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- Email customerservice@PhysicalTherapy.com
Cancer Rehabilitation: Overview & Essentials

Stephen Wechsler, PT, DPT
Board Certified Neurologic Clinical Specialist
Memorial Sloan Kettering Cancer Center
July 12, 2019

Disclosures
None
Learning Outcomes

After this course, participants will be able to:

- Describe the current data trends indicating need for increased cancer rehabilitation services
- Develop a hypothesis for the appropriate stages of rehabilitation in respect to a cancer diagnosis, prognosis, and treatment
- Identify "red flags" requiring immediate referral when evaluating a patient with a history of cancer
- List precautions/safety considerations when working with a patient with a history of cancer
- Indicate side effects of chemotherapy, radiation therapy, surgery, and hormone therapy that are amenable to rehabilitation interventions

A Growing Trend

- Cancer rates are high
  - People are living longer
  - People are living unhealthy lifestyles
  - Environmental factors
- 2018: estimated 1,735,350 new cases diagnosed with 609,640 deaths
  - Versus 1,220,100 and 552,200 in the year 2000
- Approximately 38.4% of men and women will be diagnosed with cancer at some point during their lifetimes
- 2017 national expenditures for cancer care in the US: $147.3 billion

National Cancer Institute
5-Year Survival Rate

1975-1977: 49%
2004-2010: 68%

Credit: National Cancer Institute

Figure 1: Estimated cancer prevalence by age in the US population from 1975 (216 M) to 2040 (360 M)

Signifies the year at which the first baby boomers (those born 1946-1964) turned 65 years old

Credit: National Cancer Institute
Unmet Needs

- Self-reported limitation in functioning
  - 20% of childhood cancer survivors
  - 53% of adult-onset cancer survivors

Cheville, 2017

Unmet Needs

- As many as 2/3 of breast cancer survivors experience 1+ long-term adverse sequelae
  - Fatigue, lymphedema, pain, contractures
- Increased rates of impairment with metastatic disease
- Cohort of 163 pts receiving tx for stage IV breast cancer
  - 92% endorsed at least 1 physical impairment
  - Mean number of impairments: 3.3

Cheville, 2008
Unmet Needs = Increased Costs

- Cancer care is expensive
  - For individuals, families, and our healthcare system
  - National cost could reach $174 billion in 2020
- ↑ Physical disability → ↓ Return to work
- Cancer survivors: 1.4x more likely to be unemployed
  - Psychological needs cannot be overlooked

  de Boer et al., 2009

And yet...

Treatment rates for cancer-related disablement...

1% to 2%!

Cheville et al, 2017
Why the disparity?

- Low detection of physical needs
- Difficulty documenting
  - Standardized language?
- Paucity of literature
  - Rapidly changing
- Low referral rates
  - Lack of awareness?
  - Under-recognition of potential benefits of rehab?

Systemic Issues:

- Shortage of cancer rehab specialists
  - Lack of standardized education/training?
- Rapidly expanding cancer survivor population
  - Difficulty keeping pace

Barriers

- Patients already managing multiple providers
  - Multiple comorbidities and impairments
  - Limited fiscal and energetic resources
- Shift in cancer care model to a community-based delivery system
  - Dissemination of cancer rehabilitation services into this setting has been limited

Alfano et al., 2012
“In effect, the medical system creates a situation where high-functioning individuals are given life-prolonging treatments and then left to struggle with how to recover from the toxic adverse effects”

Silver et al, 2011

Supporting Evidence

- Sedentary behavior before a diagnosis of cancer
  - Increased risk: colorectal, endometrial, lung, & breast cancer
  - Increased risk of all-cancer mortality
- Physical activity before a diagnosis of cancer
  - Decreased risk of all-cancer mortality

Lynch et al, 2017
Supporting Evidence

- Patients who exercised after a diagnosis of cancer
  - Lower relative risk of cancer mortality
  - Lower relative risk of recurrence
  - Fewer/less severe adverse effects

Cormie et al, 2017

Supporting Evidence

- Exercise after a diagnosis of cancer
  - Significant benefits on QoL & physical function
  - Comparable effects across patients with different demographic and clinical characteristics
  - Supervised > unsupervised interventions

Buffart et al, 2017
So how do we begin to think about individualizing a cancer rehab plan of care...

