Treatment Modalities: Radiation Therapy & Bone Marrow Transplant

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Objectives
Discuss the role radiation therapy and hematopoietic cell transplant in the treatment of cancer.

1. Principles of radiation therapy
2. Assessment
3. Radiation safety precautions
4. Transplant process basics
5. Patient teaching and preparation for transplant for the community oncology nurse
6. Follow-up care for the community oncology nurse

Radiation
Radiation is the emission or transmission of energy in the form of waves or particles through space or through a material medium

Sources of Radiation

Ionizing: has enough energy to remove electrons from atoms, creating ions
- Alpha particles α
- Beta particles β
- Gamma rays γ
- X-rays
- Neutrons
- Protons
Radiation as Cancer Treatment

- Damages DNA directly or creates free radicals which damage DNA
- May affect normal and tumor cells

Goals of Radiation therapy

- **Definitive**: primary cancer treatment
- **Neoadjuvant**: given prior to surgery
- **Adjuvant**: after chemo or surgery
- **Prophylaxis**: to prevent spread to high risk tissues
- **Control**: slow growth and spread of tumor
- **Palliation**: decrease symptoms related to disease

Cancers treated with Radiation

- Breast
- Lung
- GI
- Cervical
- Lymphoma
- Prostate
- Brain
- Sarcoma
- Head/Neck
- Renal Cell
- Pancreatic Cancers
- Thyroid

Radiosensitivity

Bergonie and Treibondeau’s Law: Radiosensitivity is highest in tissues with the highest mitotic index, and lowest in well-differentiated tissues.

<table>
<thead>
<tr>
<th>Tumor</th>
<th>Radiosensitivity</th>
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</thead>
<tbody>
<tr>
<td>Lymphoid, bone marrow, blood, testes, ovaries, intestines</td>
<td>High</td>
</tr>
<tr>
<td>Skin, cornea, oral, esophagus, rectum, bladder, vagina, cervix, ureters</td>
<td>Fairly High</td>
</tr>
<tr>
<td>Stomach, vasculature, growing bone and cartilage</td>
<td>Moderate</td>
</tr>
<tr>
<td>Salivary glands, lung, kidneys, liver, breast, pancreas, thyroid, adrenals, pituitary</td>
<td>Fairly Low</td>
</tr>
<tr>
<td>Muscle, brain, spinal cord</td>
<td>Low</td>
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RadioSensitivity

Well-oxygenated tumors are more radiosensitive

Medications effects:
• Radiosensitizers: 5-Flouracil; cisplatin, metronidazole and analogues
• Radioprotectors: Amifostine

Types of Radiation

• Photon Radiation
  • X-Rays
  • Gamma Rays

• Particle Radiation
  • Alpha
  • Beta
  • Proton
  • Neutron
  • Electron
  • Carbon

Treatment dosing

Measured in “Gray” (Gy): the absorption of one joule of radiation energy per one kilogram of matter

1/100th of Gray: “Centigray” (cGy) =100 rad

Example: Typical treatment dose for breast cancer may be 50-60 Gy.

Radiation Therapy Team

• Radiation Tech: delivers daily dose of radiation treatments
• Radiation Dosimetrist: has an understanding of radiation therapies, physics, and works with the physicist and MD to calculate radiation doses
• Nurse: symptom management, care coordination, patient and family education
• Physicist: expert in physics, radiation equipment, radiation dosimetry
• Radiation Oncologist: Physician specializing in radiation for cancer treatment


External Beam Radiation

Radiation delivered by a machine
X-Ray Therapy or Particle Beams
Most common type of radiation therapy
Often delivered a linear accelerator

External Beam Radiation: Simulation & Treatment Planning

Imaging: CT, MRI, or PET to obtain details about tumor and surrounding tissues
Simulation of a treatment
Tattoos or ink markings to denote treatment area
Blocks created
Body Molds/Masks may be created
Dosimetry calculations

