Sharma<sup>5</sup>, Sangeeta Desai<sup>6</sup>, Meenakshi Thakur<sup>7</sup>, Gunjan Baijal, Rajiv Sarin, Indraneel Mittra<sup>4</sup>, Jaya Ghosh<sup>1</sup>, Rajendra Badwe<sup>4</sup> and other  
*Locoregional Panel Members*

Departments of Radiation Oncology, <sup>1</sup>Medical Oncology, <sup>4</sup>Surgical Oncology, <sup>6</sup>Pathology, and <sup>7</sup>Radiology, Tata Memorial Hospital, Parel, Mumbai, <sup>2</sup>Director, Breast Health Clinic University of Washington/Seattle Cancer Care Alliance, Chair and Director, Breast Health Global Initiative, <sup>3</sup>Department of Clinical Oncology, Institute of Cancer Research and The Royal Marsden Hospital, Surrey UK, <sup>5</sup>Department of Radiation Oncology, PGI, Chandigarh, Punjab, India

## Address for correspondence:

Dr. Anusheel Munshi,  
Department of Radiation Oncology,  
120, Tata Memorial Hospital, Parel,  
Mumbai 400 012, India.  
E-mail: anusheel8@hotmail.com

## ABSTRACT

**Background:** Limited guidelines exist for breast cancer management in developing countries. In this context, the Women's Cancer Initiative - Tata Memorial Hospital (WCI-TMH) organised its 8<sup>th</sup> Annual Conference to update guidelines in breast cancer. **Materials and Methods:** Appropriately formulated guideline questions on each topic and subtopic in the surgical, radiation and systemic management of primary breast cancer were developed by the scientific committee and shared with the guest faculty of the Conference. Majority of the questions had multiple choice answers. The opinion of the audience, comprising academic and community oncologists, was electronically cumulated, followed by focussed presentations by eminent national and international experts on each topic. The guidelines were finally developed through an expert panel that voted on each guideline question after all talks had been delivered and audience opinion elicited. Separate panels were constituted for locoregional and systemic therapy in primary breast cancer. **Results:** Based on the voting results of the expert panel, guidelines for locoregional therapy of breast cancer have been formulated. Voting patterns for each question are reported. **Conclusions:** The updated guidelines on locoregional management of primary breast cancer in the context of developing countries are presented in this article. These recommendations have been designed to allow centers in the developing world to improve the quality of care for breast cancer patients.

**Key words:** Breast cancer, developing countries, guidelines, locoregional therapy

## INTRODUCTION

A number of international guidelines currently exist in

breast cancer, all aiming to ensure uniformity and quality in the delivery of care to patients with breast cancer.<sup>[1-4]</sup> The majority of guidelines have been developed in the context of evidence and clinical practice in the Western world. There is little representation from developing countries, if any, in the expert panels that formulate these guidelines. Clinical practice in developing countries, however, continues to be largely guided by these guidelines as they are based on high-quality evidence with expert appraisal. Many of these guidelines are not literally applicable to developing countries because of constraints on resources and/or expertise.

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The Women's Cancer Initiative is a non-governmental organization that focuses on the cause of women's cancers. Women's Cancer Initiative – Tata Memorial Hospital – (WCI-TMH) has organized focussed theme-based Annual Breast and Gynecological Cancers Conferences for the past 8 years. This Conference invites and receives participation from national and international experts and academic and community oncologists from all disciplines. The Steering Committee of WCI-TMH decided, in view of the paucity of relevant guidelines, to commit the 2010 Annual Conference to the development of guidelines for the management of primary breast and cervical cancers in the express context of India and other developing countries. We report herein the results of the expert panel for the development of guidelines for locoregional therapy in primary breast cancer.

## MATERIALS AND METHODS

The scientific committee of the Conference met over several sessions in the early part of 2010 to discuss the methodology for the development of these guidelines and important issues to be discussed. Members of the committee developed a series of appropriately formulated questions on each topic and subtopic in the surgical, radiation and systemic management of primary breast cancer. The majority of questions could be answered in the form of multiple choice answers, with the chosen answer amenable to formulation as a guideline, called the guideline questions.

It was decided that the best existing evidence on each question would be appraised in the Conference prior to the formulation of guidelines. It was decided to invite national and international experts to deliver focussed talks that will appraise the relevant evidence in the context of the previously decided questions. It was also decided that members of the audience would be invited to opine on the guideline questions through electronic voting prior to each talk. The final development of the guidelines would be done through an expert panel that will electronically vote on each guideline question after all talks had been delivered and audience opinion elicited. Although the majority of the panel time was to be allocated to voting, members of the panel would be allowed to make dissenting or consenting comments. Separate panels were constituted for locoregional and systemic therapy in primary breast cancer. This manuscript deals with the guidelines related to locoregional therapy in primary breast cancer.

## RESULTS

The guideline questions (Appendix I) were developed and

sent to the invited experts many months in advance of the Conference that was held from 22 to 24 October 2010. The experts were repeatedly reminded about the context of developing countries while preparing their presentations. The experts delivered talks that directly appraised the relevant evidence with respect to each question, preceded by audience voting on each of them. The expert panel on locoregional therapy convened and voted on the guideline questions on 22<sup>nd</sup> October 2010 after the completion of expert presentations and audience vote.

### Pathology guidelines

#### *Routine performance of HER2 testing in all breast tumors*

The panel recommended (84% vs. 16%) that all breast tumors in developing countries be subjected to routine HER2 testing by immunohistochemistry (IHC). This was considered important for guiding the choice of systemic HER2-targeted therapy in primary breast cancer, if the latter was feasible. The panel also suggested that there was some prognostic and predictive capability (for anthracycline benefit) of HER2 testing.<sup>[5-7]</sup> In cases with a 2+ score on IHC, the panel advised performance of fluorescent *in situ* hybridization (FISH), if the latter capability is available at the institution/laboratory. The experts suggested that the American Society of Clinical Oncology and College of American Pathologists guidelines be followed in the performance of HER2 testing.<sup>[8]</sup>

#### *Incorporation of multigene assays in clinical decision making*

The expert panel voted (68% vs. 26%) against the routine incorporation of multigene assays like Recurrence Score (RS, Oncotype DX™) in clinical decision making, including prognostication and prediction of chemotherapy benefit. The panel considered the fact that RS had been shown to accurately prognosticate node-negative, hormone receptor-positive patients in retrospective validated analyses and to predict the benefit from chemotherapy in hormone receptor-positive patients, both in node-negative and node-positive situations.<sup>[9-11]</sup> However, the high cost and the current lack of prospective level 1 evidence for such tests weighed in the final decision of the majority of the panel. A minority of the panel members expressed the opinion that the use of such tests should be discussed with selected patients in developing countries based on financial feasibility.

