Cure or Curse?
A review of long-term side effects from pelvic radiation therapy

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June 2018

Objectives
1. Current treatment modalities which cause long-term complications in pelvic radiation therapy patients.
2. Complications which affect quality of life of pelvic radiation therapy patients.
3. Known techniques which reduce long-term post-pelvic radiation therapy complications.
5. Specific strategies a medical dosimetrist can consider using to help patients reduce long-term side effects from pelvic radiation therapy.
New Pelvic Cancers in 2016

- Gynecologic
  - Cervix: 13,000
  - Uterus: 60,000
  - Vaginal: 4600
  - Vulva: 6000
- Prostate: 181,000
- Bladder: 77,000
- Anal/rectal/testicular/urethral: 58,000


Jane’s Story

Jane is a 44 year old thin female, who presented with Stage IB-2 squamous cell carcinoma of the cervix. Medical history unremarkable. Non-smoker. She completed pelvic radiotherapy to 45Gy, Cisplatin x 5 cycles and 5 intracavitary brachytherapy treatments. Two years post-treatment she presents with thoughts of suicide secondary to sexual dysfunction which is manifested by decreased libido and painful intercourse plus bowel toxicity complications of chronic diarrhea, pain, fecal incontinence and partial intermittent small-bowel obstruction episodes. Her comment, “Had I known life would be like this now, I would not have undergone treatment.”
**Treatment Modalities**

- External beam radiation
  - Standard
  - IMRT
  - IGRT
- Brachytherapy
  - LDR vs HDR
  - CT vs MRI vs ViewRay
- Radiosensitizing chemotherapies
  - Cisplatin
  - Gemcitabine
  - Fluoropyrimidines

*Bansal, et al (2013)*

**Pelvic Radiation Therapy**

- Standard 4-field
  - Quick
  - More normal tissue radiated
- 3D-CRT
  - IMRT: Less normal tissue radiated; increased costs
  - IGRT: Even less normal tissue radiated; costly
- Proton
  - No prospective head to head comparison (proton vs IMRT)
Radiation Field Comparison to Anatomic Model

“Normal” 4-field RT pelvis

“Normal” (Female) Anatomic Pelvis

Example: Isodose Distribution of a “normal” 4-field pelvis to 45Gy
Example: Isodose Distribution of an IMRT plan on Tomotherapy to 45Gy

Brachytherapy

- X-ray
  - Quickest
  - Cheap
  - Radiation exposure
  - Images poor quality
- CT
  - Quicker
  - More expensive than plain film
  - Radiation Exposure
  - Images good quality
Brachytherapy

- MRI/ViewRay
- Not so quick
- Expensive
- No radiation exposure
- Imaging excellent quality
- High vs Low dose
  - Low: cheaper??, radiation exposure to staff, hospital costs, patient inconvenience, side effects related to hospitalization as well as radiation
  - High: expensive, quick, fewer treatment side effects

Radiosensitizing Chemotherapy

- Cisplatin
- Gemcitabine
- Fluoropyrimidines

Raviraj, et al 2014
Complications of Pelvic RT

- Bowel dysfunction
- Sexual dysfunction
- Bladder dysfunction
- Pelvic bone changes
- Skin changes
- Lumbosacral plexopathy

Before Radiation

Roof = epithelium (inner layer)
Muscle
Submucosa
Foundation (outer layer)
Chimney = Papilla
After Radiation

Roof = epithelium (inner layer)

Chimney = Papilla

Submucosa

Muscle

Foundation (outer layer)

Radiation Enteritis

Risk Factors for Bowel Complications

- Cancer site
- Volume of tissue treated
- Treatment schedule
- Total dose
- Dose per fraction
- Type of RT
- Previous pelvic surgeries
- Pelvic inflammatory disease
- Comorbid illness
  - IBD
  - Vascular disease
  - Active collagen disease
- Tobacco


Acute Radiation Enteritis

- Acute < 3mo post RT
- Onset w/in 2 weeks of starting pelvic RT
- Peaks 4-5 weeks
- Resolves after 2-6 months
- Affects 60-80% patients

Morris, et.al. (2015)
Radiation Enteritis:
Acute Signs and Symptoms
- Nausea
- Vomiting
- Tenesmus
- Bowel cramping
- Mucous discharge
- Fecal urgency
- Decreased appetite
- Bleeding

Radiation Enteritis:
Acute Treatment
- Bulking agents
- Probiotics
- Anti-kinetics
- Anticholinergics/Anti-spasmotics
- Analgesics
- Rehydration
Chronic Radiation Enteritis