External Beam Treatments

• Treatment are often daily M-F for 2-10 weeks
• Pt must lie still during treatments
• Radiation therapist remains in the next room during treatments
• Treatment may last 15-30mins due to set-up though the radiation is only 1-5 minutes
• Pt is NOT radioactive

External Beam Radiation

• 3D-Conformal Radiation Therapy (3D-CRT)
• Intensity Modulated Radiation Therapy (IMRT)
• Image-guided Radiation Therapy (IGRT)
• Intensity Modulated Proton Therapy (IMPT)
• Stereotactic Radiosurgery & Stereotactic Body Radiation Therapy (SRS & SBRT): Gamma Knife, Cyberknife
Fractionation

Division of total dose of radiation into smaller doses called “fractions”
- Hyperfractionation: Smaller doses given more often: (2x/day)
- Hypofractionation: Large doses given less often over a shorter period of time

Goal to maximize tumor kill while minimizing impacts on surrounding tissues.

The 4 R’s of Fractionation

- **Repair**: Allows time between doses for normal tissues to repair themselves
- **Redistribution**: Cell cycle redistribution, increasing tumor radiosensitivity
- **Repopulation**: New growth of normal tissues occurs
- **Reoxygenation**: Allows oxygenation of tumor, increasing radiosensitivity


Brachytherapy: Internal Radiation

- Delivery of radiation directly to the tumor or in nearby tissues via a sealed source (ie: implant, seed)
  - Interstitial Radiation: ex: Mammosite for breast CA, seed implants for prostate CA
  - Intracavitary Radiation: ex: vaginal cylinder for uterine CA
  - Radioembolization for cancers of the liver

General Radiation Safety with Internal Radiation

- Patients may be radioactive for a short time
- May be instructed to avoid small children and pregnant women or to keep a distance from others for a short time
- Body fluids are not usually radioactive (exception: some types of radioembolization)
- If implant removed, patient is no longer radioactive
- If permanent implants are placed, radioactivity decays over time until gone

Source: ACR SIR practice parameter for radioembolization with microsphere brachytherapy device (RMBD) for treatment of liver metastases.
Brachytherapy: Mammosite

- After lumpectomy, a saline filled balloon with attached catheter is inserted into the lumpectomy pocket
- Radiation is delivered via a "seed" that is inserted into the catheter during treatments and then removed.
- Balloon is typically left in place for 5 days


Brachytherapy: Prostate Seed Implants

- Seeds are implanted in the prostate
- May be removed or left in place
- Urinary incontinence, rectal discomfort, diarrhea, or erectile dysfunction are potential side effects
- Avoidance of children on lap and wearing condoms may be recommended

Systemic Radiation Therapy

- Radioactive antibody infusions:
  - Ibritumomab Tiuxetan (Zevalin)
- Radiopharmaceutical Infusions:
  - Radium 223, Strontium 89- used for bone metastases
- Radioactive iodine (I-131) treatments for thyroid cancer

I-131 Radiation Treatments

- Pt is radioactive
- If hospitalized, rooms are covered with plastic or paper covering to protect from body fluids
- Cover personal electronics or belongings with plastic
- Men should sit to use the toilet
- Flush toilet twice & use separate bathroom
- Avoid sharing utensils & disposable trays in hospitalized
- Sleep alone for a period of time
- Minimize time with pregnant women and children for several days

Assessment for Acute Radiation Toxicities

- Fatigue
- Pain
- Esophagitis/Mucositis
- Diarrhea
- Skin erythema
- Wet Desquamation
- N/V

- Pneumonitis
- Myelosuppression
- Reproductive changes
- Sexual dysfunction
- Alopecia
- Increased cerebral edema
- Cystitis

Acute Toxicities: Think Site

General: Fatigue, Skin Care

Head/Neck XRT: Mucositis

Brain: Neuro cognitive changes

Breast: Skin care

Pelvic cancer: Sexual impacts, infertility

GI: Diarrhea, dehydration

Management of Skin Toxicities

- Erythema & pigmentation. May progress to dry and wet desquamation.
- Wash with mild soap and water
- Wear loose fitting clothes over the area
- Avoid razors
- Avoid sun
- Moisturize, but not before treatments
- If moist desquamation- hydrocolloid or silicone dressings may be applied.


