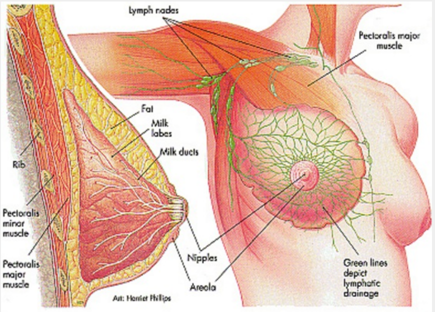
Breast Anatomy



Anatomy

Most of the breast tissue extends from the edge of the sternum to the anterior axillary line and from the second or third to the sixth or seventh costal edge. It overlies the second to the sixth ribs and pectoralis major muscle.

Production and secretion of milkare the primary functions of the mammary glands.

The human breast consists of approximately 20 separate glands or lobes, each with its own duct opening separately onto the surface of the nipple.

The **medial limit** is the sternum.

The **lateral limit** is the anterior axillary line.

Mammary tissue also overlies the pectoralis major muscle on the anterior chest wall and is attached to it by a layer of connective tissue.

Lymph drains into the axillary, supraclavicular, internal mammary and abdominal lymph nodes.

More than 75% of lymph from the breast drains to the axillary nodes, of which there are 5 sets.

Much of the remainder drains from the medial portion of the breast to the internal mammary nodes which lie para-sternally.

Anatomy (cont)

The breast is very rich in vasculature (potential for haematogenous spread). The arterial supply is via the thoracic branches of the axillary, intercostal and internal mammary arteries. Veins form an anastamosic circle around the nipple known as the Circulous Venosus. From here, branches drain blood to the circumference of the breast and empty into the axillary and internal mammary veins.

Predisposing factors

Genetic factors - a family history of breast cancer, especially in a mother or sister; carrying a mutation in either of the two recognized breast cancer genes BRCA1 or BRCA2

Hormones –prolonged oestrogen exposure in early menarche, late menopause, nulliparity (never having borne a child), delayed pregnancy (having first child after age 35) or the use of HRT

Previous cancer in one breast

Exposure to ionising radiation

Diet and weight

Viruses

Histology and Pathology

The majority of breast carcinomas are adenocarcinomas and are generally classified on morphology as either ductal or lobular

Most cancers in the breast originate in the ducts.

Either **in situ** (non-invasive) or **infiltrating** (invasive)

Invasive ductal carcinoma with no special features is the most common type of breast cancer comprising more than 80% of all cases

Invasive tumours are further classified according to their microscopic appearance and histological grade such as **Medullary, Tubular, Mucinous and Papillary.**

Histology and Pathology (cont)

Inflammatory breast cancer is a rare form of invasive carcinoma with poor prognosis.

Pagets disease of the nipple is a variation of ductal carcinoma in situ commonly associated with an underlying invasive ductal carcinoma.

(40%) originate in the upper outer quadrant of the breast, 30% occur in the central part of the breast, 15% in the upper inner quadrant, 10% in the lower outer quadrant and 5% in the lower inner quadrant.

Simultaneous bilateral breast cancer is rare.

Diagnosis

Regular mammography is an integral part of early detection of breast cancer.

Younger women have denser breast tissue, making it radio-graphically more difficult to detect malignant change.

Breast screening is aimed at women in the age groups of 40 – 69.

Women with a genetic/family history of breast cancer may undergo screening early.

After a suspect lump is located and mammograms confirm that the lump may be malignant, a pathological diagnosis is required.

A **biopsy or Fine Needle Aspirate (FNA)** will be performed to obtain a histological diagnosis.

Staging

Often follows the **TNM staging system**.

There is much debate in the area of surgical staging on whether **sentinel lymph node biopsy** or **axillary lymph node dissection** is the desired procedure to determine the extent of metastasis to the axillary lymph nodes

Staging (cont)

If a diagnosis of breast cancer was invasive, an **axillary lymph node dissection** would determine if the cancer has spread to the lymph nodes underneath the arm. The surgeon makes an incision underneath the arm, and removes the bulk of the lymph node tissue that drains from the breast.

