PRINCIPLES AND PRACTICE OF CANCER REHABILITATION

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Disclosures:
None
Cancer Rehabilitation
Job Description

A specialist in the identification, evaluation, and rehabilitation of neuromuscular, musculoskeletal, pain, and functional disorders associated with cancer and it’s treatment emphasizing the restoration and maintenance of function and quality of life.
Cancer Rehabilitation
Contemporary Perspective: United States

- 14 million cancer survivors in 2014\(^1\)
- 18.1 million cancer survivors by 2020\(^2\)
- 273,000 spinal cord injury survivors in 2013\(^3\)
- Approximately 68% of persons diagnosed with cancer today can expect to live at least 5 years after diagnosis compared with only 49% in the 1970’s and 35% in the 1950’s.\(^4\)

Cancer Rehabilitation

US Estimate of Survivors vs. New Cancer Diagnoses and Deaths in 2014

- Survivors: 1.66 Million
- New Cancers: 0.58 Million
- Cancer Deaths: 14.0 Million

Practice of Cancer Rehabilitation
Cancer Rehabilitation
Success Requires and Understanding of:

• Cancer

• Cancer treatment
  – Surgery
  – Chemotherapy
  – Radiation Therapy

• Pre-existing disorders

• The interrelationship between all of the above
Cancer Rehabilitation
“The Dirty Little Secret”

The principles and practice of cancer rehabilitation are generally similar to those of general rehabilitation...
Cancer Rehabilitation

Neuromuscular, Musculoskeletal, and Pain Disorders Commonly Seen in Cancer Survivors

• Neuromuscular
  – Cerebropathy
  – Myelopathy
  – Radiculopathy
  – Plexopathy
  – Neuropathy
    • Polyneuropathy
    • Mononeuropathy
    • Mononeuropathy Multiplex
    • Ganglionopathy
    • Small Fiber
  – Myopathy
  – Disorders of Neuromuscular Transmission

• Musculoskeletal
  – Rotator Cuff Tendonitis
  – Adhesive Capsulitis
  – Epicondylitis
  – De Quervain's Tenosynovitis
  – Neuroforaminal/Central Stenosis
  – Spinal Instability
  – Fracture/Impending Fracture
  – Arthritis
  – Enthesopathy
  – Osteoporosis
  – GVHD
  – Scoliosis
  – Bony Metastases
Cancer Rehabilitation

Functional Disorders Commonly Seen in Cancer Survivors

- Lymphedema
- Fatigue
- Myalgia
- Fibromyalgia
- Autonomic dysfunction
- Cardiac dysfunction
- Pulmonary dysfunction
- Endocrine dysfunction
- Gastrointestinal dysfunction
- Genitourinary dysfunction
- Cognitive dysfunction
- Psychiatric dysfunction
- Psychosocial dysfunction
Cancer Rehabilitation
Spectrum of Need in Cancer Survivors

Mild       Moderate       Severe
Impending Fracture
Pathologic Fracture
Impending Fracture Risk

• Why prevent fractures?
  – Concept first prophylactic fixation of impending fracture was first presented by Griessman in 1947.¹
  – Though unproven, the proposed benefit to patients include²
    • Technically easier operation
    • Decreased operating time
    • Less blood loss
    • Decreased complication
    • Decreased pain
    • Convenience

Pathologic Fracture
Impending Fracture Risk

• Osteolytic
  – Characterized by lysis or bone destruction
  – Secretion of proteases directly stimulate bone resorption or the release of osteoclast-stimulating factors

• Osteoblastic
  – Characterized by new bone growth
  – Appear dense on X-ray and CT
  – Bone produced is not good quality
  – Thought to be less prone to fracture
Pathologic Fracture
Impending Fracture Risk

• Radiographic Detection of Bone Tumors
  – X-Ray
  – Bone Scan
  – CT
  – PET - CT
  – MRI
Pathologic Fracture
Impending Fracture Risk

• X-Ray
  – Relative poor screening test for metastasis
  – Up to 50% of bone needs to be destroyed before lytic lesion is visible on radiographs
  – Can identify collapse deformities in the spine
Pathologic Fracture
Impending Fracture Risk

• Bone Scan
  – More sensitive than plain films for detecting metastasis
  – Often also abnormal by disease processes other than tumor-degenerative change
  – Some tumors such as multiple myeloma or those limited to the marrow or soft tissue may not be detected
Pathologic Fracture
Impending Fracture Risk

