- Breast cancer must be considered as systemic disease

- 10% of breast cancer diagnoses as stage-IV

- Locally advanced breast cancers are at risk for both distant and locoregional failure
CARCINOMA BREAST

LOCAL
Nearer to surgical bed

REGIONAL
Axillary node
Supraclavicular node
Internal mammary node

DISTANT
Skeletal metastasis
Visceral metastasis
TUMOR SPREAD
Breast tumor grows
Travel along the duct
Eventually breaking through basement membrane of the duct
Invading adjacent lobules, ducts, facial strands and the mammary fat
Spreading through the breast lymphatics and peripheral lymphatics
Tumor grow through the wall of the blood vessels
• Halsted model – orderly progression to regional lymph nodes and from there to distant metastatic site.

• Keynes and Crile et. Al. – Systemic disease.

• Fisher – systemic process involving host-tumor interaction based on laboratory and clinical study.

• Hellman – Breast cancer is a heterogeneous disease that metastases are a function of tumor growth and progression factors even when detected as every small lesion.
The majority of the metastasis occur within 5 years after the diagnosis of the primary disease but it can be extent as long as 20-30 years after the initial diagnosis.

The time to appearance of a metastatic disease is depend upon

- Initial primary tumor size
- Axillary status
- Hormonal receptor status
FACTORS RELATED WITH RECURRENCE

- Young age at diagnosis
- African American women
- Tumor > 2 c.m.
- Multicentric disease
- Extracapsular invasion
- Medial quadrant of breast
- Sentinel lymph-node metastasis >2m.m.
- Lymphatic-vascular invasion
- -ve hormonal receptor
- High fraction of cells in S-phase
- Thymidine labelling index
- High mitotic index
- Proliferating cell nuclear antigen
- Her-2/neu proto-oncogene
- Ki-67
- High EGFR
- P-53 tumor suppression gene mutation
- Serum markers such as CA 15-3 and CA 27-29
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COMMON SITES OF METASTASIS

- **REGIONAL FAILURE**
  - AXILLARY NODES
  - INTERNAL MAMMARY NODES
  - SUPRACLAVICULAR NODES

- **DISTANT METASTASIS**
  - SKELETAL
  - VISCERAL (lung, liver, brain, adrenal gland, orbit, skin, ovary, stomach, any region of the body)
Haagensen’s autopsy series on the detectable metastasis at the various sites

- Lung - 70%
- Liver - 65%
- Bone - 70%
- Adrenal gland - 50%
- Brain - 20%

Other sites 10-20%
- Ovaries
- Heart
- Peritoneum
- Skin
- Lymph nodes
DIAGNOSTIC TESTS FOR DETECTING METASTASIS

- X-ray Chest
- Ultrasonography of Abdomen and Pelvis
- Computerised Tomography of Chest, Abdomen, Pelvis, Brain
- PET-CT scan
- Haemogram
- Renal Function Tests
- Liver Function Test (assessing physiologic function)
TREATMENT GOAL FOR METASTATIC BREAST CANCER

- To palliate symptoms
- Arrest tumor growth to prevent symptoms due to increasing pressure
- To improve quality of life
- To prolong survival

Prompt supportive measures should be offered according to an individual needs.
TREATMENT MODALITIES

Radiotherapy machine in use
Types of treatment modality depend upon

- Site and extent of metastatic disease
- Hormone receptor status
- Disease – free interval
- Age of patient
- Menopausal status
• LOCAL CONTROL BY

RADIOThERAPY

SURGERY

• SYSTEMIC CONTROL BY

HORMONAL THERAPY
- Hormone receptor +ve patient with no life threatening condition

CHEMOTHERAPY
- Hormone receptor –ve
- Symptomatic visceral disease
- Life-threatening condition

TARGETED THERAPY
Complete remission can be achieved in 5-15%
LOCAL RECURRENCE
LOCATION

- Close to the site of the original tumor
- Tumor cells aggregates close to the surgical bed
FACTORS RELATED WITH LOCAL RECURRENCE