10 to 15 lymph nodes are removed with this operation. The remaining tissues underneath the arm tend to “leak” some lymph fluid when the lymph nodes are removed; a post operative drain is left in place for 2-3 weeks. Approximately 5-10% of the patients who undergo an axillary lymph node dissection experience chronic problems related to the dissection such as arm swelling (**lymphoedema**), or pain or discomfort in the area of the dissection. Almost all women will have some residual numbness under the inside of the arm.

Sentinel lymph node biopsy was developed as an alternative to the dissection.

The lymph ducts of the breast usually drain to one lymph node first, before draining through the rest of the lymph nodes underneath the arm.

That first lymph node is called the **sentinel lymph node**. That is the lymph node that helps sound the warning that the cancer has metastasised. Lymph node mapping helps identify that lymph node, and a **sentinel lymph node biopsy** removes only that lymph node.

The sentinel lymph node is identified in one of two ways, either by a weak radioactive dye (technetium-labeled sulfur colloid) that can be measured by a hand held probe, or by a blue dye (isosulfan blue) that stains the lymph tissue a bright blue so it can be seen. Most breast cancer surgeons use a combination of both.

Management of Breast Cancer

Can involve a combination of surgery, chemotherapy, hormone therapy and radiation therapy.

The majority of the breast cancer patients that seen in Radiation Therapy centres will be treated post operatively.

Breast cancer management decisions are based around key patient characteristics:

-Age
-Tumour classification
-Tumour grade
-Tumour size
-Oestrogen receptor (ER) status: positive or negative
-Pre or post menopausal

All treatment modalities endeavour to improve conservation of the breast, minimize side effects and enhance the cosmetic outcome for the patient

Surgical Management

The aim is **to eradicate the primary tumour and any local extension in the hope of achieving total disease control**

Two options: **conservative surgery**: wide local excision, and **total mastectomy**: complete excision of the breast parenchyma with preservation of the underlying pectoral muscles

Completeness of excision minimises the risk of local recurrence.

The size of the tumour must be taken into consideration when deciding between lumpectomy and mastectomy.

Breast conserving surgery with post operative radiation is accepted as being equivalent to mastectomy in terms of reducing local recurrence for node negative disease.

There is no absolute limit to the size of a tumour which can be locally excised without incurring a high risk of recurrence; 3–4cm is often regarded as a practical limit.

Surgical Management (cont)

Mastectomy is also preferred when there may be extensive intra ductal carcinoma or DCIS which is of high grade and cannot be excised with clear margins and also in patients where there are widespread breast calcification that may make mammogram follow up difficult.

Relativity of tumour size to breast size and the achievement of an acceptable cosmetic result are equally important considerations.

Axilla staging – Axillary lymph node status is the most powerful single variable in the estimation of prognosis

Axilla staging – Axillary lymph node status is the most powerful single variable in the estimation of prognosis. Axillary lymph node involvement is related to worse overall survival.Axillary clearance provides information about nodal status for both prognosis and the planning of adjuvant treatment. Axillary clearance is a standard procedure accompanying mastectomy.

The aims of axillary clearance: Eradication of metastatic disease within the axillary nodes, Assessment of nodal status for evaluation of prognosis, Assessment of nodal status to determine adjuvant therapy

Hormone Therapy

The goal is to **block the action of oestrogen on the tumour cells** either by inhibiting oestrogen from binding to the specific oestrogen receptor or by inhibiting its synthesis.

Tamoxifen is the most widely used hormone-related drug to treat breast cancer both in the adjuvant and metastatic settings.

Tamoxifen blocks the uptake of oestrogen and thus inhibits cell growth.

Hormone Therapy (cont)

Tamoxifen is more effective in both pre and post menopausal women who have tumours classified as oestrogen –receptor positive. Women with oestrogen receptor (ER)–rich tumours have 3 – 10 times the benefits of ER-poor patients.

Optimal treatment duration is still undecided but current evidence suggests probably 5 years

Tamoxifen has relatively few significant side effects in most patients. There may be mild nausea or weight gain and younger women may have annoying menopausal symptoms such as hot flushes and vaginal dryness.

Randomised clinical trials are ongoing to investigate the role of aromatase inhibitors as an alternate hormonal therapy that either replaces or are used in sequence with Tamoxifen.

Immunotherapy

The goal is to **help the body produce antibodies** to attack breast cancer cells.