### Radiology guidelines

#### *Local imaging prior to surgery – mammography and ultrasound*

The panel voted (82% vs. 18%) for the routine use of both mammography and breast ultrasound in the evaluation of

cases with early operable breast cancer. The panel agreed that the cornerstones of accurate local staging of breast cancer involved a good physical examination and bilateral mammography. The panel agreed that the addition of diagnostic breast ultrasound to mammography increases the accuracy and diagnostic yield, especially in patients with dense breasts and asymmetric densities in addition to providing image guidance for diagnostic procedures such as biopsies.<sup>[12]</sup>

### ***Routine breast magnetic resonance imaging prior to breast conservation***

The panel recommended against the routine use (89% vs. 11%) of breast magnetic resonance imaging (MRI) prior to breast conservation therapy (BCT). The panel considered the randomized trial evidence that revealed a lack of benefit from routine pre-operative breast MRI and the relatively high rate of false positives with this technique.<sup>[13-16]</sup> The panel, however, also suggested that the use of breast MRI be considered in special situations like evaluation of dense breasts in very young women and in patients with lobular carcinomas.

### ***Positron emission tomography-computed tomography for routine staging in early and locally advanced breast cancer***

The panel recommended against the routine use of PET and positron emission tomography-computed tomography (PET-CT) (88% vs. 12%) for pre-treatment staging assessment of patients with early or locally advanced breast cancer. The panel considered the benefits of metabolic imaging, but the lack of good evidence for improvement in patient outcome measures and the possibility for confusion due to false-positive results weighed in its majority opinion. This recommendation is identical to the recent update in the National Comprehensive Cancer Network guidelines for the use of PET-CT imaging.<sup>[1]</sup>

## **Surgical guidelines**

### ***Routine use of breast conserving therapy in developing countries***

The panel voted in favor of offering breast conserving surgery to all eligible patients (88% vs. 12%) in developing countries. The panel noted that there was overwhelming evidence for the equivalent safety and efficacy of BCT compared with mastectomy in appropriately selected patients.<sup>[17,18]</sup> The panel considered the fact that tumors in these parts of the world are most often not screen detected, larger and there is variable availability of expertise for undertaking breast conservation.<sup>[19]</sup> However, the panel recommended that even in the latter situation, the option of BCT should at least be discussed with the patient, with the possibility of referral to centers that possess requisite expertise.

### ***Importance of potential cosmetic outcome in decision making for BCT***

The panel could not reach a majority verdict on the preference between a potentially cosmetically poor BCT and mastectomy (50% vs. 50%). The panel noted that number of patients and tumor and treatment-related factors are known to influence the cosmetic outcome after BCT,<sup>[20,21]</sup> and the fact that cosmesis could itself potentially affect physical, social, sexual and other domains in a patient's life. Some members discussed the element of subjectivity in evaluation of cosmesis, with patients sometimes rating their cosmesis better than the healthcare providers.

### ***Separate incisions for primary and axillary surgery***

The panel recommended that communication of the axillary dissection with the breast cavity be avoided as far as possible (78% vs. 22%) in order to prevent transfer of seroma fluid between these locations and to improve the cosmetic outcome. This is in agreement with the recommendations of the National Surgical Adjuvant Breast and Bowel Project.<sup>[22]</sup>

### ***Use of oncoplastic procedures***

The panel recommended (83% vs. 17%) that oncoplastic procedures be considered only in specialized centers with multidisciplinary expertise in these techniques. Oncoplastic surgery refers to techniques involving volume displacement and replacement in order to achieve superior cosmetic outcomes.<sup>[23-25]</sup> The panel noted that close cooperation among expert oncosurgeons, plastic surgeons, pathologists and radiation oncologists is required in order to achieve satisfactory cosmetic outcomes. The panel also suggested that surgical decisions like those on the type of incisions (linear versus quadrilateral), flap reconstruction and reduction mammoplasty could be important in achieving optimal results. The panel suggested that advanced centers with expertise could help to train individuals from developing countries in these techniques.

### ***Defining adequacy of margins in primary breast surgery***

The panel voted that the extent of margins after BCT was irrelevant as long as it was technically free (62% vs. 32%). A positive margin has often generated debate and controversy with respect to its significance related to local control rates and disease-free survival.<sup>[26-29]</sup> Guidelines have variously defined an adequate margin in breast conservation from 1 mm to 10 mm or more.<sup>[28-31]</sup> Interestingly, the rate of finding Invasive Ductal Carcinoma in the revised specimens has been in the range of only 30–40%.<sup>[32]</sup> Although there are conflicting reports, it is evident that obtaining a wide negative margin is desirable. However, a focally involved

margin, particularly when re-excision is not technically feasible, as may be the case with a focally involved deep margin at the pectoralis fascia, is not a contraindication to planned therapy.

#### **Management of positive posterior (chest wall) margin after mastectomy**

The panel recommended (52% vs. 36%) that the posterior margin after an otherwise adequate mastectomy be revised wherever possible if it is reported to be grossly positive and if the area to be re-excised can be localized by the surgeon. Because this finding predicts for increased rates of local recurrence, all such patients should receive post-operative radiotherapy.<sup>[33,34]</sup>

#### **Surgery after neoadjuvant chemotherapy**

The panel voted for marking the initial location and extent of tumor (94% vs. 6%) using techniques like biopsy scar, clips, tattoos, etc. in patients being planned for neoadjuvant chemotherapy (NACT). The panel noted that this facilitates ease of subsequent surgery and has a bearing on local control.<sup>[35,36]</sup>

The panel recommended (88% vs. 12%) that BCT is a valid option in selected cases of large or locally advanced breast cancer who achieve excellent response after NACT. The panel noted that this recommendation was not based on randomized level 1 evidence but on the low local recurrence rates in single-arm prospective series<sup>[37]</sup> and the non-randomized use of BCT in trials that evaluated NACT.<sup>[38]</sup> The panel also noted that there is likely to have been careful selection of good prognostic patients for post-NACT BCT in the latter reports and, therefore, similar selection be applied during routine use of this procedure in patients with large and locally advanced breast cancer.