• Computed Tomography
  – Useful for assessing the degree of bone destruction
  – Can often use the CT obtained for other reasons, i.e., CT of the chest, abdomen, or pelvis
  – Information on soft tissues provided
Pathologic Fracture
Impending Fracture Risk

• Positron Emission Tomography – Computed Tomography (PET – CT)
  – Correlates the distribution of metabolic or biochemical activity with anatomy.
  – Same benefits of CT with the correlated metabolic/biochemical information.
Pathologic Fracture
Impending Fracture Risk

• Magnetic Resonance Imaging (MRI)
  – Noninvasive
  – High tissue contrast
  – Multiplanar capabilities
  – Most sensitive and specific modality for imaging spine abnormalities
  – Not particularly good for imaging bone and assessing fracture risk
  – Good for imaging the spine, particularly epidural disease and intramedullary or leptomeningeal disease if gadolinium provided
Pathologic Fracture
Impending Fracture Risk

• Risk Factors
  – Anatomic site
    • i.e., long bones
  – Pain
    • i.e., biologic, functional
  – Primary tumor type
    • i.e., multiple myeloma
  – Amount of bony destruction
    i.e., 50% cortical destruction, >2.5 cm diameter
  – Lytic vs. blastic

Pathologic Fracture
Impending Fracture Risk

• Risk Factor Caveats
  – Lesions not static and tend to progress
  – Degree of bone destruction difficult to measure
  – Amount of weight bearing placed on a bone difficult to measure
  – A collapsed vertebral body can still support weight
  – Chemotherapy has improved
  – Steroids and other osteoporosis-inducing drugs common
  – Radiation therapy has improved but can cause radio-osteonecrosis
  – Bisphosphonates are standard therapy in bone metastases

Pathologic Fracture
Impending Fracture Risk

<table>
<thead>
<tr>
<th>Variable</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td>Site</td>
<td>Upper limb</td>
</tr>
<tr>
<td>Pain</td>
<td>Mild</td>
</tr>
<tr>
<td>Lesion</td>
<td>Blastic</td>
</tr>
<tr>
<td>Size</td>
<td>&lt;1/3</td>
</tr>
</tbody>
</table>

The Malignant Spine
The Malignant Spine
Tumor Location

The Malignant Spine
Epidural Disease from Metastatic Prostate Cancer
The Malignant Spine
Leptomeningeal Disease from Metastatic Breast Cancer
The Malignant Spine
Intramedullary Ependymoma
The Malignant Spine
Epidural Spinal Cord Compression
The Malignant Spine
Definition of Spinal Instability

The Spine Oncology Study Group (SOSG) defines spine instability as loss of spinal integrity as a result of a neoplastic process that is associated with movement-related pain, symptomatic or progressive deformity, and/or neural compromise under physiologic loads.

The Malignant Spine
Mechanical Instability vs. Biologic Pain

Mechanical Instability

• Requires Surgery
• Defined by level of tumor involvement
• Involves release of chemical mediators, elevated intraosseous pressure, and stretching or irritation of the periosteum
• Movement Related
• Exacerbated increased axial load (sitting, standing)
• Not helped by steroids

Biologic/Tumor

• Involves release of chemical mediators, elevated intraosseous pressure, and stretching or irritation of the periosteum
• Worse at night and when recumbent
• Responds to steroids

### The Malignant Spine

**Spinal Instability Neoplastic Score (SINS)**

<table>
<thead>
<tr>
<th>SINS Component</th>
<th>Description</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Location</strong></td>
<td>Junctional (Occ-C2, C7-T2, T11-L1, L5-S1) Mobile (C3-6, L2-4) Semirigid (T3-10) Rigid (S2-5)</td>
<td>3</td>
</tr>
<tr>
<td><strong>Pain</strong></td>
<td>Yes* Occasional non-mechanical pain No</td>
<td>3, 1, 0</td>
</tr>
<tr>
<td><strong>Bone Lesion</strong></td>
<td>Lytic Mixed Blastic</td>
<td>2, 1, 0</td>
</tr>
<tr>
<td><strong>Alignment</strong></td>
<td>Subluxation / translation De novo deformity Normal</td>
<td>4, 2, 0</td>
</tr>
<tr>
<td><strong>Vertebral Body</strong></td>
<td>&gt;50% collapse &lt;50% collapse No collapse with &gt;50% VB involved None of above</td>
<td>3, 2, 1, 0</td>
</tr>
<tr>
<td><strong>Posterolateral Involvement of Spinal Elements†</strong></td>
<td>Bilateral Unilateral None</td>
<td>3, 1, 0</td>
</tr>
</tbody>
</table>