Only **monoclonal antibodies (MAbs)** have been approved for use against breast cancer so far. But many other forms of treatment are being studied.

25% of breast cancer patients have tumours that are **HER2+ (Human Epidermal growth factor Receptor 2 positive)**. HER2+ tumours tend to grow and spread more quickly.

Women with HER2+ breast cancer:
-May be less likely to respond to certain breast cancer treatments
-May be more likely to have a recurrence

The MAb trastuzumab (**Herceptin**) is used in women with breast cancer whose cancer cells have too many copies of the HER2/neu gene

Immunotherapy (cont)

These genes make extra receptors for growth-stimulating factors on the cells, which results in a more aggressive form of breast cancer. Trastuzumab attaches to the receptors, blocking the access of the growth factors to the cancer cells and slowing their growth. Other HER2/neu antibodies are now being studied in clinical trials.

Radiation Therapy

Radiation Therapy (RT) is indicated in all patients who have undergone Breast Conserving Surgery (BCS) and are node negative. Significant reductions in the risk of local recurrence.

A common dose fractionation regime used for breast cancer patients is 50Gy in 25 fractions to the whole breast and/or SCF (if required).

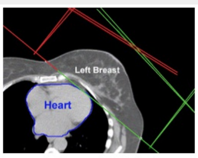
45-50Gy could control 95% of subclinical disease.

Doses above 45Gy delivered in 1.8 Gy fractions resulted in permanent control of subclinical disease in approximately 80% of patients.

Radiation therapy is generally confined to the chest wall and relevant regional nodes.

The internal mammary (IM) nodes are often excluded unless they are known to be positive, due to the high risk of cardiac damage. (Eg. Patients with left sided tumours and those who have had Adriamycin chemotherapy). If treatment of the IM nodal chain, which extends from the 1 – 3 intercostal space, is warranted, electrons can be utilized to minimize the underlying dose.

Radiation Therapy



The image above illustrates a cross sectional CT slice through the chest wall, showing the left breast with the green and red lines representing the radiation beams to be used for treatment and the underlying heart that needs to be avoided to reduce any radiation dose. The red and green beams are angled, this is called tangents.

Radiation Therapy

An **electron/photon mix** can be employed to utilize the characteristics of an electron beam as well as decrease the skin dose.

However, these field arrangements are subject to matching difficulties causing dose irregularities at the junction. The treatment of the IM nodes can also be incorporated in the photon tangent beams. This is generally not desirable, due to the significant increase of lung volume irradiated.

Supraclavicular nodal irradiation is commonly given to those patients who have undergone axillary clearance where there is extensive axillary nodal disease (eg >/= 4 nodes)

The supraclavicular nodes are usually encompassed with a single anterior-oblique field. The field is angled medially to avoid the trachea, oesophagus and spine or alternatively larynx shielding can be utilised. Irradiation of the entire axilla is indicated if an axillary dissection is not performed, incomplete or if more that 50% of axillary nodes are involved. In order to boost the mid axillary lymph nodes, an opposing posterior axilla field may be used with consideration of divergence issues and the dose to the brachial plexus.

A breast boost is a supplementary dose of radiation delivered to the tumour bed. Rationale for the boost is that most local recurrences are at or near the primary site.

Post mastectomy patients may not need radiotherapy.

Only if: tumours greater than 5cm, axillary node positive disease, lympho-vascular invasion, high-grade tumour, positive margins, muscle invasion

Simulation

The position that the patient will be planned and treated in will depend on the size of the patients' breast.

The patient is normally treated **supine** on the couch top. The patient may have the **ipsilateral arm** raised above their head, or both. The arm must be abducted away from the chest wall to allow access for the treatment beams laterally. Having both arms up can make the patient too wide to fit through the CT doughnut.A device may be required for the patient to grasp with their hand, and possibly a **Vac Bag** to support the arm and ensure consistent positioning.

A patient with large, pendulous breasts represents a challenge to treat as gravity pushes the breast laterally of the chest wall, and sometimes superiorly. To treat the entire breast in this position would mean treating a larger portion of healthy tissues laterally, or superiorly the chin. Neither situation is acceptable.They are pos0itioned on an inclined plane. This will move the breast anteriorly and inferiorly on the chest wall.