#### **Extent of post-NACT margins**

The panel could not arrive at a majority decision (50% vs. 50%) on whether post-NACT BCT should be based on pre-chemotherapy or post-chemotherapy tumor volume. The panel noted that the administration of NACT often obscures the initial tumor size and makes planning of BCT difficult.<sup>[39,40]</sup> The panel also noted that some institutions have reported successful surgery based on post-chemotherapy tumor volume.<sup>[40]</sup>

#### **Full axillary dissection as a routine standard of care**

The panel recommended (59% vs. 41%) that a full axillary clearance that includes level III lymph nodes be undertaken as a standard procedure in breast cancer surgery in developing countries. The panel noted the relative abundance of large, non-screen-detected cancers and locally advanced breast cancers in these regions, with

a high possibility of axillary nodal involvement being an important factor in this recommendation.<sup>[41]</sup> The panel also noted that there was high-quality evidence that the clearance of involved axillary lymph nodes improves overall survival.<sup>[42]</sup> The panel was cognizant of the reports that extensive axillary procedures could lead to increased incidence of adverse effects like shoulder stiffness and arm edema.<sup>[43,44]</sup>

#### **Sentinel lymph node procedure and axillary sampling in breast cancer patients**

The panel recommended (74% vs. 26%) that the sentinel lymph node technique could be considered in carefully selected patients with early breast cancer and clinically negative axilla in centers that have this expertise. The panel noted that there was now sufficient evidence regarding the oncological safety of this procedure from high-quality trials.<sup>[45,46]</sup> However, the panel recommended that in order to establish the safety of this procedure in developing countries, centers that undertake these procedures should regularly audit their outcome with adequate patient follow-up.

The panel recommended (54% vs. 46%) that anatomically defined sampling of lower-level axillary lymph nodes could be considered an alternative to the sentinel node technique. The boundaries of such a sampling would be intercostobrachial nerve cranially, insertion of latisimus dorsi pedicle into the muscle caudally, chest wall medially and lateral border of latisimus dorsi muscle laterally. Caveats for the sentinel technique, including those of careful patient selection and follow-up, apply to axillary sampling. The panel noted single-institution non-randomized reports of the safety of this procedure in selected patients.<sup>[47,48]</sup>

#### **Depot hydroxyprogesterone prior to surgery for primary breast cancer**

The panel voted against (65% vs. 35%) the adoption of pre-operative injection depot hydroxyprogesterone as a standard of care in patients with operable breast cancer. The panel acknowledged that a recently presented large randomized trial had suggested statistically significant and clinically meaningful improvement in disease-free and overall survival in patients with node-positive operable breast cancer with this intervention.<sup>[49]</sup> It also noted that a number of retrospective analyses had suggested improvements in outcome for surgery performed during the luteal phase of the menstrual cycle, although there had also been reports of no benefit.<sup>[50-52]</sup> The panel felt that the results would need to be published and replicated in other centers before pre-operative progesterone could be recommended as a routine standard of care.

**Radiation therapy guidelines*****Use of radiation in patients with one to three positive axillary nodes after mastectomy***

The panel recommended (50% vs. 33%) that among post-mastectomy patients with one to three positive nodes, patients with additional poor risk features (young age, vessel invasion, inadequate axillary lymph node dissection) should receive radiotherapy. This was based on the subgroup analysis from the Danish study that showed a survival benefit in these (one to three node positive) patients equivalent to those with more than three involved nodes involved and other studies that have tried to analyze specific risk factors in these patients.<sup>[53-56]</sup> The panel acknowledged that there is continuing controversy on the use of radiation in patients with one to three positive nodes.<sup>[55]</sup>

***Benefit of modern radiation techniques in terms of local adverse effects and cosmesis***

The panel voted (88% vs. 12%) in favor of newer radiation techniques (like three-dimensional conformal radiotherapy (3D CRT), intensity modulated radiotherapy (IMRT)) for achievement of better cosmesis and fewer local reactions when feasible and in specific situations.<sup>[57-59]</sup> The panel noted that larger breast sizes and left-sided breast cancer merited more careful planning and specialized radiotherapy techniques. On the question of the best technique for IMRT, the panel voted (60% vs. 40%) for forward planning IMRT as being the most suitable.

***Use of Cobalt (Co) machines for radiation therapy after BCT and mastectomy***

The panel voted (57% vs. 29%) that the Cobalt (Co)<sup>[60]</sup> machine could be used for post-BCT radiation in selected patients, especially in those with small breasts (interfield separation <17 cm).<sup>[61]</sup> The panel considered the fact that cosmesis is an important outcome after BCT, and a number of radiation machine-related factors like beam energy and regional field separation play an important part in achievement of optimal outcomes.<sup>[21]</sup> The panel recognized that some studies have shown better cosmetic outcome for patients treated on linear accelerators compared with cobalt therapy units, especially in those with large breast size.<sup>[20]</sup> The panel also voted (62% vs. 38%) that the Co<sup>[60]</sup> unit was a valid option for radiotherapy after mastectomy when such treatment was indicated.

***Adoption of hypofractionated radiation schedules as standard therapy***

The panel initially voted in favor of hypofractionated radiotherapy (50% vs. 33%) based on recent reports of its equivalent efficacy in comparison with standard schedules in terms of local control and cosmesis.<sup>[62,63]</sup> However, some

panellists expressed concern regarding the lack of long-term safety data (>10 years) with these techniques. After deliberation, the panel qualified its initial vote in favor of hypofractionated schedules, to state that such techniques be used only in centers with advanced simulation and planning systems.

***Use of tumor bed boost after BCT***

The panel recommended (50% vs. 33%) that tumor bed boost be given to all patients after whole breast radiotherapy, based on randomized evidence that its use improves local failure rates.<sup>[64]</sup> Radiotherapy boost after breast conservation can be given by various techniques including external beam conformal photon RT, interstitial implantation and use of electrons. As no technique has been shown to be better than others,<sup>[65]</sup> the panel recommended that any reasonable locally available technique could be used.

On the question of whether higher boost dose could compensate for the deleterious effect of a positive margin, the panel felt that this was not the case (50% vs. 43%).

***Use of axillary nodal radiation after surgery***

The panel voted (79% vs. 14%) for the omission of routine axillary radiation after adequate surgical clearance. This was primarily based on the low rates of axillary failure in such patients and the increased risk of arm edema and shoulder morbidity with the use of both modalities.<sup>[66-71]</sup> Thus, axillary radiation should be reserved for patients who have not undergone adequate axillary dissection.

***Use of internal mammary radiation***

The panel recommended (44% vs. 38%) that internal mammary radiation may be given only to a select group of breast cancer patients with adverse factors like large, inner quadrant tumors with heavy nodal burden that place them at higher risk of internal mammary nodal involvement. The panelists noted that a definitive European Organization for Research and Treatment of Cancer study has addressed this issue in a randomized design, and its results are expected soon. The panel also suggested that other factors such as pulmonary and cardiac comorbidities should be taken into account before delivering internal mammary radiation. Internal mammary lymphatics are relatively uncommon sites for recurrences, and radiation of this field is best omitted in patients with cardiac concerns, consistent with other guidelines.<sup>[71]</sup> The panel also noted a recent trial with 3 years follow-up that reported good tolerance to internal mammary radiation, including cardiac safety, but with higher rates of lung fibrosis and pneumonitis.<sup>[72]</sup>

***Use of accelerated partial breast radiation***

The panel voted (56% vs. 37%) for the use of (accelerated partial breast radiation (APBI) in a highly selected group