### Clinical and Radiographic data from 30 patients reviewed by members of the Spine Oncology Study Group on 2 occasions at least 6 weeks apart using SINS

<table>
<thead>
<tr>
<th></th>
<th>Stable</th>
<th>Potentially Unstable</th>
<th>Unstable</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-6</td>
<td>7-12</td>
<td>13-18</td>
</tr>
</tbody>
</table>

### SINS demonstrated near-perfect inter- and intra- observer reliability in determining three clinically relevant categories of stability

*Pain improved with recumbency and/or pain with movement/loading of spine
†Facet, pedicle, or costovertebral joint fracture or replacement with tumor

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Radiation Fibrosis Syndrome
Radiation Fibrosis Syndrome
Common Clinical Sequelae

- Myelo-radiculo-plexo-neuro-myopathy
- Cervical dystonia
- Neck extensor weakness ("dropped head syndrome")
- Trigeminal neuralgia
- Cervical plexopathy
- Trismus (oropharyngeal dystonia)
- Mononeuropathies
- RTC tendonitis/adhesive capsulitis
- Lymphedema

Radiation Fibrosis Syndrome
Myelo-Radiculo-Plexo-Neuro-Myopathy from Mantle Field Radiation for Hodgkin Lymphoma
Radiation Fibrosis Syndrome
Management of Neck Extensor Weakness

• Education
• Physical Therapy
  – Neuromuscular Reeducation
    • Postural correction
    • Proprioceptive reeducation
    • Core strengthening
    • Scapular retraction/depression
    • Muscle balancing
  – MLD
  – Soft Tissue Mobilization
    • Advanced myofascial techniques
    • “Facia is the arch-nemeses”
• Medications
  – Nerve stabilizers, muscle relaxants, opioids
• Orthotics
  – Headmaster Cervical Collar

A 57 year old man with largely right sided nasopharyngeal carcinoma diagnosed in 2002 and treated with 5-Fu and IMRT 7020 cGy to the primary disease and neck now with right sided cervical dystonia and mild to moderate upper trunk brachial plexopathy.
Radiation Fibrosis Syndrome

Trismus

• Trismus is defined as the inability to fully open the mouth

• \( \leq 35\text{mm} \) cut-off point for defining trismus has a sensitivity of 0.71 and a specificity of 0.98\(^1\)

• Patients with trismus may have difficulty with eating, speaking, maintaining oral hygiene, being surveyed for cancer recurrence, engaging in oral intimacy, or a variety of other important aspects of daily life

• The incidence of trismus may be as high as 28% in HNC patients 1 year after treatment \(^2\)


Radiation Fibrosis Syndrome
Management of Radiation-induced Trismus

- Education
- Physical Therapy
  - Soft Tissue Mobilization
    - Advanced myofascial techniques
  - Neuromuscular Reeducation
    - Postural correction
    - Proprioceptive reeducation
    - Muscle balancing
  - MLD
- Medications
  - pregabalin, gabapentin, duloxetine
- Orthotics
  - Dynasplint, Therabite
- Injections
  - Botulinum Toxin Injection

Radiation Fibrosis Syndrome

Jaw Opening Devices for Trismus

- Tongue Depressors
- Cork Screw Device
- Therabite® Trismus System
- Dynasplint® Trismus System

# Radiation Fibrosis Syndrome

Changes in Maximal interincisal Distance (MID) Before and After Treatment with Dynasplint Trismus System

<table>
<thead>
<tr>
<th>Patients</th>
<th>No.</th>
<th>Pretreatment Score Median (Range)</th>
<th>Posttreatment Score Median (Range)</th>
<th>Difference in Scores Median (Range)*</th>
<th>p-value†</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>20</td>
<td>16.5 (9 to 41)</td>
<td>23.5 (10 to 47)</td>
<td>5 (-4 to 15)</td>
<td>.0003</td>
</tr>
<tr>
<td>Compliant</td>
<td>15</td>
<td>16 (11 to 41)</td>
<td>27 (11 to 47)</td>
<td>7 (0 to 15)</td>
<td>.0001</td>
</tr>
<tr>
<td>Noncompliant</td>
<td>5</td>
<td>17 (9 to 30)</td>
<td>22 (10 to 26)</td>
<td>-1 (-4 to 5)</td>
<td>.88</td>
</tr>
</tbody>
</table>

*Based on the difference of the preintervention and postintervention values for each individual patient.