Cancer Rehabilitation
Overview & Essentials

This is a medically complex population

Once safety and scope of practice are established...

You have the skills needed to treat this population!
A Focused Review of Safety Considerations in Cancer Rehabilitation
Maltser, Cristian, Silver, Morris, Stout
PM&R September 2017

Safety Considerations

- Metastatic disease
- Osteoporosis/bone loss
- Myelosuppression
- DVT/PE
- Cachexia/Malnutrition
- Active malignancy

Maltser et al, 2017
Bone Metastases

- Most common: breast, lung, prostate
- Lesions in long bones and spine present greatest risk of pathologic fracture
- General safety measures
  - No MMT in affected limb
  - No progressive resistive exercises through affected limb
  - Offloading WBing through affected limb with AD
  - Spinal precautions (BLT)
  - Monitor for increasing functional pain*

Maltser et al, 2017

Bone Metastases

Rehab interventions are generally safe and effective and do not increase the risk for fractures!

Osteoporosis and Bone Loss

- Most common in hormonally driven cancers
  - Prolonged exposure to hormone therapy
- Increases risk of fracture
- WBing exercise may have a protective effect

Cachexia

- Common with advanced cancer
- Symptoms
  - Marked weight loss
  - Loss of lean muscle
  - Muscle atrophy
  - Fatigue
  - Weakness
  - Loss of appetite
- Exercise in the absence of appropriate energy balance may pose a risk for further functional decline
Modalities & Manual Therapy Precautions

- Impaired sensation
  - Heat, cold, TENS, NMES
- Skin fragility
  - Manual therapy, heat, cold
- Bone fragility
  - Manual therapy, joint manipulation
- Active malignancy
  - NMES, low-level light laser, ultrasound, heat

Malterer et al, 2017

“Red Flags” - Reasons to Refer

- Newly onset pain
  - Unrelenting
  - Nocturnal
  - “Atypical”
- Atypical SOB
  - Hemoptysis
- Change in neuro signs
  - Bowel/bladder
  - Acute focal/diffuse weakness
  - Altered reflexes
- Sudden change in cognitive/functional status
- Possible POD?
- Urgent versus Emergent
Onco-
logic Emergencies

Structure/mechanically induced

- **Spinal Cord Compression**
  - Localized back pain
  - Thoracic region
  - Night pain, increased with thoracic pressure
  - Presentation like SCI

- **Malignant Pericardial Effusion**
  - Primary pericardial tumor
  - Metastatic pericardial disease
  - Reduced cardiac output
  - Dyspnea, cyanosis, hypotensive, tachycardic

- **Superior Vena Cava Syndrome**
  - Tumor burden creates impaired blood flow via superior vena cava
  - Swelling in upper thorax, face, neck, jugular v distension

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Maltser et al, 2017

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Onco-
logic Emergencies

Metabolic

- **Hypercalcemia**
  - May be due to bony mets
  - Diffuse symptoms
    - Lethargy, fatigue, bone pain, abdominal pain, polyuria, weakness

- **Tumor lysis syndrome**
  - Typically 6-72 hrs s/p chemo
  - N/V, weakness, cramping

Hematologic

- **Neutropenic fever**
  - Plus s/s of infection

- **Venothrombotic events**
  - DVT, PE
  - LEs or UEs
A Call for Clinical Reasoning

- We are fighting to establish autonomy
- Direct access continues to expand and grow
- If we can safely and effectively screen and manage patients independently, minimizing external referrals, we can decrease health care costs, decrease potentially unnecessary and harmful testing, improve quality of life of our clients

Ross et al, 2010

Cancer 101
“Cancer is a group of diseases characterized by uncontrolled growth and spread of abnormal cells.”