**Table 1: Summary of the guidelines for developing countries for locoregional treatment of breast cancer**

| Treatment field/treatment question  | Panel recommendation  |
|---|---|
| Pathology   |   |
| Her2 reporting  | Should be reported in all patients  |
| Multigene assays  | Should not be used routinely and maybe discussed on a case to case basis with the patient   |
| Radiology   |   |
| Use of diagnostic ultrasound and mammography  | Use of both modalities is suggested for accurate staging after a good physical examination  |
| Use of magnetic resonance imaging   | Routine use not recommended. May be considered in young women with dense breasts and in those with lobular cancers  |
| Use of positron emission tomography   | Routine use for pre-treatment staging of breast cancer not recommended  |
| Surgical therapy  |   |
| Use of BCT in developing countries  | Should be offered to all eligible patients. Patients should be referred to centers with adequate expertise  |
| Potential cosmetic outcome and decision for BCT   | The panel was split and could not reach a verdict   |
| Incisions for primary and axilla  | Separate incisions should be used for primary and axilla  |
| Oncoplastic techniques  | Should be used in multidisciplinary centers with adequate expertise. Time should be spent on planning such treatments   |
| Adequate margins for primary  | As long as technically free, the margins may be considered adequate   |
| Positive posterior (chest wall) margins after mastectomy  | Gross residual tumor should be resected when possible   |
| Marking tumors before neoadjuvant chemotherapy  | Location and extent of tumors should be marked with a suitable technique that is locally available  |
| Breast conservation post-NACT in large or locally advanced breast cancers                               | BCT is a reasonable option in selected cases of large or locally advanced breast cancer who achieve excellent response after NACT when post-lumpectomy radiation therapy is available   |
| Extent of resections post NACT  | The panel could not arrive at a majority decision on whether post-NACT BCS should be based on pre-chemotherapy or post-chemotherapy tumor volume  |
| Full axillary dissection as a standard of care  | Full axillary clearance that includes level III lymph nodes be undertaken as a standard procedure in breast cancer surgery in developing countries  |
| Sentinel lymph node procedure   | Sentinel lymph node technique should be considered in selected patients with early breast cancer with clinically negative axilla in centers that have this expertise  |
| Axillary sampling procedures as an alternative form of reduced axillary surgery                         | Anatomically defined sampling of lower level axillary lymph nodes could be considered an alternative to the sentinel node technique. The boundaries of such a sampling would be intercostobrachial nerve cranially, insertion of Lattisimus dorsi pedicle into the muscle caudally, chest wall medially and lateral border of lattisimus dorsi muscle laterally |
| Depot hydroxyprogesterone prior to surgery for primary breast cancer                                    | Pre-operative injection of depot hydroxyprogesterone cannot be adopted as a standard of care in patients with operable breast cancer until confirmation of results in other trials  |
| Radiation therapy   |   |
| Radiation in patients with 1–3 positive axillary nodes after mastectomy                                 | Among post-mastectomy patients with 1–3 positive nodes, only patients with additional poor features (young age, extranodal extension, vessel invasion and inadequate axillary lymph node dissection) should receive radiotherapy  |
| Modern radiation techniques in terms of side-effects and cosmesis                                       | Voted in favor of newer techniques in specific situations   |
| The best technique for IMRT   | Forward planning IMRT is the most suitable technique for performing breast IMRT   |
| Use of Cobalt <sup>60</sup> (Co <sup>60</sup> ) machines for radiation therapy after BCS and mastectomy | Cobalt machines can be used for a select group of patients, especially in those with small breasts with interfield separation <17 cm  |
| Hypofractionated radiation schedules  | Hypofractionated radiotherapy with schedules like those used by the START Trialists Group can be used in centers with an advanced set up  |
| Tumor bed boost after BCS   | Tumor bed boost should be given to all patients after whole breast radiotherapy   |
| Axillary nodal radiation after surgery  | Axillary portals for radiation should be omitted if adequate clearance of axilla had been done  |
| Use of internal mammary radiation   | Internal mammary irradiation should be given only to breast cancer patients with adverse factors (e.g., large, inner quadrant tumors with positive axillary nodes)  |
| Use of accelerated partial breast irradiation (APBI)  | APBI could be used as a standard technique in a highly selected group of patients such as those recommended by ASTRO  |
| Follow-up   |   |
| Need for follow-up after primary treatment  | All breast cancer patients needed to be followed-up regularly with institution-dependent protocols  |
| Use of investigative modalities during follow-up  | In clinically asymptomatic patients, mammogram was the only required investigation during follow-up   |

of patients with low risk features (such as age >65 years, pathological tumor size <2 cm and negative axillary nodes), which is consistent with the recent American Society of Therapeutic Radiation Oncology Guidelines.<sup>[79]</sup> There has been recent interest in using brachytherapy as the sole modality of radiation to decrease the treatment time and toxicities without compromising control.<sup>[73-77]</sup> The American Brachytherapy Society recommends a total dose of 34 Gy in 10 fractions to the clinical tumor volume and high dose rate brachytherapy is used as the sole modality.<sup>[78]</sup> The panel felt that considering present evidence, it is not possible to determine a subgroup of patients otherwise suitable for APBI who would not need any radiotherapy at all.

### Follow-up of patients after primary treatment

#### *Need for follow-up after primary treatment*

The panel voted (67% vs. 33%) for the regular post-treatment follow-up of all patients with primary breast cancer. The panel recognized that there is lack of evidence from randomized trials supporting any particular follow-up sequence or protocol. The panel however felt that regular follow-up would help to ensure continuity of care, including early detection of local recurrences, contralateral breast cancer, management of therapy-related complications and facilitation of psychological support to enhance return to normal life after breast cancer.<sup>[80,81]</sup>

#### *Use of investigative modalities during follow-up*

The panel voted (67% vs. 33%) for annual mammogram as the only routinely required investigation during follow-up in patients who are asymptomatic and have a normal physical examination. This was based on evidence from two randomized trials that failed to prove any benefit from more extensive investigations during follow-up care.<sup>[82,83]</sup> The panel also suggested that the follow-up protocol could be institution based, and stressed the importance of good history taking and physical examination. Some panelists commented that the use of other investigations like imaging is occasionally useful in detecting early relapse in some patients.

## SUMMARY AND CONCLUSIONS

The development of evidence-based and effective breast cancer treatment techniques and guidelines is of great importance in developing countries. This is especially important for optimizing the efficacy of available therapies and early referral of selected patients to expert centers. The recommendations of the WCI-TMH Expert Panel have been summarized here. These recommendations have been designed to allow centers in the developing world to improve the quality of care for breast cancer patients. It needs to be noted that even though the guidelines are meant for developing countries, the bulk of evidence

utilized for formulating these guidelines is generated from studies done in developed countries. Adoption of these guidelines and consistent collection of patient, disease, treatment and outcome data in developing countries would allow evaluation of the public health impact of guideline adherence in these regions [Table 1].