†P values were calculated for differences in the pretreatment and posttreatment scores using the Wilcoxon signed-rank test.

Radiation Fibrosis Syndrome
Lymphedema in HNC Patients

- Often underdiagnosed and neglected
- Can be external (face, neck, chest) or internally (larynx, pharynx, oral cavity)
- Has adverse cosmetic and psychosocial consequences (infections, breathing or swallowing difficulties, etc.)
- Diagnosed on clinical grounds (external) or by endoscopic evaluation (internal)
- In one study 75.3% of HNC patients have secondary lymphedema
  - 9.8% isolated internal lymphedema
  - 39.4% isolated external lymphedema
  - 50.8% combined internal and external lymphedema


Radiation Fibrosis Syndrome
Radiculoplexopathy Following Single Fraction Radiation with 2400 cGy for Metastatic Papillary Thyroid CA
Neuropathy
Neuropathy in Cancer
Spectrum of Neuropathy in Cancer Survivors

Mild
Moderate
Severe

Normal
Femoral Mononeuropathy from Metastasis
POEMS
# Neuropathy in Cancer

## Common Neurotoxic Chemotherapeutics

<table>
<thead>
<tr>
<th>Category</th>
<th>Drugs</th>
</tr>
</thead>
</table>
| **Platinum Analogues** | - Cisplatin  
                  |     - Carboplatin  
                  |     - Oxaliplatin  |
| **Vinca Alkaloids**   | - Vincristine  
                  |     - Vinblastine  
                  |     - Vinorelbine  
                  |     - Vindesine  |
| **Taxanes**           | - Paclitaxel  
                  |     - Abraxane  
                  |     - Docetaxel  |
| **Others**            | - Bortezomib  
                  |     - Ixabepilone  
                  |     - Thalidomide  
                  |     - Lenalidomide  |

Neuropathy in Cancer
Incidence of Neuropathy by Agent

- **Taxanes**
  - Paclitaxel: 57%-83% overall; 2%-33% severe
  - Docetaxel: 11%-66% overall; 3%-14% severe
- **Vinca alkaloids**
  - 30%-47%
- **Platinum Analogues**
  - Cisplatin: 28%-100%
- **Capecitabine (unknown)**
- **Capecitabine + Ixabepilone (microtubulin-targeting agent)**
  - 67% overall; 21% severe
- **Paclitaxel + Carboplatin**
  - 67%

Neuropathy in Cancer
Vinca Alkaloids (vincristine, vinblastine, vinorelbine)

• Indications:
  – Solid tumors, lymphoma, leukemia

• Mechanism of action:
  – Binds tubulin and blocks its polymerization into microtubules
  – Arrests mitosis in metaphase

• Clinical Features:
  – Distal symmetric sensorimotor axonal PN
  – Affects large and small fibers
Neuropathy in Cancer
Taxanes (paclitaxel, docetaxel)

• From Pacific Yew Tree (*Taxus brevifolia*)
• Indications:
  – Solid tumors (i.e., ovarian and breast cancer)
• Mechanism of action:
  – Binds tubulin and blocks its polymerization into microtubules
  – Arrests mitosis in metaphase
• Clinical Features:
  – Distal symmetric sensorimotor axonal PN
  – Affects large fiber > small fiber functions
Neuropathy in Cancer
Platinum Analogues (cisplatin, carboplatin, oxaliplatin)

• Indications:
  – Solid tumors (ie, ovarian, testicular, & bladder cancer)

• Mechanism of action:
  – Binds and cross-links DNA, inhibits protein synthesis, and impairs axonal transport

• Clinical Features:
  – Preferential damage to dorsal root ganglion
  – Distal symmetric predominately sensory axonal PN
  – Affects large fiber > small & sensory > motor fibers
  – Sensory ataxia
  – Symptoms can appear after treatment and progress for months following treatment
Neuropathy in Cancer
Compressive Causes of Radiculopathy

- Disk Herniation
- Central Stenosis
- Facet Arthropathy
- Spondylolisthesis
Neuropathy in Cancer
Causes of Non-compressive Radiculopathy