- Age < 40 years
- Tumor > 3 c.m. size
- Multicentric disease
- Positive surgical margin
- Extensive intraductal component
- LCIS component
- Peritumoral lymphatic infiltration
- Grade-3 disease
- >3 positive axillary lymph node
- ER/PR –ve
- BRCA 1-2
- P-53 overexpression
LOCAL RECURRENCE AFTER CONSERVATIVE BREAST SURGERY

- Salvage mastectomy with or without post-operative radiotherapy

- Second breast conserving surgery with interstitial brachytherapy
CHEST WALL
RECURRENCE FOLLOWING MRM

RADIOTHERAPY
is treatment of choice
- To control bleeding
- To control discharge
- Reduces ulceration
- To decrease bulk of tumor

CHEMOTHERAPY
- Loco-regional relapse with distant metastasis
- Previously irradiated patient
- Palliation with radiotherapy unsatisfactory
RADIOTHERAPY TECHNIQUE

- Parallel opposed pair of tangential field
- Direct electron beam field with 6-8 Mev
  With 2 c.m. margin all around

DOSE-FRACTIONATION SCHEDULES

- 30 Gy in 10 Fr
- 20 Gy in 5 Fr
SIMULATOR FILM OF TANGENTIAL FIELD
DRAINING LYMPHATIC AREAS
FACTORS RELATED WITH AXILLARY NODE

- Age < 60 year
- Tumor > 1 c.m.
- Outer quadrant location
- Infiltrating ductal histologic type
- M.D./P.D. nuclear grade
- Presence of lymphatic-vascular invasion
- Aneuploidy
- High fraction of cells in S-phase
FACTORS RELATED WITH SUPRACLAVICULAR NODE

- Age < 40 year
- Tumor size > 3 c.m.
- High histologic grade
- Angiolymphatic invasion
- > 4 positive L-I & II axillary lymph node
- Gross extranodal extension of axillary node
- Negative estrogen receptor
- DNA synthetic fraction > 4%

Supraclavicular node failure < 1% in prophylactically treated nodes
FACTORS RELATED WITH INTERNAL MAMMARY NODE

- Age < 40 year
- Tumor > 2 c.m.
- Inner quadrant tumor
- Positive axillary node

Clinical parasternal recurrences appear more slowly than axillary and supraclavicular recurrences; the delay probably due to the size of tumor necessary before it can be palpated between the costal cartilages as parasternal mass.
RADIATION TECHNIQUE

- Single field on cobalt with bolus
  
  Or

- Single field with electron depend upon depth of tumor

With 2 c.m. margin all around

RADIATION DOSE

- 30 GY / 10 #

- 20 GY / 5 #

- Additional dose should be delivered through reduced field to the site of residual palpable disease
SYSTEMIC FAILURE
The systemic spread of the disease is common in breast carcinoma with high metastatic potential.

It is considered as an ominous sign but expected lifetime is still good and every effort should be made.

Treatment of metastatic breast cancer generally focuses on relieving symptoms and extending woman’s lifetime.
FACTORS RELATED WITH SYSTEMIC FAILURE

- Larger local tumor size
- Higher histologic grade
- >3 axillary lymph node metastasis
- Negative hormone receptor tumor

Micrometastasis was detected in 30.6% of patient. It was an independent predictor of poor outcome.
SKELETAL METASTASIS

- Bone metastasis is seen in almost 33% of breast cancer cases clinically where as in autopsy series as high as 70%.
- Bone as a preferred site of metastasis due to high blood flow in areas of red marrow. (breast drains principally by azygos venous system communicating with Batson’s paravertebral plexus)
- Most patient with breast cancer have predominantly osteolytic lesion but at least 15-20% have predominantly osteoblastic lesion
- Bone metastasis due to breast cancer patient are still alive for 5 years after discovery
SKELETAL METASTASIS