Do not raise the incline plan to the extent that it produces a breast fold inferiorly. The tissue fold will produce a build-up effect increasing the skin dose in the Infra mammary fold and ultimately the toxicity for the patient.

Simulation (cont)

Other options for moving the breast into a different position are **breast rings.** tubes of polyethylene, looped around the base of the breast and attached with Velcro around the patient. This physically lifts the breast, but is associated with a slight increase in skin reaction from treating through the tube. It is possible that the placement of the ring varies at daily treatment delivery, therefore compromising the accuracy of the radiation therapy. This is minimised to a certain extent if a tracing of the ring position is taken at simulation in relation to the tattoos/skin marks.

A **compression sock** can be used, **micropore tape**, and even **Orfit thermoplastic casts** can be used to move the breast into position. The accuracy of these methods can vary on a daily basis.

The radiation oncologist defines the treatment fields on the patient's skin. Palpating the breast tissue, and giving this a 1.5 – 2 cm margin, and marking this as the field edge. Defining the treatment volume (a PTV) on CT is difficult, as it is hard to define were breast tissue starts and stops based on density changes alone. Therefore the traditional technique of field definition on patient's skin continues. For post-mastectomy patients, the intact breast is often used as a reference for the field definition.

The breast cancer treatment technique is often known as **"Tangents"**. This is from the radiation fields being tangential in nature. To treat the entire breast, the radiation fields are angled across the patients' chest wall, thereby minimising the dose to the underlying healthy lung and heart. There will be a small amount of lung tissue within the tangent fields to adequately cover the chest wall.

Field technique

Intact breast

The radiation oncologist will define the treatment fields

Chest wall

For mastectomy patients, there is less tissue within the treatment volume, often making the task of homogeneous dosimetry difficult. There is also an increased risk of seeding – recurrence in the surgical scar for mastectomy patients.

To increase the dose to the skin surface and reduce the risk of recurrence, the radiation oncologist will so often prescribe the treatment to include bolus across the entire treatment area. The thickness and frequency of application may vary between centres and doctors.

Chest wall field delineation recommendations by RANZCR suggest covering all breast tissue (or where it would have been) from approximately the midline anteriorly, to the mid axillary line laterally, 2cm inferior to the lower pole of the breast and to just beyond its upper pole or about the second rib.

'The tangential nature of the fields minimises lung and heart involvement but ensures the underlying pectoral muscles are included'

Fields may be outlined clinically on skin and a CT virtual simulation used to confirm field placement and coverage of underlying breast tissue, lung and heart

Field Technique (Tangents + Supra Clavicular field)

There are numerous techniques that are applied to achieve a junctional technique for three and four field treatment techniques. The technique can either involve two isocentres, or a common isocentre using asymmetric collimators.

Field technique (cont)

Two isocentres means that the fields will diverge towards each other.

Overlap of the SC field and the tangent fields will result in a hot spot, which is not acceptable. Some centres will rotate the couch, or collimators to match the divergence of the beams at the junction, thereby minimising the risk of hot spots. Another technique uses a common isocentre to achieve a junction match. This includes a non-divergent upper level of the tangents, centring at this level, matching to the non-divergent lower level of the SC field.

If the patient is having the supraclavicular field, the upper level of the tangent field will junction with the SC field at the level of the second intercostal space. The tangent fields will otherwise be defined as described above for the two-field technique.

The field is often angled 1- 15 degrees to angle away from spinal cord, also minimising dose to the trachea and oesophagus. Some radiation oncologists prefer to leave the gantry on zero, but get the patient to move their neck away from the field to attempt the same result.

There may be some shielding placed along the medial edge if there is still spinal cord in the field, or if the radiation oncologist is shielding the larynx. The SC field is unlikely to be wide enough to include any other the humerus. If the is required to cover particular disease, then a humeral head shield is to be added without compromising nodal coverage. Shielding may also be used to reduce the dose to the apex of the lung.

4 Field Technique

Field technique (cont)

The option of irradiating both the SC and axillary nodes is made by the radiation oncologist based upon the number of positive nodes found at axillary clearance, and the size of the positive nodes. The four-field technique can be associated with an increased risk of toxicity, therefore this will be discussed with the patient prior to simulation.