Arachnoiditis from Epidural Catheter

Waldenström's Macroglobulinemia

IgM MGUS

CIDP
Upper Body Pain Disorders
Common Diagnoses

- Neuromuscular
  - Cervical Radiculopathy
  - Brachial Plexopathy
  - Polyneuropathy
  - Mononeuropathy
  - Post-mastectomy pain syndrome
  - Complex regional pain syndrome

- Lymphovascular
  - Lymphedema
  - Axillary web syndrome
  - Post-thrombotic syndrome

- Musculoskeletal
  - Post-surgical pain
  - Rotator cuff disease
  - Bicipital tendonitis
  - Adhesive capsulitis
  - Bony metastases
  - Epicondylitis
  - DeQuervain’s tenosynovitis
  - Arthralgias
  - Arthritis

- Integumentary
  - Cellulitis
  - Radiation dermatitis

Upper Body Pain Disorders
Shoulder Pain and Dysfunction Cycle

Breast Surgery
Radiotherapy
Neurotoxic Chemotherapy
Advanced Age
Recurrent Disease

C-5 or C-6 Radiculopathy
Upper Trunk Brachial Plexopathy

Shoulder Pain
Rotator Cuff Weakness
Decreased Shoulder Movement
Foreshortened Pectoral Soft Tissues

Adhesive Capsulitis

Rotator Cuff Tendonitis

Exercise and Lymphedema
“Some of the psychological and physiological challenges faced by cancer survivors can be prevented, attenuated, treated or rehabilitated through exercise”

• Exercise is Safe
  – During and after cancer treatments*
  – Results in improvements in
    • Physical functioning
      – Aerobic fitness
      – Muscular strength
      – Flexibility
    • Quality of life
    • Cancer-related fatigue
    • Body image & composition
    • Anxiety

Lymphedema
Upper Extremity Exercise for Breast Cancer Survivors

Upper body exercise has historically been discouraged in breast cancer survivors following axillary lymph node dissection and/or radiation for fear of precipitating or exacerbating lymphedema.

Lymphedema

Dragon Boat Racing

McKenzie DC. Abreast in a boat--a race against breast cancer. CMAJ 1998;159(4):376-8
Lymphedema
Weight Lifting in Women with Breast Cancer-Related Lymphedema

- 141 Breast Cancer survivors with lymphedema
  - 71 twice weekly weight lifting
    - No upper limit on progression
    - Instructed to wear compression garment
  - 70 controls
    - Instructed not to change their exercise during the study

Lymphedema
Weight Lifting in Women with Breast Cancer-Related Lymphedema

• Primary Outcome
  – 5% change in hand/arm swelling at 1 year

• Secondary Outcomes
  – Exacerbations of lymphedema
  – Amount and severity of lymphedema symptoms
  – Muscle strength

Lymphedema

Weight Lifting in Women with Breast Cancer-Related Lymphedema

• Results: Primary Outcome
  – Compared with Controls, weight lifters did not have worsening of their lymphedema (11% vs. 12%)

• Results: Secondary Outcomes
  – Exacerbations of lymphedema decreased (14% vs. 29% in controls)
  – Amount and severity of lymphedema symptoms decreased (p=0.03)
  – Upper- and lower-body strength increased (p<0.001)

Lymphedema
Weight Lifting in Women at risk for Breast Cancer-Related Lymphedema

• 154 Breast Cancer survivors 1-5 years post-breast cancer surgery (including lymph node removal) with **no clinical signs of lymphedema**
  – 72 randomized to weightlifting in a community fitness center (usually a YMCA) with 13 weeks supervised instruction and 9 months unsupervised
  – 75 controls

Lymphedema
Weight Lifting in Women at risk for Breast Cancer-Related Lymphedema

• Primary Outcome
  – 5% change in hand/arm swelling at 1 year

• Results
  – No increase incidence of lymphedema
  – 11% (8/72) in the weight lifting group vs. 17% (13/75) in the control group developed lymphedema (p=0.04)
  – In women with ≥5 lymph nodes removed 7% (3/45) in the weight lifting group vs. 22% 11/49 in the control group developed lymphedema (p=0.003)

Lymphedema
Compression Garments and Exercise

• The National Lymphedema Network position paper on exercise states “current understanding of the underlying physiology provides strong support for the use of compression garments”

• The systematic review by Kwan et al. states that “a clear evidence-based recommendation for use of compression garments cannot be made based on this current review”

Thank You