- Tumor cells in bone
- Production of parathyroid hormone related peptide
- Activates osteoblasts and osteoclasts in bone
- Osteoclast
  - destroy bone matrix
  - releasing embedded growth factor
- Further stimulates tumor cells
Osteolytic lesion can cause

- severe pain
- pathological fracture
- life threatening hypercalcemia
- spinal cord compression
- other nerve compression syndrome
COMMON SITES

- SPINE
- PELVIS
- FEMUR
- HUMERUS

INVESTIGATION

- X-RAYS
- RADIO-OPAQUE ISOTOPE SCAN
- CT-SCAN
- MRI
MULTIPLE BONE METASTASIS
TREATMENT

Depend upon

- Patient’s general status
- Site of metastatic lesion
- Pathological fracture

RT indicated for long term management for localised bony metastasis

- To relieve bone pain (60-80%)
- Prevention of fracture at critical site
- Recalcification process in the destroyed bone matrix
- Improves morbidity
TYPES OF TREATMENT

- Restoration of musculoskeletal stability
- Various types of internal fixation
- Immobilization casts
- Rehabilitation
- Radiotherapy
RADIOThERAPY PORTAL

- Single or parallel opposed fields with 2 c.m. margin

RADIATION DOSE

- 30GY/10FR
- 20GY/5FR
- 8GY/single fraction
- LHBI 8GY/2FR
FRACTURE OF HUMERUS
BONE UNION
ROLE OF RT TO SHOULDER
HUMERUS
2000 RAD TD
1 WEEK

RADIUS OR ULNA
2000 RAD TD
1 WEEK
RIBS

3000 RADS GD

1 WEEK

or

800 RADS GD x 2

2 DAYS
FEMUR
3000 RADS TD
2 WEEKS
ROLE OF RT TO HEMIPELVIS
HemiPelvis or HipJoint

3000 RADS TD

2 Weeks
MULTIPLE BONE METASTASIS IN PELVIS
TO AVOID BOWEL

TIBIA
2000 RADS TD
1 WEEK

LOWER PELVIS
2000 RADS TD
1 WEEK

WHOLE PELVIS
3000 RADS TD
2 WEEKS

SHOULDER
2000 RADS TD
1 WEEK

LOWER CERVICAL SPINE
2000 RADS TD
1 WEEK

DORSAL SPINE
2000 RADS TD
1 WEEK

TO AVOID ANAL AREA
A typical metastatic lesion of a long bone destroys a segment of medullary structures and corresponding cortical bone.

The cortical defects can not bear the normal torsional and weight bearing forces.

Treated with prophylactic internal fixation followed by external beam radiotherapy to inhibit tumor growth and prevent fracture.
SPINAL CORD COMPRESSION

SITE
- Extradural
- Rarely intradural
- Metastasis to spinal cord and cauda equina (5-10%)
- Epidural cord compression (adenocarcinoma)
- Thoracic spine most frequent site
PRESENTATION

- Pain
- Weakness
- Sensory loss
- Sphincter disturbances
- Radicular or referred pain
- Various neurological deficits

INVESTIGATION

- X-ray spine (vertebral collapse)
- Bone scan
- CT scan
- MRI
TREATMENT

- High dose steroid with localized external beam radiotherapy

- Neurological decompression spinal stabilization procedures should be followed by radiotherapy
RADIATION TECHNIQUE

- Direct single posterior field
- Oblique wedge field
  The portal should include at least one vertebra above and below the involved site

RADIATION DOSE

- 30GY /10FR
- 20GY /5FR
- 8GY/FR
  The dose is calculated at a depth of
  (cervical 3 c.m.
  dorsal 4 c.m.
  lumber 5 c.m.)
Sr-89 is an analog of calcium and concentrates in osteoblastic bone carcinoma lesion.

After intravenous injection of ionic Sr-89 it is cleared rapidly from the blood; approximately 50% of injected activity is deposited in bone and remain for as long as 100 days.