## ACKNOWLEDGMENTS

Members of the Panel are listed at the end of manuscript. All members were present at the voting panel during the conference. The manuscript draft was sent to all the panellists for their approval. Dr. P K Julka was not present during the panel voting but gave his approval to the content of the manuscript. The authors of this manuscript want to thank the delegates of the 8<sup>th</sup> Tata Memorial Hospital - Women's Cancer Initiative (TMH-WCI) Conference for their contribution and useful comments.

### Locoregional therapy consensus panel

- R A Badwe, Director, Tata Memorial Center, Department of Surgical Oncology, Tata Memorial Hospital
- Benjamin Anderson: Professor and Director, Breast Health Clinic University of Washington/Seattle Cancer Care Alliance. Chair and Director Breast Health Global Initiative
- Anurag Srivastava, Department of Surgical Oncology, Tata Memorial Hospital, Mumbai, India
- Mandar Nadkarni: Head Breast Surgery at Kokilaben Dhirubhai Ambani Hospital and Medical Research Centre, Mumbai
- Hemant Raj: Head, Department of Surgery, Apollo Hospital, Chennai, India
- John Yarnold: Professor of Clinical Oncology, Institute of Cancer Research and The Royal Marsden Hospital, Surrey UK. (Representative of ESTRO at the conference)
- P K Julka, Professor, Department of Radiation Oncology, All India Institute of Medical Sciences, New Delhi, India
- Stephen Johnston, Professor, Department of Medical Oncology, Royal Marsden Hospital, Sutton, UK
- Sanjiv Sharma, Department of Radiation Oncology, Bangalore Institute of Oncology, Bangalore, India
- Charlotte Coles, Department of Clinical Oncology, Royal Marsden Hospital, Sutton, UK
- Sangeeta Desai, Professor, Department of Pathology, Tata Memorial Hospital, Mumbai, India
- Vivek Kaushal, Professor, Department of Radiation Oncology, Medical College, Rohtak, India
- Puneeta Lal, Professor, Department of Radiation Oncology, SGPGI, Lucknow, India

- G V Giri, Department of Radiation Oncology, Kidwai Institute, Bangalore, India
- Seigo Nakamura, Professor, Department of Breast Surgical Oncology, Showa University, Japan
- Indraneel Mitra, Professor Emeritus, Department of Surgical Oncology, Tata Memorial Hospital, Mumbai, India
- S C Sharma, Professor, Department of Radiation Oncology, PGIMER, Chandigarh, India
- Seema Medhi, Assistant Professor, Department of Radiology, Tata Memorial Hospital, Mumbai, India
- Rakesh Jalali, Associate Professor, Department of Radiation Oncology, Tata Memorial Hospital, Mumbai, India
- Nuran Bese, Professor in Radiation Oncology, Istanbul University, Cerrahpasa Medical School, Fatih Istanbul, Turkey

## APPENDIX: GUIDELINE QUESTIONS

1. Should Her2 be considered a standard in all histopathology reports?
2. Is extent of margin for infiltrating ductal carcinoma irrelevant as long as the margin is technically free?
3. Should gene profiling be pursued as a prognostic and predictive option?
4. What imaging should patients of primary breast cancer ideally undergo?
5. Should MRI be routinely done before surgery in patients undergoing breast conservation?
6. Is PET CT a standard during work up for large and locally advanced breast cancer?
7. Should BCT be offered as a standard to all eligible patients?
8. Is a cosmetically poor BCT a preferable alternative to a mastectomy?
9. Oncoplastic techniques in developing countries: 1) Should be used in all oncology centers, 2) Should be used only with good pathology, plastic and related services, 3) Do not know.
10. Is level III clearance a must in routine practice of large and locally advanced cancers?
11. Should communication with the breast cavity be avoided as far as possible during axillary dissection?
12. Is sentinel lymph node biopsy a standard of care in a select group of breast cancer patients?
13. Can axillary sampling be considered a preferred alternative to sentinel lymph node biopsy?
14. Is there a role of sentinel lymph node biopsy after neoadjuvant chemotherapy?
15. Should we mark the initial tumor/tumor size in some way before giving neoadjuvant chemotherapy?
16. Should the margin of resection in BCT after NACT be based on the initial lump size/clinical local findings?
17. Should the margin of resection in BCT after NACT be based on the initial lump size?
18. Is breast conservation a valid option for selected large and locally advanced breast cancer after neoadjuvant chemotherapy?
19. Should margin-positive bases be reexcised after otherwise adequate mastectomy?
20. Can solitary focal IDC margin positivity after breast conservation be safely ignored?
21. Does surgery in a particular phase of ovulatory cycle affect outcome in breast cancer?
22. Should administration of Proluton (hydroxyprogesterone) before surgery be considered a standard of care?
23. Is cobalt machine an option in select group of patients post BCT?
24. Can hypofractionated external beam radiotherapy be adopted as a standard of care at present?
25. Which should be the preferred technique of doing whole breast IMRT?
26. Should boost be given to all breast cancer patients who undergo conservation?
27. Can a higher radiotherapy boost dose abrogate the effect of a positive margin?
28. Is APBI a standard technique for a select group of patients?
29. Would some patients suitable for APBI not need any radiotherapy at all?
30. Regarding post-mastectomy, patients with 1–3 positive axillary nodes: 1) All should receive RT, 2) None should receive RT, 3) Only patients with additional poor features should receive RT, 4) Do not know.
31. Is a cobalt machine as good as a linear accelerator for chest wall radiotherapy?
32. Should axillary radiation be done after adequate axillary dissection in patients otherwise requiring post-operative radiotherapy?
33. Should internal mammary radiation be given to breast cancer patients who are otherwise eligible for LRRT?
34. Have modern radiotherapy machines improved local reactions and cosmetic outcome after breast conservation?
35. Do we need to do any other investigation (besides a mammogram) in follow-up when patients are clinically asymptomatic?
36. Do we need to regularly follow-up breast cancer cases?

## REFERENCES

1. Carlson RW, Allred DC, Anderson BO, Burstein HJ, Carter WB, Edge SB, *et al.* Breast cancer. Clinical practice guidelines in oncology. J Natl Compr Canc Netw. 2009;7:122-92.