Staging: TNM System

- **T**: Tumor
  - TX: Main tumor cannot be measured.
  - T0: Main tumor cannot be found.
  - T1-4: Refers to the size and/or extent of the main tumor.
- **N**: Nodes
  - NX: Cancer in nearby lymph nodes cannot be measured.
  - N0: There is no cancer in nearby lymph nodes.
  - N1-3: Refers to the number and location of lymph nodes that contain cancer.
- **M**: Metastases
  - MX: Metastasis cannot be measured.
  - M0: Cancer has not spread to other parts of the body.
  - M1: Cancer has spread to other parts of the body.
Other Ways of Staging

- **In situ**
  - Abnormal cells are present but have not spread

- **Localized**
  - Cancer is limited to the place where it started

- **Regional**
  - Cancer has spread to nearby LN, tissues, or organs

- **Distant**
  - Cancer has spread to distant parts of the body

- **Stage 0**
  - Abnormal cells present but have not spread

- **Stage I**
  - Cancer is small/localized, no LN involvement

- **Stage II**
  - Tumor is >Stage 1, possible LN involvement

- **Stage III**
  - Regional spread + local LN

- **Stage IV**
  - Metastatic disease

Malignant versus Benign

**Malignant**
- Able to spread locally
- Able to invade locally
- Able to metastasize throughout the body via the blood or lymphatic systems
- Can be recurrent

**Benign**
- Space-occupying tumors
- Do not spread, invade, or metastasize
- Usually do not grow back if surgically removed
- Can still be life threatening
Implications of Cancer Stage/Type

- Size of tumor at diagnosis
- Benign vs malignant
- Progressing slowly vs quickly
- Local vs metastatic

Why Stage & Type Matter to Us

- The patient's status along the continuum of cancer care will affect assessment, goals, and treatment plan
  - May dictate duration and frequency
- Survivorship continuum
  - Pretreatment: Recently diagnosed, no tx initiated
  - Active care: Actively receiving tx
  - Maintenance: Long-term antineoplastic therapy
  - Postcare/Remission: Considered “NED”
  - Palliative/Hospice
Palliative Care vs Hospice Care

**Palliative Care**
- Goal is to relieve symptom burden and optimize quality of life
- All ages and stages
  - Curable
  - Chronic
  - Life-threatening

**Hospice Care**
- A specific type of palliative care for people at the end stage of their illness
- Typically offered to patients with less than 6 months life expectancy

PT’s role: Symptom control and management of physical impairments

Common goal: Quality of life

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**Stages of Rehabilitation**

- **Preventative**
  - Reduce the impact/severity of anticipated effects of treatment
  - Can be pre-operative/"Prehab", but not limited to this
  - Assists the individual in learning how to cope, manage, reduce risk

- **Restorative**
  - Interventions to return patients to previous levels of function
  - Varies across the continuum of acute care to survivorship

- **Supportive**
  - Interventions to help patients accommodate for existing impairments and limit further functional changes
  - Assistive devices, cognitive strategies, prosthetics, home services

- **Palliative**
  - Interventions to optimize quality of life for patients and families
  - Pain control, energy conservation, skin care, caregiver training

*Dietz, 1980*
Case Studies

Cancer Rehabilitation
Overview & Essentials

Case Study

1. 56 y.o. female diagnosed with R sided stage III breast cancer (T1N3M0), s/p chemotherapy, mastectomy and axillary lymph node dissection, breast reconstruction with saline implant, radiation therapy to R axilla/chest wall, currently taking an aromatase inhibitor.
2. 70 y.o. male diagnosed with stage I lung cancer (T1N0M0) in R upper lobe, s/p wedge resection tumor removal via video-assisted thoracotomy surgery (VATS) complicated by pneumothorax. Patient then received radiation to tumor bed in R upper lobe.

3. 60 y.o. male diagnosed with stage II oropharyngeal squamous cell carcinoma (T2N2M0) s/p excision via modified radical neck dissection, with adjuvant radiation therapy.
Case Study

4. 29 y.o. female diagnosed with a cerebellar medulloblastoma (Grade II) s/p subtotal resection, radiation to posterior fossa, and chemotherapy.

Cancer Treatments and Rehab Implications
Chemotherapy

Photo by Captain Frank Hurley. (Public domain) (left) Rhoda Baer (Photographer) (Public domain) (right)

How Chemo Works

- Chemotherapy = cytotoxic
- NCI’s definition:
  - “Anticancer drugs that kill cells, especially cancer cells.”
- Techniques of administration:
  - Neoadjuvant: Prior to surgery/radiation
  - Adjuvant: After surgery/radiation
  - To treat primary, recurrent, or metastatic cancer

National Cancer Institute
Chemotherapy & Rehab Implications

Acute Side Effects

- Myelosuppression
  - Thrombocytopenia
    - Platelets
  - Neutropenia/Leukopenia
    - WBC
  - Anemia
    - RBC