Management of Mucositis

- Basic oral care
- Saline or baking soda rinses
- Keep tissues moist
- Topical lidocaine mouth rinses
- Pain control
- Swallowing exercises
- Secretion management
- Consult nutrition for support
Patient Teaching

Emphasize Treatment Adherence:
- Missing treatments can negatively impact disease control
- Missing even one treatment in head/neck cancer treatment may decrease local control of tumor by 1.4%


Radiation Safety for Staff

- ALARA: As low as reasonably achievable
- Dosimetry monitoring for staff
- Fetal dosimeter monitor for pregnant staff
- Dosimetry monitoring required for those that might get 10% of annual limit (0.5 rem/year) or staff that enter high radiation areas.
- Geiger counters

Radiation Safety Principles

- Time
- Distance
- Shielding
- Containment

Hematopoietic Stem Cell Transplant
Why a Transplant?

- High risk disease features at diagnosis
- Relapsed or refractory disease with standard treatments
- Correction of malfunctioning component of the immune or hematopoietic system
- Curative potential

HSCT Process

1. Planning phase
2. Preparing for transplant
3. Conditioning
4. Transplant
5. Awaiting Engraftment
6. Post-engraftment recovery
7. Long-term follow-up

Indications for HSCT

- Non-malignant diseases:
  - Hematologic Disorders (ex: Aplastic Anemia, Sickle Cell Anemia)
  - Congenital Immunodeficiencies (ex: SCID, Wiskott Aldrich Syndrome, HLH)
  - Inborn Errors of Metabolism (ex: Hurler’s Syndrome)
  - Autoimmune Diseases (ex: Systemic Sclerosis, Multiple Sclerosis)

- Malignant diseases:
  - Acute and Chronic Leukemia
  - Hodgkin’s lymphoma and Non-Hodgkin’s lymphoma
  - Myelodysplastic Syndromes
  - Multiple myeloma
  - Selected solid tumors

Approaches to Transplant

- Autologous

- Allogeneic
  - Related or Unrelated
  - Myeloablative
  - Non-myeloablative
Autologous vs Allogeneic

**Autologous**
- High dose chemo and/or radiation
- Stem cells “rescue” the ablated marrow
- Risk for tumor in stem cell product
- Avoid graft-vs-host disease

**Allogeneic**
- **Standard:** High Dose Chemo and/or radiation. Stem cells “rescue” the marrow.
- **Non-myeloblastic:** Lower dose chemo and/or radiation.
- Risk for graft versus malignancy effect
- Risk for graft versus host disease

Stem Cell Sources

<table>
<thead>
<tr>
<th>Stem Cell Source</th>
<th>Advantages</th>
<th>Disadvantages</th>
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<tbody>
<tr>
<td>Bone Marrow</td>
<td>Good source of stem cells</td>
<td>Less risk of cGVHD</td>
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<tr>
<td></td>
<td>Anaesthesia &amp; surgical risks for donor</td>
<td>Longer time to engraftment than PBSC</td>
</tr>
<tr>
<td>Peripheral Blood</td>
<td>Most abundant source of stem cells</td>
<td>Faster engraftment</td>
</tr>
<tr>
<td></td>
<td>Growth factors given to healthy donors</td>
<td>Higher risk of cGVHD</td>
</tr>
<tr>
<td>Umbilical Cord Blood</td>
<td>Readily available</td>
<td>HLA mismatch more acceptable</td>
</tr>
<tr>
<td></td>
<td>Lack of donor risks</td>
<td>Delayed engraftment</td>
</tr>
<tr>
<td></td>
<td>Smaller “dose” of stem cells</td>
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Autologous HSCT: Mobilization and Apheresis

- **Mobilization:** A technique used to increase the number of circulating hematopoietic stem cells from the bone marrow into the bloodstream
  - High Dose Chemotherapy + G-CSF ± plerixafor
  - G-CSF
- **Apheresis:** The method for stem cell collection using a dialysis-type machine with cell separators that are programmed to collect stem cells