2. Aebi S, Davidson T, Gruber G, Castiglione M. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. *Ann Oncol* 2010;21(Supplement 5): V9-14.
3. Goldhirsch A, Ingle JN, Gelber RD, Coates AS, Thürlimann B, Senn HJ. Thresholds for therapies: Highlights of the St Gallen International Expert Consensus on the Primary Therapy of Early Breast Cancer 2009. *Ann Oncol* 2009;20:1319-29.
4. Harnett A, Smallwood J, Titshall V, Champion A. Diagnosis and treatment of early breast cancer, including locally advanced disease--summary of NICE guidance. *BMJ* 2009;338:b438.
5. Slamon DJ, Clark GM, Wong SG, Levin WJ, Ullrich A, McGuire WL. Human breast cancer: Correlation of relapse and survival with amplification of the HER2/neu oncogene. *Science* 1987;235:177-82.
6. Paik S, Bryant J, Tan-Chiu E, Yothers G, Park C, Wickerham DL, *et al.* HER2 and choice of adjuvant chemotherapy for invasive breast cancer: National Surgical Adjuvant Breast and Bowel Project Protocol B-15. *J Natl Cancer Inst* 2000;92:1991-8.
7. Pritchard KI, Shepherd LE, O'Malley FP, Andrulis IL, Tu D, Bramwell VH, *et al.* HER2 and responsiveness of breast cancer to adjuvant chemotherapy. *N Engl J Med* 2006;354:2103-11.
8. Wolff AC, Hammond ME, Schwartz JN, Hagerty KL, Allred DC, Cote RJ, *et al.* American Society of Clinical Oncology/College of American Pathologists guideline recommendations for human epidermal growth factor receptor 2 testing in breast cancer. *J Clin Oncol* 2007;25:118-45.
9. Paik S, Shak S, Tang G, Kim C, Baker J, Cronin M, *et al.* A multigene assay to predict recurrence of tamoxifen-treated, node-negative breast cancer. *N Engl J Med* 2004;351: 2817-26.
10. Paik S, Tang G, Shak S, Kim C, Baker J, Kim W, *et al.* Gene expression and benefit of chemotherapy in women with node-negative, estrogen receptor-positive breast cancer. *J Clin Oncol* 2006;24:3726-34.
11. Albain KS, Barlow WE, Shak S, Hortobagyi GN, Livingston RB, Yeh IT, *et al.* Prognostic and predictive value of the 21-gene recurrence score assay in postmenopausal women with node-positive, oestrogen-receptor-positive breast cancer on chemotherapy: A retrospective analysis of a randomised trial. *Lancet Oncol* 2010;11:55-65.
12. Harris JR, Lippman ME, Morrow M, Osborne CK. Diseases of the breast. Philadelphia: Lippincott Williams and Wilkins; 2004.
13. Turnbull L, Brown S, Harvey I, Olivier C, Drew P, Napp V, *et al.* Comparative effectiveness of MRI in breast cancer (COMICE) trial: A randomised controlled trial. *Lancet* 2010;13:375: 563-71.
14. Gundry KR. The application of breast MRI in staging and screening of breast cancer. *Oncology* 2005;19:159-69.
15. Esserman L. Integration of imaging in breast cancer. *J Clin Oncol* 2005;23:1601-2.
16. Houssami N, Ciatto S, Macaskill P, Lord SJ, Warren RM, Dixon JM, *et al.* Accuracy and surgical impact of magnetic resonance imaging in breast cancer staging: Systematic review and meta-analysis in detection of multifocal and multicentric cancer. *J Clin Oncol* 2008;26:3248-58.
17. Fisher B, Anderson S, Bryant J, Margolese RG, Deutsch M, Fisher ER, *et al.* Twenty-year follow-up of a randomized trial comparing total mastectomy, lumpectomy, and lumpectomy plus radiation for the treatment of invasive breast cancer. *N Engl J Med* 2002;347:1233-41.
18. Veronesi U, Zucali R, Luini A. Local control and survival in early breast cancer: The Milan trial. *Int J Radiat Oncol Biol Phys* 1986;12:717-20.
19. Leong SP, Shen ZZ, Liu TJ, Agarwal G, Tajima T, Paik NS, *et al.* Is breast cancer the same disease in Asian and Western Countries? *World J Surg* 2010;34:2308-24.
20. Sarin R, Dinshaw KA, Shrivastava SK, Sharma V, Deore SM. Therapeutic factors influencing the cosmetic outcome and late complications in the conservative management of early breast cancer. *Int J Radiat Oncol Biol Phys* 1993;27: 285-92.
21. Munshi A, Kakkar S, Bhutani R, Jalali R, Budrukkar A, Dinshaw KA. Factors influencing cosmetic outcome in breast conservation. *Clin Oncol* 2009;21:285-93.
22. Taylor ME, Perez CA, Halverson KJ, Kuske RR, Philpott GW, Garcia DM, *et al.* Factors influencing cosmetic results after conservation therapy for breast cancer. *Int J Radiat Oncol Biol Phys* 1995;31:753-64.
23. Nicholson RM, Leinster S, Sassoon EM. A comparison of the cosmetic and psychological outcome of breast reconstruction, breast conserving surgery and mastectomy without reconstruction. *Breast* 2007;16:396-410.
24. Fischbacher C. Immediate versus delayed breast reconstruction. *STEER*. 2002;2:4-18.
25. Drucker-Zertuche M, Robles-Vidal C. A 7 year experience with immediate breast reconstruction after skin sparing mastectomy for cancer. *Eur J Surg Oncol* 2007;33:140-6.
26. Heimann R, Powers C, Halpem HJ, Michel AG, Ewing CA, Wyman B, *et al.* Breast preservation in stage I and II carcinoma of the breast. The University of Chicago experience. *Cancer* 1996;78:1722-30.
27. Peterson ME, Schultz DJ, Reynolds C, Solin LJ. Outcomes in breast cancer patients relative to margin status after treatment with breast-conserving surgery and radiation therapy: The University of Pennsylvania experience. *Int J Radiat Oncol Biol Phys* 1999;43:1029-35.
28. Obedian E, Haffty BG. Negative margin status improves local control in conservatively managed breast cancer patients. *Cancer J Sci Am* 2000;6:28-33
29. Vicini FA, Goldstein NS, Pass H, Kestin LL. Use of pathologic factors to assist in establishing adequacy of excision before radiotherapy in patients treated with breast-conserving therapy. *Int J Radiat Oncol Biol Phys* 2004;60:86-94.
30. Arriagada R, Lê MG, Rochard F, Contesso G. Conservative treatment versus mastectomy in early breast cancer: Patterns of failure with 15 years of follow-up data. Institut Gustave-Roussy Breast Cancer Group. *J Clin Oncol*. 1996;14: 1558-64.
31. Fisher ER, Anderson S, Redmond C, Fisher B. Pathologic findings from the National Surgical Adjuvant Breast Project protocol B-06. 10-year pathologic and clinical prognostic discriminants. *Cancer*. 1993;71:2507-14.
32. Skripinova S, Layfield LJ. Initial margin status for invasive ductal carcinoma of the breast and subsequent identification of carcinoma in reexcision specimens. *Arch Pathol Lab Med* 2010;134:109-14
33. Freedman GM, Fowble BL, Hanlon AL, Myint MA, Hoffman JP, Sigurdson ER, *et al.* A close or positive margin after mastectomy is not an indication for chest wall radiation except in women aged fifty or younger. *Int J Radiat Oncol Biol Phys* 1998;41:599-605.
34. Katz A, Strom EA, Buchholz TA, Thames HD, Smith CD, Jhingran A, *et al.* Loco-regional recurrence patterns following mastectomy and doxorubicin-based chemotherapy: Implications for postoperative radiation. *J Clin Oncol* 2000;18:2817-27.
35. Oh JL, Nguyen G, Whitman GJ, Hunt KK, Yu TK, Woodward WA, *et al.* Placement of radiopaque clips for tumor localization in patients undergoing neoadjuvant chemotherapy and breast conservation therapy. *Cancer* 2007;110:2420-7.
36. Lannin DR, Grube B, Black DS, Ponn T. Breast tattoos for planning surgery following neoadjuvant chemotherapy. *Am J Surg* 2007;194:518-20.
37. Parmar V, Krishnamurthy A, Hawaldar R, Nadkarni MS, Sarin R, Chinoy R, *et al.* Breast conservation treatment in women with locally advanced breast cancer - Experience from a single centre. *Int J Surg* 2006;4:106-14.