Information to be recorded to ensure that the patient is treated correctly each fraction.

-Patient Position
-UL reference line – this maintains the correct arm position
-Tattoo/skin mark location
-Isocentre position in relation to anatomical landmarks
-Clinical volume delineated by radiation oncologist – this is the shielding that is to be maintained each fraction
-Photos of the skin mark the doctor marked as a permanent reference for any possible queries at a later stage.

Virtual Simulation

For those departments without a traditional simulator the process for breast cancer patients is similar to that described above.

The Radiation Oncologist marks the field size, which are delineated for the CT images by radio-opaque wires. CT slices will be acquired at a spacing and thickness of a minimum of 5 mm. The determination of shielding/MLCs, and treatment angles will be done on the CT slices – our virtual patient.

Boost to surgical site a boost dose of 16Gy after a 50Gy whole breast treatment decreased the rate of 5-year local recurrence from 7.3% to 4.3%

The largest clinical benefit in patients <40 years of age, reducing LRR from 19.5% to 10.2%.

To boost the dose received by the surgical site, electrons are often used.

Field technique (cont)

he radiation oncologist will mark the field size to include the tumour bed and scar by 1 –2 cm to allow for the dosimetry of electrons belling in. This clinical mark up is now often combined with the CT obtained in the planning of the tangent beams. By putting the electron field on to the CT, the treatment depth and coverage of any surgical clips can be confirmed. It is possible the field delineated in simulation will be altered to include/exclude tissue information that the CT has provided. Some centres will use ultrasound to confirm the depth to the chest wall. A tracing, photos and measurements of field centre will be recorded to be able to reproduce the electron field on treatment.

Planning

As with all radiation therapy you want to deliver the entire dose to the treatment volume, while minimising the dose to the critical/healthy structures. For breast cancer this is achieved by angling the radiation fields across the chest wall. In this manner the entire breast tissue can be included within the fields, and the underlying lung and heart can be shielded out. To compensate for the contour variation in the anterior-posterior direction a wedge is placed on the lateral field, with the hot-edge posteriorly.

3D Optimisation

Not only is there contour variation in the Ant-Post direction, it is present in the sup-inf direction.

A patient usually has the greatest separation around the nipple region of the breast. It is at this level that the lowest total dose is found, and the TD that dictates the prescription.

Planning (cont)

Superior and inferior to this level, the separation decreases. The difference in the reference conditions means that there as an increase in the dose deposited at the smaller separations. This can mean that the dose received is up to 10 % greater than the prescribed dose. These higher doses can lead to an increased risk of tissue and lung fibrosis and increased skin reaction. Ultimately this will impact on the cosmetic outcome that the patient will achieve after their course of radiation therapy.

Beam-in-Beam uses the asymmetric collimation or multi-leaf collimators (MLCs) moved into the treatment area, for a portion of the treatment from each angle. The beam in beam using asymmetric jaws requires that the entire UL or LL are hot, because that entire region will be cooled down. Therefore it can't be used for every patient, but MLCs can be used to the same effect, but with greater degrees of freedom as to how they are positioned.

Beam attenuators (BAs) are thin pieces of lead that are placed on the patient's shielding tray. They attenuate the beam by a percentage, depending on the number of thickness used. These BAs can be positioned on the BEV on the planning system to reduce the dose received at the hot spot regions. The benefit over using asymmetrical jaws is that they can be positioned anywhere in the beam and made in any shape.

A method of confirming that the **correct wedge size** has been selected is by analysing the hot spots on the central axis slice. If the volumes (size) of the hot spots are similar magnitude at the medial, lateral and anterior edges of the target volume, then the wedge and weighting of the plan are appropriate for the patient.

Planning (cont)

Compensators are another form of dose optimisation that is used to a lesser degree. They are constructed from cement or steel. These have to be calculated automatically by the planning system.

IMRT is a complex form of radiation therapy that allows the dose to be tightly "Sculpted" to the tumour volume, while having quick fall off of dose to keep the dose to healthy structures as low as possible. The beam is broken up into tiny segments and the MLCs move to different positions within the field, often while the beam is on. This produces a beam profile that was determined by the planning system.