Allogenic Stem Cell Collection

- Donor apheresis procedure after receiving several days of filgrastim injections
  - Stem cells collected over 1-2 days
- Donor bone marrow harvest
  - Surgical procedure under anesthesia
  - Multiple aspirations of marrow are taken
  - Volume collected is based on recipient weight but may be between 300-1000cc
  - Bone marrow regenerates in about 4-6 weeks

Transplant Planning in the Community

• Patient & Donor Planning
  • Oncologist reviews transplant with patient & family
  • Transplant center consultation
  • Address fertility now, if needed
  • HLA type patient & siblings if needed
  • Search the donor registries

Transplant Planning in the community

• Other Preparations
  • Assess finances (insurance coverage or pay cash)
  • Select transplant center (statistics on NMDP website)
  • Select a caregiver
  • Make plans for relocation if necessary

HLA Typing

Degree of compatibility between donor and patient

• Important HLA markers for HSCT are A, B, C, & DRB1
• Matched or mismatched donor options
• 25% chance that each sibling will be an HLA-match
• 70% of people do not have suitable family donors

Preparative Phase

• Medical and psycho-social evaluations.
• Evaluation of disease status and ability to tolerate transplant procedure.
• Family Conference & Informed Consent Process
• Preparation of the Family and Caregiver
• Orientation to center; Caregiver classes & support groups
• Central Line Placement
### Conditioning
- **Chemotherapy**
  - Myeloablative
  - Myelosuppressive

  Common Drugs: Melphalan, Fludarabine, Cyclophosphamide, Etoposide, Busulfan

- **Radiation**
  - Total Body Irradiation
  - “Mini” TBI

### Transplant
- Stem cell infusion administered like an RBC transfusion
- Cryopreserved
  - Preserved with DMSO
    - Can cause hemolysis
    - Causes garlic breath
    - Transfusion reactions
- Fresh

### Awaiting Engraftment
- Nausea, Vomiting, Diarrhea
- Mucositis
  - May effect the entire length of GI tract
  - May need PCA & TPN
- Infections
- Transfusion support
- Rare: Graft Failure

### Allogeneic HSCT: Post Engraftment Recovery
- Patients are closely followed at the transplant center for several months
- Acute GVHD and infection are major concerns
- Seen daily to once/week for medical evaluation and blood tests
- Management of symptoms
- Infusion therapy
- At approximately day +80, patients are completely evaluated for disease state and complications and prepared for discharge home
Infections and HSCT

- **Pre-engraftment**: HSV, gram negative bacilli, staphylococcus epidermidis, GI-tract streptococci, candida, aspergillus
- **Early Engraftment**: candida, staphylococcus epidermidis, aspergillus, CMV, pneumocystis jiroveci
- **Late Phase**: CMV, VZV, encapsulated bacteria, aspergillus, pneumocystis jiroveci

Immune reconstitution after HSCT

- Innate immunity usually returns by day 100
- Adaptive Immunity:
  - CD4+ helper T-cells numbers may take months to return to normal levels
  - Serum immunoglobulins may take months to years normalize and gain full functionality
  - Immunosuppressants and chronic GVHD further impair immune reconstitution

Acute Graft vs. Host Disease (aGVHD)

Donor T lymphocytes (the graft) recognize the antigens and cells in the transplant recipient (the host) as foreign and mount an immunologic attack.

Estimated incidence between 35-80%.