- Fatigue
- Nausea/Vomiting
- Mouth/throat sores
- GI distress
- Cognitive Changes

National Cancer Institute

Myelosuppression & Rehab Implications

- Thrombocytopenia
  - <150,000 cells/µL: Symptom-based, monitor tolerance
  - >50,000: Progressive exercise as tolerated (aerobic, resistive), monitoring for s/s bleeding
  - >30,000: AROM, moderate exercise, aquatic therapy
  - >20,000: Light, walking, ADLs, assess fall risk
  - <20,000: Walking, light ADLs (may warrant transfusion)

Maltser, 2017
Myelosuppression & Rehab Implications

- Neutropenia
  - Typically occurs 3-7 days after chemotherapy
  - Increased risk of infection
  - Signs/symptoms may not be present
    - Fever typically earliest sign
  - No compelling evidence that rehab is contraindicated due to neutropenia
  - Interventions should be self-limited by patient
  - Consider use of public vs private therapy space

Maltser, 2017

Myelosuppression & Rehab Implications

- Anemia
  - Reduces exercise tolerance/endurance
  - May have increased HR/RR to maintain adequate O2
  - Hgb <11 g/dL: Establish baseline vital signs
    - May be tachycardic/orthostatic hypotensive
    - Symptom-based approach, monitor RPE
  - Hgb <8 g/dL: Close monitoring of vital signs
    - Short periods of intervention
    - Symptom-limited
    - Education for energy conservation

Maltser, 2017
Chemotherapy & Rehab Implications

Sub-Acute & Chronic Side Effects

- Alopecia (hair loss)
- Soft tissue fibrosis
  - Possible if IV-administered chemo infiltrates local area
- Cardiopulmonary toxicity
- Peripheral Neuropathy (CIPN)
  - Stocking-Glove
  - Sensory > motor
  - Balance impairment

Cardiopulmonary Toxicity

- Can be multifactorial
- Need to consider pre-morbid cardiopulmonary function and comorbidities
- Certain chemotherapies
  - Anthracyclines
- Symptoms
  - Systemic edema, SOB, dyspnea, lung congestion

Childhood/adolescent cancer survivors: 50% demonstrate cardiac-related comorbidity that compromises function 20-30 years after completion of treatment

Maltser, 2017
Chemotherapeutic Agents

Taxanes (Taxol, Paclitaxel)
- Breast, ovarian, lung, bladder, prostate, melanoma, esophageal
- Common rehab impact: Peripheral neuropathy, heart block/bradycardia, respiratory distress

Vinca Alkaloids (Vincristine)
- Acute leukemia, Hodgkin’s/non-Hodgkin’s lymphoma, brain tumors, Ewing’s sarcoma, multiple myeloma, chronic leukemias, thyroid cancer
- Common rehab impact: Peripheral neuropathy (sensorimotor)
  - Wrist/foot drop

Platinums (Cisplatin, Carboplatin)
- Advanced bladder cancer, metastatic ovarian/testicular cancer, head & neck cancer, lung cancer
- Common rehab impact: Ototoxicity, peripheral neuropathy

Cancer Rehabilitation
Overview & Essentials

Time frame and dosing schedule may impact POC
We must assist in monitoring for toxicities
Exercise may increase effectiveness of chemo
Exercise may improve tolerance of chemo
Many side effects amenable to rehabilitation
Case Study

1. 56 y.o. female diagnosed with R sided stage III breast cancer (T1N3M0), s/p chemotherapy, mastectomy and axillary lymph node dissection, breast reconstruction with saline implant, radiation therapy to R axilla/chest wall, currently taking an aromatase inhibitor.

Hormone Therapy
How Hormone Therapy Works

Systemic therapy used to target some types of breast cancer and prostate cancer

**Breast Cancer**

About 2/3 of breast cancers are hormone receptor-positive

- For these cancers, high estrogen levels help the cancer cells grow and spread

**Goals:**

- Reduce levels of estrogen
- Stop estrogen from acting on breast cancer cells

**Prostate Cancer**

Androgens (male sex hormones) stimulate growth of normal and cancerous prostate cells

- Testosterone

**Goals:**

- Reduce levels of androgens
- Stop them from acting on prostate cancer cells

Hormone Therapy Goals

- **Neoadjuvant:** Make tumor smaller before surgery or radiation
- **Adjuvant:** Lower the risk that cancer will recur
- **To treat cancer directly,** especially if cancer has recurred or spread
Hormone Therapies