The standard dose is 40-60 micro Ci (1.48-2.22 MBq) per kg body weight given intravenously.
BIPHOSPHONATES

- Biphosphonates should be used in bony metastatic disease
- To prevent progression of lytic disease.
- To delay skeletal related events.
- To decrease pain
- Zoledronic acid (4mg by 15 min. infusion)
- Pamidronate (90mg by 2 hr. infusion)
VISCERAL METASTASIS
CNS METASTASIS

- It is considered as late metastasis of systemic disease
- CNS (brain, cranial nerve, leptomeninges, spinal cord) sanctuary site for metastasis
- Clinically symptomatic metastasis to CNS is 10-15% but occult metastasis is common
- Patient with Her-2 positive breast tumor have been reported to develop CNS metastasis at higher rates
TREATMENT

- Whole brain radiotherapy (to kill the cells and shrink the tumors so decreases pain)
- SRS boost (to improve functional autonomy)
- Neurosurgery
- Judicious use of corticosteroids (reduces peritumoral oedema and provide symptomatic relief)
Breast cancer is the second most common cause of metastasis to the brain after lung cancer. Median time to development of the brain secondaries is about 1-1.5 years.

SITE

- Supratentorial cerebrum
- Cerebellum
- Leptomeningeal carcinomatosis
- Extradural deposits in vertebral column
BRAIN METASTASIS
BRAIN METASTASIS

PRESENTATION

- Headache
- Impaired higher function
- Cranial nerve palsies
- Loss of motor function

INVESTIGATION

- CT scan of brain
- MRI brain
MANAGEMENT OF BRAIN METASTASIS

- Judicious use of steroids
- Mannitol
- Anticonvulsants
- Antiemetic therapy
BRAIN METASTASIS
MANAGEMENT OF SOLITARY METASTASIS

- Surgical resection only after PET-CT scan with post operative radiotherapy
- Whole brain radiotherapy (30GY/10#) with boost by SRS
Role of SRS in Solitary Brain Metastasis

- Stereotactic radio surgery (SRS)
- Palliative radiotherapy – 30 Gy / 10 # followed by SRS boost
- Single fraction (12-15 GY)
Stereotactic Radiosurgery

The delivery of a single, high dose of irradiation to a small and critically located intracranial volume, sparing normal structure
INDICATION

- Small target volume (<3 c.m.)
- Sharply defined target
- High conformity
- Sensitive structures excluded from the target
Co-planar vs. Non-coplanar beams

- tolerance of normal tissue depends upon both the dose and volume of the tissue irradiated
- normal tissue irradiation can be minimized through stereotactic definition of target and sharply focused, multiple, non-coplanar beams

A. Parallel opposed beams
B. Coplanar arcs (bilateral 100°)
C. Non-coplanar beams
Advantages

- Enhances clinical outcome
- Improves quality of life
- Time factor
The Time Factor

Open Surgery
2-4 days ICU
10-16 days hospitalization
4-6 weeks convalescence

Gamma Knife Surgery

Symptom Diagnosis
Quality of Life

- Minimally invasive
- Less trauma
- Faster recovery
- Minimal hospitalization
- Fewer complications
- Documented efficacy
Gamma Knife
RADIATION DELIVERY THROUGH SRS
MULTIPLE BRAIN METASTASIS
MULTIPLE BRAIN METASTASIS
MANAGEMENT OF MULTIPLE METASTASIS

- Whole brain radiotherapy (30 GY/10 FR)
  With or without TEMOZOLAMIDE

METASTASIS WITH SIGNIFICANT MASS EFFECT

- Produces consequent hydrocephalus or herniation
- Requires urgent surgical intervention
PORTALS OF RADIOTHERAPY

- Radiotherapy plays a major role in brain secondaries and in leptomeningeal carcinomatosis.