Electron Boosts. The beauty of CT-planning is that the affect of the patient's lung can be seen with the electron boost. It is common that a mix of electron energies is used to treat the boost, because the chest wall depth is between the two treatment depths. For example, a 9 MeV beam does not cover the chest wall depth, yet a 12 MeV beam treats too much lung. If the boost is planned with half of the dose delivered from each beam, the dose to depth can be optimised to satisfy the radiation oncologist's prescription.

Internal Mammary Chain (IMC) Metastases to the IMC are more frequent from the inner quadrant or centrally located lesions. The IMC are at a depth of 4 – 5 cm, and can often be determined with the assistance of the planning CT. The field width is normally 5 – 6 cm, and will junction with the medial field edge of the tangential field.

Planning (cont)

Total Dose Plan is generated for any patient that is receiving treatment to junctioning treatment sites. By analysing the total contribution of all treatment sites, hot and cold spots can be located, and corrected if required. Therefore for three-, four-field and IMC patients a total dose will be done. It is most likely that each treatment site will be prescribed to a different dose, and a different TD.

Treatment

A radical prescription will be 45 - 50 Gy in 25 to 28 fractions at five fractions per week to the entire breast prescribed to an isodose line following the chest wall.

The SC/Axilla will only be taken to 45/25/5 usually. The SC region will be prescribed to a depth between 1.5 – 3 cm. With the four-field technique, the dose also needs to be delivered at the patient's mid separation.

The **international standard radiotherapy schedule** for breast cancer treatment delivers a total dose of **50Gy in 25 fractions.**

Hypo-fractionated radiotherapy and this is now becoming more commonly used for early breast cancer, with the intent of reducing overall treatment time whilst improving outcome.

Treatment is often followed by a**boost to the primary surgical site.**

The electron boost is usually prescribed **10 - 16 Gy in 5 – 8 fractions**, often prescribed to the 90% isodose line. Some centres use **bachytherapy** instead.

Heterogeneity should be between -5% and +7% of the prescribed dose.

Treatment (cont)

Typical doses for **palliative breast irradiation** are **10/1 or 50/20/5**. Another possibility is to treat to a total of **36-38 Gy treating in 3-4 Gy increments, 3 times a week.** All of the fractionation schedules aim for control of local systems, treating large fractions per increment, while minimising the inconvenience to the patient.

It is important to remember that with opposed photon fields, that any change you make to match the lateral shielding will affect the medial and vice versa. It is important therefore to check the shielding of both fields prior to irradiation.

Tangential image verification is a minimum requirement for breast cancer. This will be acquired weekly as a minimum in most centres. For those patients treated with a three or four-field technique, these fields will also be imaged to verify field position. The junction also becomes important to avoid overlap with tangent fields. Those centres with EPI (electronic portal imaging) or an OBI (on board imager) may image every field daily.

Complications

Information and communication are the keys to supportive care. It is vital that those interacting with patients deliver accurate and up to date information. It is also important that health care professionals have an understanding of the experience of breast cancer patients in order to assist in the development of coping strategies

Potential **side effects** that patients receiving radiation therapy for breast cancer are likely to experience.

Cardiac/vascular Damage

Osteitis of the Ribs is a brittleness of the ribs which occurs in up to 2 per cent of cases and can lead to spontaneous fracture.

Complications (cont)

Acute Radiation Pneumonitis s reported to range from 0.7–7 per cent. When the breast and axilla are irradiated, the risk will be at the upper end of the range because the risk increases with the amount of lung in the radiation field. It is, therefore, a rare complication.

Brachial plexopathy is a very rare complication and will only occur when the axilla and supra-clavicular fossa are irradiated.

Secondary Malignancy

Local side effects in the conserved breast may include abnormal sensation varying between discomfort and significant pain, particularly in the first two years. The end cosmetic result is affected by many factors.

There is conflicting evidence over whether chemotherapy given at the same time as radiotherapy affects the cosmetic result.

Lymphoedema of the ipsilateral arm

The diagnosis of breast cancer presents women with several **psychosocial issues** the dynamics of which often extend beyond the patient and affect those around them. The difficulties faced will vary from patient to patient as personal circumstances and disease management options differ.

Fatigue is a recognised side effect of cancer treatment that can seriously affect quality of life and hinder a patient's ability to self care and rehabilitate after treatment. Fatigue is also tentatively linked to depression.