**Breast Cancer**
- Selective estrogen receptor modulator (SERM)
  - Blocks estrogen receptors in breast cancer cells
  - Tamoxifen
- Aromatase Inhibitors
  - Typically used in postmenopausal women
  - Stop estrogen production
  - Letrozole, Anastrozole, Exemestane

**Prostate Cancer**
- Orchiectomy (surgical)
- Luteinizing hormone-releasing hormone (LHRH) agonists
  - Lower the amount of testosterone made by the testicles
- Anti-androgens
  - Bind to androgen-receptors so androgens can't

Hormone Therapy and Rehab Implications

**Common side effects:**
- **Tamoxifen**
  - Risk of blood clot
  - Bone loss
- **Aromatase Inhibitors**
  - Muscle/joint pain
- **Androgen Deprivation Therapy**
  - Osteoporosis
  - Decreased muscle mass
  - Fatigue
  - Anemia
  - Weight gain
  - Depression
Aromatase Inhibitors & Exercise

- Aerobic & Resistance training
- Healthy post-menopausal women versus women on AI
- Similar improvements:
  - Lower body strength
  - V02 max
  - Body fat mass

Gardner et al., 2014

d'Espallier et al., 2018

Androgen-Deprivation Therapy & Exercise

- Aerobic/resistance training
- Benefits
  - Muscular strength
  - Cardiorespiratory fitness
  - Functional task performance
  - Lean body mass
  - Fatigue

Gardner et al., 2014
Hormone therapy can last several years following primary treatment.

Side effects can impact daily function and QoL:
Weakness, weight gain, muscle/joint pain, fatigue, osteoporosis

Exercise can mitigate some side effects.

Patient education is key.

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**Case Study**

1. 56 y.o. female diagnosed with R sided stage III breast cancer, s/p chemotherapy, mastectomy and axillary lymph node dissection, breast reconstruction with saline implant, radiation therapy to R axilla/chest wall, currently taking an aromatase inhibitor.
Radiation Therapy

How Radiation Works

- Damages cellular DNA, killing or slowing growth of cells
  - Cells stop dividing/die
    - Broken down and removed by body
  - Cells do not die immediately
    - Takes days/weeks for DNA to become damaged enough
      - Cells continue dying for weeks/months following treatment
Techniques of Administration

- External Beam Radiation Therapy
- Internal Radiation Therapy
  - Brachytherapy Therapy (solid, radioactive seeds)
  - Systemic Therapy (liquid via blood)
- Intended Outcomes
  - Curative
  - Preventative
  - Palliative

Radiation Side Effects

Side effects:
- Myelosuppression
- Alopecia
- Fatigue
- Nausea/vomiting
- Pulmonary fibrosis
- Plexopathies/neuropathies
- Radiation myelitis/inflammation at spinal cord
- Bone loss/joint necrosis
- Muscle atrophy
- Skin irritation -> desquamation
- Soft tissue fibrosis
Radiation & Rehab Implications

- Skin irritation -> desquamation, ulceration of skin/membranes
  - Precaution should be taken with red/tender/blistered skin
  - Usually limit to AROM/AAROM, gentle therapeutic exercise
- Bone loss/joint necrosis
  - May increase risk for fracture
  - May need to consider precautions or seek input from referring MD
- Fatigue
  - Etiology is multifactorial
    - Effect of treatment?
    - Effect of treatment schedule?

Radiation-Induced Fibrosis

- Influenced by dose, volume, schedule, previous tx, genetic susceptibility, certain comorbidities (DM)
- Radiation causes microvascular injury which may lead to ischaemic hypoxia and inflammatory changes in surrounding tissue
  - Loss of tissue compliance (muscle, skin, lung)
  - Development of strictures (hollow organs)
  - Impaired gaseous diffusion (alveolae, capillaries)
Radiation-Induced Fibrosis

- Typically 6 mo-5 yrs following treatment
  - Can progress indefinitely
- Early initiation of active and passive intervention is key
- Soft tissue mobilization
  - Increase blood flow
  - Increase pliability of skin for AROM and neuro re-ed
- May impact muscle’s ability to stretch/strengthen