- Radiation portal should cover the entire cranium and basal meninges (two lateral step-ladder / German helmet) fields or slanting field.
PALLIATIVE CRANIAL RT

WIDESPREAD BRAIN METASTASES
3000 RADS TD
2 WEEKS

OR
2000 RADS TD
6 DAYS

UPPER CERVICAL SPINE
2000 RADS TD
1 WEEK
PALLIATIVE CRANIAL
WHOLE BRAIN RT
Temozolomide (TMZ)

- Oral administration
- Excellent concentration in CNS
- Encouraging antitumour activity
- Favourable toxicity profile
- Synergism with radiotherapy and other agents
RADIOThERAPY WITH TEMOZOLOMIDE

Outcome versus Toxicity

Toxicity

Local Control

Survival

What can improve the outcome Without increase in complications
CARCINOMATOUS MENINGITIS

- CM is the disseminated form of malignancy due to spread of malignant cells into cerebrospinal path involving intracranial meninges and meninges around the nerve roots of the spinal axis.

- Presented with severe backache, headache, vomiting, and neck rigidity.
TREATMENT

- Medical decompression
- Craniospinal irradiation (25-30GY in 15FR)
- Intrathecal chemotherapy
CHOROIDAL METASTASIS

- Incidence-10-40%

- Metastatize to intraocular structure than eyelids or orbit

- Two-third of the ophthalmic metastasis from BC involves the globe and choroid is more commonly involved.

- Substantial number of patients will show bilateral metastasis
PRESENTATION

INTRACHOROIDAL METASTASIS

- Distorted vision
- Diplopia
- Sudden blindness due to retinal detachment

ORBITAL METASTASIS

- Proptosis
- Periorbital swelling
- Palpable mass
- Lid lag
INVESTIGATION

- Ophthalmic examination
- Ultrasonography of eye (B-scan)
- CT scan
- MRI of orbit
- Fluorescent angiography
- FNAC
CHOROIDAL METASTASIS
TREATMENT

- Radiotherapy 30GY / 10 FR over 2 weeks by lateral portal and calculated at 2.5 c.m. depth.

- Anterolateral wedge fields used in case of orbital metastasis with eyelid extension.

- Prognosis following early radiotherapy is generally good.
RETINAL METASTASES

CAUSING

VISUAL IMPAIRMENT

4000 RADS TD

4 WEEKS
RETO-ORBITAL SPACE
3000 RADS G.D.
2 WEEKS
BRACHIAL PLEXOPATHY

- < 3% of cases.
- Pain due to involvement of lower trunk (C7, C8, D1) and upper plexus (C5, C6)
- Atrophy of muscles
- Sensory changes
- Motor loss
- Horner’s syndrome (50%) ominous sign
- Investigated by CT scan and MRI
TREATMENT

- Radiotherapy is the treatment of choice. 30GY/10FR over 2 weeks.
- Radiotherapy portal includes lower neck and supraclavicular areas extending medially to cover C5-D1 nerve roots.
- Systemic chemotherapy if general status is good.
- Steroid with other analgesics.
LIVER METASTASIS

- Ominous sign

- Presented with anorexia, malaise, weight loss, biliary obstruction, hepatic pain (due to capsular infiltration or haemorrhage)

- Treated with chemotherapy and / or radiofrequency ablation.
PULMONARY METASTASIS

- Systemic chemotherapy
- Excision if feasible and solitary nodule

PLEURAL EFFUSION

- Pleural drainage
- Sclerotherapy
- Intrapleural administration of Bleomycin
PERICARDIAL METASTASIS

- Malignant pericardial effusion and cardiac tamponade

- Investigated by CxR, ECG, echocardiogram USG-guided aspirate

- Bleomycin installed as asclerosant.
OVARIAN ABLATION

- Premenopausal Patients
- ER / PR +ve
- Surgical Oopherectomy Vs. Ovarian Ablation
- Small Pelvic field RT (Inferior border is 1 cm below the top of pubic symphysis)
- Dose: 12 – 15 Gy in 5 #
- Response is slow (2-3 months), 50-55% in ER+ve and 5-10% in ER-ve