Predictive Factors for aGVHD

- Donor/Host Factors
  - HLA disparity
  - Parity of female donor
  - Age of donor and recipient
- HSC Source
  - PBSC > BM > UCB
- Immunomodulation
  - Omission of adequate aGVHD prophylaxis
  - TBI recipients
Clinical Features of aGVHD

• Skin
  • Maculopapular rash, often beginning with palmar/plantar surfaces and extending to the face, abdomen and trunk
  • Sunburned appearance to desquamation and loss of skin integrity

• Gut
  • Anorexia, nausea and vomiting, early satiety
  • Diarrhea, intestinal bleeding and abdominal pain to ileus

• Liver
  • Elevated alkaline phosphatase and bilirubin
  • RUQ pain, hepatomegaly and jaundice to ascites and encephalopathy

Prevention of aGVHD

• Highest degree of histocompatibility from donor (when multiple donors are available.)
  • Prophylactic immunosuppression
    methotrexate, cyclosporine, mycophenolate mofetil, tacrolimus, sirolimus
  • Selective T-cell depletion

Treatment & Prognosis for aGVHD

• Steroids: Prednisone 1-2mg/kg/day usual starting dose
• Secondary therapies may include other immunosuppressive agents that impact T-cell function such as biologic agents and ATG.
• Prognosis depends upon grade of GVHD and response to initial therapy
• Patients that do not respond to treatment for aGVHD have a high risk for non-relapse mortality

Allogeneic HSCT: Long-term Follow-Up (LTFU)

Late complications
• Chronic GVHD
• Late infectious complications
• Pulmonary complications – Bronchiolitis obliterans, pulmonary fibrosis
• Neurological complications
• Psychological complications
• Cataracts
• Sexual disorders (ex: dry vaginal mucosa) and impaired fertility
• Orthopedic complications – Fragile joints due to steroids
• Secondary malignancy
Nursing Care for the LTFU Patient in the Community
- Refer to treatment plan from the discharging transplant center
- Follow guidelines from transplant center about safe living with impaired immune function
- Support psychosocial needs as patient returns to community after intense treatment at transplant center
- Monitor infection & immunosuppression
- Monitor for sx of chronic GVHD
- Immunizations
- Care coordination with transplant center and primary oncologist

Chronic GVHD
Pathophysiology is poorly understood
Immune dysfunction
- T-cells
- B-cells
Fibrotic changes
Resembles autoimmune or collagen vascular disorder
Estimated incidence between 30-70%

Predictive factors & prognosis for cGVHD
- Previous aGVHD
- PBSC
- Older donor or recipient
- HLA disparity
- Mortality in cGVHD is largely attributed to infection.
- Major morbidity is often present with extensive chronic GVHD and requires long-term therapy.

Clinical Manifestations of Chronic GVHD
- Oral Symptoms
- Skin
- Nails
- Scalp & Body Hair
- Eyes
- Genitalia
- GI Tract
- Liver
- Lung
- Muscles/Fascia/Joints
- Hematopoietic/Immune
Treatment of cGVHD

• Primary
  • Prednisone 1mg/kg/day or less, with a slow taper after improvement usually in combination with cyclosporine or tacrolimus
  • Salvage: Various other immunosuppressive agents

Supportive Care in cGVHD

• Infection prophylaxis
  • Symptom palliation
    — Manage dry skin and protect from sun
    — Artificial tears
    — Oral care
    — Gynecology consult
• Nutritional intervention
  • PT and OT
  • Massage
  • Psychosocial support

Donor-Host Tolerance

• Donor-host tolerance can develop
• If no GVHD evident, patients can be tapered off immunosuppression slowly under medical supervision while watching to see if GVHD occurs
• Patients are educated to notify physician between visits if GVHD sx occur

Transplant Survivorship Concerns

• Fatigue
• Fertility & Sexuality
• Growth and development for children
• Secondary Cancers
• Finances & employment
• Caregiver burnout
• Intimacy
• Learning and memory problems
• Late organ damage
Factors influencing HSCT outcomes

- Diagnosis
- Disease status at time of transplant
- Co-morbidities
- Severity of GVHD

Web resources for outcome statistics:
www.bmtinfonet.org
www.bethematch.org
www.cibmtr.org

Resources:

- National Marrow Donor Program
  www.bethematch.org
- “Understanding Cancer” topics
  www.cancer.gov
- Seattle Cancer Care Alliance
  www.seattlecca.org
- American Society for Radiation Oncology
  www.astro.org
- Oncology Nursing Society
  www.ons.org

Questions?

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