38. Fisher ER, Wang J, Bryant J, Fisher B, Mamounas E, Wolmark N. Pathobiology of preoperative chemotherapy: Findings from the National Surgical Adjuvant Breast and Bowel (NSABP) protocol B-18. *Cancer* 2002;95:681-95.
39. Buchholz TA, Hunt KK, Whitman GJ, Sahin AA, Hortobagyi GN. Neoadjuvant chemotherapy for breast carcinoma: Multidisciplinary considerations of benefits and risks. *Cancer* 2003;98:1150-60.
40. Chen AM, Meric-Bernstam F, Hunt KK, Thames HD, Oswald MJ, Outlaw ED, *et al.* Breast-conserving therapy after neoadjuvant chemotherapy: The M.D. Anderson Cancer Center experience. *J Clin Oncol* 2004;22:2303-12.
41. Greco M, Crippa P, Agresti R, Seregini E, Gerali A, Giovanazzi R, *et al.* Axillary lymph node staging in breast cancer by 2-fluoro-2-deoxy-D-glucose-positron emission tomography: clinical evaluation and alternative management. *J Natl Cancer Inst* 2001;93:630-5.
42. Orr RK. The impact of prophylactic axillary node dissection on breast cancer survival--A Bayesian meta-analysis. *Ann Surg Oncol* 1999;6:109-16.
43. Vinh-Hung V, Verschraegen C. Breast-conserving surgery with or without radiotherapy: Pooled-analysis for risks of ipsilateral breast tumor recurrence and mortality. *J Natl Cancer Inst* 2004;96:115-21.
44. Clarke D, Martinez A, Cox RS, Goffinet DR. Breast edema following staging axillary node dissection in patients with breast carcinoma treated by radical radiotherapy. *Cancer* 1982;49:2295-9.
45. Krag DN, Anderson SJ, Julian TB, Brown A, Harlow SP, Costantino JP, *et al.* Primary outcome results of NSABP B-32, a randomized phase III clinical trial to compare sentinel node resection (SNR) to conventional axillary dissection (AD) in clinically node-negative breast cancer patients. *J Clin Oncol* 2010;28:18s,(suppl; abstr LBA505).
46. Mansel RE, Fallowfield L, Kissin M, Goyal A, Newcombe RG, Dixon JM, *et al.* Randomized multicenter trial of sentinel node biopsy versus standard axillary treatment in operable breast cancer: The ALMANAC Trial. *J Natl Cancer Inst* 2006;98:599-09.
47. Forrest AP, Everington D, McDonald CC, Steele RJ, Chetty U, Stewart HJ. The Edinburgh randomized trial of axillary sampling or clearance after mastectomy. *Br J Surg* 1995;82:1504-8.
48. Parmar V, Hawaldar R, Nadkarni MS, Badwe RA. Low axillary sampling in clinically node-negative operable breast cancer. *Natl Med J India* 2009;22:234-6.
49. Badwe R, Hawaldar R, Parmar V, Nadkarni M, Shet T, Desai S, *et al.* Single-injection depot progesterone before surgery and survival in women with operable breast cancer: A randomized controlled trial. *J Clin Oncol* 2011;29:2845-51.
50. Senie RT, Rosen PP, Rhodes P, Lesser ML. Timing of breast cancer excision during the menstrual cycle influences duration of disease-free survival. *Ann Intern Med.* 1991;115:337-42.
51. Veronesi U, Luini A, Mariani L, Del Vecchio M, Alvez D, Andreoli C, *et al.* Effect of menstrual phase on surgical treatment of breast cancer. *Lancet* 1994;343:1545-7.
52. Grant CS, Ingle JN, Suman VJ, Dumesic DA, Wickerham DL, Gelber RD, *et al.* Menstrual cycle and surgical treatment of breast cancer: Findings from the NCCTG N9431 study. *J Clin Oncol.* 2009;27:3620-66.
53. Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, *et al.* Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy: Danish Breast Cancer Cooperative Group 82b Trial. *N Engl J Med* 1997;337:949-55.
54. Ragaz J, Olivetto IA, Spinelli JJ, Phillips N, Jackson SM, Wilson KS, *et al.* Locoregional radiation therapy in patients with high-risk breast cancer receiving adjuvant chemotherapy: 20-year results of the British Columbia randomized trial. *J Natl Cancer Inst* 2005;97:116-26.
55. Truong PT, Olivetto IA, Kader HA, Panades M, Speers CH, Berthelet E. Selecting breast cancer patients with T1-T2 tumors and one to three positive axillary nodes at high post mastectomy locoregional recurrence risk for adjuvant radiotherapy. *Int. J Radiat Oncol Biol Phys* 2005;61:1337-47.
56. Overgaard M, Nielsen HM, Overgaard J. Is the benefit of postmastectomy radiation limited to patients with four or more positive nodes, as recommended in international consensus reports? A subgroup analysis of the DBCG 82 bandc randomized trials. *Radiother Oncol* 2007;82:247-53.
57. Pignol JP, Olivetto I, Rakovitch E, Gardner S, Sixel K, Beckham W, *et al.* A multicenter randomized trial of breast intensity-modulated radiation therapy to reduce acute radiation dermatitis. *J Clin Oncol.* 2008;26:2085-92.
58. Donovan E, Bleakley N, Denholm E, Evans P, Gothard L, Hanson J, *et al.* Randomised trial of standard 2D radiotherapy (RT) versus intensity modulated radiotherapy (IMRT) in patients prescribed breast radiotherapy. *Breast Technology Group. Radiother Oncol* 2007;82:254-64.
59. Harsolia A, Kestin L, Grills I, Wallace M, Jolly S, Jones C, *et al.* Intensity-modulated radiotherapy results in significant decrease in clinical toxicities compared with conventional wedge-based breast radiotherapy. *Int J Radiat Oncol Biol Phys* 2007;68:1375-80.
60. Clarke M, Collins R, Darby S, Davies C, Elphinstone P, Evans E, *et al.* Effects of radiotherapy and of differences in the extent of surgery for early breast cancer on local recurrence and 15-year survival: An overview of the randomised trials. *Lancet* 2005;366:2087-106.
61. Munshi A, Pai RH, Phurailatpam R, Budrukkar A, Jalali R, Sarin R, *et al.* Do all patients of breast carcinoma need 3-dimensional CT-based planning? A dosimetric study comparing different breast sizes. *Med Dosim.* 2009;34:140-4.
62. START Trialists' Group, Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, *et al.* The UK Standardisation of Breast Radiotherapy (START) Trial A of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. *Lancet Oncol* 2008;9:331-41.
63. START Trialists' Group, Bentzen SM, Agrawal RK, Aird EG, Barrett JM, Barrett-Lee PJ, *et al.* The UK Standardisation of Breast Radiotherapy (START) Trial B of radiotherapy hypofractionation for treatment of early breast cancer: A randomised trial. *Lancet* 2008;371:1098-107.
64. Bartelink H, Horiot JC, Poortmans P, Struikmans H, Van den Bogaert W, Barillot I, *et al.* Recurrence rates after treatment of breast cancer with standard radiotherapy with or without additional radiation. *N Engl J Med* 2001;345:1378-87.
65. Poortmans P, Bartelink H, Horiot JC, Struikmans H, Van den Bogaert W, Fourquet A, *et al.* The influence of the boost technique on local control in breast conserving treatment in the EORTC 'boost versus no boost' randomised trial. *Radiother Oncol* 2004;72:25-33.
66. Overgaard M, Hansen PS, Overgaard J, Rose C, Andersson M, Bach F, *et al.* Postoperative radiotherapy in high-risk premenopausal women with breast cancer who receive adjuvant chemotherapy: Danish Breast Cancer Cooperative Group 82b Trial. *N Engl J Med* 1997;337:949-55.
67. Ragaz J, Jackson SM, Le N, Plenderleith IH, Spinelli JJ, Basco VE, *et al.* Adjuvant radiotherapy and chemotherapy in node-positive premenopausal women with breast cancer. *N Engl J Med* 1997;337:956-62.
68. Mehta K, Haffty BG. Long-term outcome in patients with four or more positive lymph nodes treated with conservative surgery and radiation therapy. *Int J Radiat Oncol Biol Phys* 1996;35:679-85.
69. Taghian A, Jeong JH, Manounas E, Anderson S, Bryant J, Deutsch M, *et al.* Patterns of locoregional failure in patients with operable breast cancer treated by mastectomy and adjuvant chemotherapy with or without tamoxifen and