Cancer Rehabilitation, Stubblefield, O’Dell

Radiation-Induced Fibrosis Precautions

- Use of modalities
  - Decreased blood supply
  - Decreased sensation
- Manual techniques in areas of skin breakdown
- Lymphedema precautions when indicated
- Weight bearing precautions when indicated

Stubblefield, 2011
Cancer Rehabilitation
Overview & Essentials

Remain anatomically-focused - Know the irradiated area

Establish all structures within this area

Go 1-2 steps outside of the radiated area

Think big picture - Relate to function

Potentially progressive - Patient education is key

Case Study

2. 70 y.o. male diagnosed with stage I lung cancer in R upper lobe, s/p wedge resection tumor removal via video-assisted thoracotomy surgery (VATS) complicated by pneumothorax. Patient then received radiation to tumor bed in R upper lobe.
Surgery

Credit: U.S. Army photo by Marcy Sanchez (photographer)

How Surgery Works

- Surgeons resect part of/all cancerous tissue
  - Soft tissue
  - Bony tissue
- Goals of surgical intervention:
  - Total resection of tumor
  - Debulking in conjunction with other treatments
  - Palliative
  - Prophylactic

National Cancer Institute
Cancer Surgery Considerations

- Was bone removed?
- Was muscle sacrificed?
- Were muscles transferred?
- Were specific nerves sacrificed?
- Was a lobe of the brain impacted?
- Were lymph nodes removed?
- Weight bearing status?
- Lifting precautions?
- ROM precautions?
- Functional potential/prognosis?

Cancer Rehabilitation, Stubblefield, O’Dell

Cancer Rehabilitation
Overview & Essentials

Remain anatomically-focused
Consider impact of scar tissue
External and internal
Need to facilitate tissue healing, prevent restrictions in function and optimize functional status
How will surgical report impact goal setting?
Case Study

3. 60 y.o. male diagnosed with oropharyngeal squamous cell carcinoma s/p excision via modified radical neck dissection, with adjuvant radiation therapy.

Cancer Rehab Cheat Sheet

1. Chart review
   a. Understand the patient’s cancer stage
      i. Where are they in the continuum?
2. Form a hypothesis re: the appropriate rehab stage
   a. This can be a dynamic and working hypothesis
3. Listen to the patient’s subjective and history
   a. Are the patient’s chief complaints indicative of any potential red flags?
   b. Are the patient’s goals in line with your hypothetical rehab stage?
4. Screen for red flags/concerns (yours or patient’s)
5. Assess and treat the patient’s chief complaint while not losing sight of the patient as a whole
Cancer Rehabilitation Overview & Essentials

Cancer Rehab Cheat Sheet

1. Chart review
   - Reason for referral
   - Medical history
   - Oncologic history
   - Surgical precautions
     - ROM/lifting restrictions
   - Weight bearing considerations
     - Bony involvement
   - Lab values
   - Psychosocial considerations

2. Form a hypothesis re: the appropriate rehab stage
   - This should be a dynamic and working hypothesis

3. Listen to the patient’s subjective and history
   - Are the patient’s chief complaints indicative of any potential red flags?
   - Are the patient’s goals in line with your hypothetical rehab stage?

4. Screen for red flags/concerns (yours or patient’s)

5. Assess and treat the patient’s chief complaint while not losing sight of the patient as a whole
Cancer Rehabilitation
Overview & Essentials

**Cancer Rehab Cheat Sheet**

2. Form a hypothesis re: the appropriate rehab stage
   - Preventative
   - Restorative
   - Supportive
   - Palliative

   *This *should* be a dynamic and working hypothesis*

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**Case Study**

4. 29 y.o. female diagnosed with a cerebellar medulloblastoma (Grade II) s/p subtotal resection, radiation to posterior fossa, and chemotherapy.
Cancer Rehab Cheat Sheet

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Cancer Rehabilitation
Overview & Essentials

**Cancer Rehab Cheat Sheet**

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5. Assess and treat the patient’s chief complaint while not losing sight of the patient as a whole

This is a medically complex patient population
There must be certain considerations to maintain safety

Once safety and scope of practice is established…
you HAVE the skills needed to treat this population!
These patients have been through or are currently on a challenging journey

Each patient’s experience and ‘cancer story’ is unique and important

We have the opportunity to provide a positive environment, a positive experience, and to make a positive change in their journey

References

References