- without radiotherapy: Results from 5 National Surgical Adjuvant Breast and Bowel Project randomized clinical trials. *J Clin Oncol* 2004;22:4247-54.
70. Chang DT, Feigenberg SJ, Indelicato DJ, Morris CG, Lightsey J, Grobmyer SR, *et al.* Long-term outcomes in breast cancer patients with ten or more positive axillary nodes treated with combined-modality therapy: The importance of radiation field selection. *Int J Radiat Oncol Biol Phys* 2007;67:1043-51.
  71. Beese SN, Munshi A, Buddrukar A, Elzawawy A, Perez CA. Breast radiation therapy guideline implementation in low and middle income countries. *Cancer(suppl)* 2008;113:2305-14.
  72. Matzinger O, Heimsoth I, Poortmans P, Collette L, Struikmans H, Van Den Bogaert W, *et al.* Toxicity at three years with and without radiation of the internal mammary and medial supraclavicular lymph node chain in stage I to III breast cancer (EORTC trial 22922/10925). *Acta Oncol* 2010;49:24-34.
  73. Orecchia R, Ciocca M, Lazzari R, Garibaldi C, Leonardi MC, Luini A, *et al.* Intraoperative radiation therapy with electrons (ELIOT) in early-stage breast cancer. *Breast* 2003;12:483-90
  74. Vaidya JS, Baum M, Tobias JS, Houghton J. *Lancet*. Targeted intraoperative radiotherapy;1999. Available from: <http://www.thelancet.com/journals/lancet/misc/protocol/99PRT-47>. [Last accessed on 2011 Apr 10].
  75. Wolmark N, Curran WJ. On behalf of NSABP and RTOG of the American College of Radiology (ACR). NSABP Protocol B-39. RTOG Protocol 0413. A randomized phase III study of conventional whole breast radiation versus partial breast radiation for women with stage 0, I, or II breast cancer. National surgical adjuvant breast and bowel project (NSABP). Trial protocol 2007. p. 1-132.
  76. OCOG. Ontario Clinical Oncology Group (OCOG), Canadian Institutes of Health Research (CIHR), Canadian Breast Cancer Research Alliance. RAPID: Randomized Trial of Accelerated Partial Breast Radiation; 2008.
  77. Yarnold J, Coles C. On behalf of the IMPORT LOW Trial Management Group: Intensity Modulated and Partial Organ Radiotherapy. Randomised trial testing intensity modulated and partial organ radiotherapy following breast conservation surgery for early breast cancer. Trial Protocol, version 4. Sutton, Surrey, UK: The Institute of Cancer Research, Royal Cancer Hospital; 2008. p. 1-74.
  78. Nag S, Kuske RR, Vicini FA, Arthur DW, Zwicker RD. The American Brachytherapy Society recommendations for brachytherapy for carcinoma of the breast. *Oncology* 2001;15:195-207.
  79. Smith BD, Arthur DW, Buchholz TA, Haffty BG, Hahn CA, Hardenbergh PH, *et al.* Accelerated Partial Breast Radiation consensus statement from The American Society For Radiation Oncology (ASTRO). *Int J Radiation Oncology Biol Phys* 2009;74:987-1001.
  80. Aebi S, Davidson T, Gruber G, Castiglione M. Primary breast cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. ESMO Guidelines Working Group. *Ann Oncol* 2010;21 Suppl 5:v9-14.
  81. Grunfeld E, Hodgson DC, Del Giudice ME, Moineddin R. Population-based longitudinal study of follow-up care for breast cancer survivors. *J Oncol Pract* 2010;6:174-81.
  82. Grunfeld E, Mant D, Yudkin P, Adewuyi-Dalton R, Cole D, Stewart J, *et al.* Routine follow up of breast cancer in primary care: Randomised trial. *BMJ* 1996;313:665-9.
  83. Palli D, Russo A, Saieva C, Ciatto S, Rosselli Del Turco M, Distante V, *et al.* Intensive vs clinical follow-up after treatment of primary breast cancer: 10-year update of a randomized trial. National Research Council Project on Breast Cancer Follow-up. *JAMA* 1999;281:1586

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