- Chronic 6mo-3years – 3 decades
- Cross over with acute phase
- “Late” reacting tissues

Radiation Enteritis: Chronic Signs and Symptoms

- Bowel urgency
- Malabsorption
- Fecal incontinence
- Bleeding
- Fistulas
- Strictures
- Ulcerations
- Bowel thickening
Radiation Enteritis: Chronic Treatment

- Low fat
- Low fiber
- Low residue
- Adequate calories
- Anti-inflammatories
- Hydration
- Steroid enemas
- Bile salt absorption
- Argon plasma coagulation

Steps to Bowel Recovery

- Patient education
- Food diary
- Anti ..... 
- Vitamin B12
- Referral to gastroenterology
- Referral for nutritional evaluation
- Hyperbaric therapy

Paul’s Story

Paul is a 74 year old male, with h/o diabetes and tobacco abuse, diagnosed with adenocarcinoma of the prostate. Gleason score 4+5. Treated with robotic nerve sparing radical prostatectomy. Experienced post-surgery incontinence and erectile dysfunction. Stage T3aN0M0. 6 mo follow-up notes PSA now 4.2 which warrants pelvic RT. 10 mo post-RT follow-up Paul c/o urinary frequency, nocturia, ongoing erectile dysfunction despite use of medications and bleeding with bowel movements.
Proctitis

- **Acute**
  - Occurs within 6 weeks of pelvic RT completion
  - Affects 8-13% with brachytherapy and 21% with EBRT and brachytherapy
  - Dose <45Gy few side effects while >70Gy significant long-term side effects
  - SSx: diarrhea, mucous discharge, urgency, tenesmus and bleeding

- **Chronic**
  - Occurs 9-14 months post RT and up to 30 years
  - SSx: same as above but worse; may also have bowel strictures, fistulas, bleeding

Viswanathian, et al. 2014

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Proctitis

- **Treatment**
  - Supportive comfort care
  - Metronidazole
  - Enemas (sucralfate or glucocorticoids)
  - Argon plasma coagulation (APC)
  - Hyperbaric therapy
Risk Factors for Bladder Toxicity

- Obesity
- Previous GU surgeries
- Tobacco use
- Radiation type, dose, volume of tissue (think balloon)

Bladder Dysfunction: Acute Signs and Symptoms

- Dysuria
- Urgency
- Frequency
- Nocturia

Bradley & McHaffie, [2015]
Bladder Dysfunction: Acute Treatment

- Evaluate and treat UTI
- Anti-inflammatories
- Anticholinergics/Anti-spasmodics
- Cranberry juice
- Peri-bottle/Sitz bath

Bladder Dysfunction: Chronic Signs and Symptoms

- Decreased bladder capacity leads to
  - Urgency
  - Frequency
- Loss of tissue compliance
- Hemorrhagic cystitis
- Ureter and/or urethra stricture
- Bladder stones
Bladder Dysfunction: Chronic Treatment

- Referral to Urology or Uro-Gynecologist
- Pelvic floor PT
- Hyperbaric therapy

Sexual Complications
Men’s Sexual Health

- Partial or complete loss of erectile function
- Sex bother
- Loss of libido
- Ejaculation changes
- Reduced penile length, sensation and curvature

Sexual Health Treatments

- Men
  - Oral medications (Viagra, Sialis)
  - Penile vacuum devices
  - Penile injections
  - Intraurethral medications
  - Penile prosthesis
  - Other: antidepressant, anti-anxiety, etc.
  - Pelvic floor PT
  - **Counseling
Women’s Sexual Health

- Dyspareunia
- Vaginal dryness
- Scarring
- Post-coital spotting/bleeding
- Decreased or absent libido

Sexual Health Treatments

- Women
  - Dilators
  - Lubricants/moisturizers
  - Hormone replacement therapy
  - Oral medications: PDE-5, Addyi, DHEA
  - Mona Lisa Laser Therapy, EROS, etc.
  - Other: antidepressant, anti-anxiety, etc.
  - Pelvic floor PT

- **Counseling

A Woman’s Touch: https://sexualityresources.com/
Pelvic Floor Physical Therapy

Used by permission by http://sequencewiz.org/

Pelvic Floor Physical Therapy

Toned pelvic floor “hammock”

Droopy pelvic floor “hammock”

Used by permission by http://sequencewiz.org/
Other complications

- Hematologic (blood)
- Osteologic (bone)
- Dermatologic (skin)
- Lumbosacral plexy (nerve)

Risk factors for Bone Complications

- Age
- Sex
- Menopause
- Osteopenia or osteoporosis
- Steroid use
- Smoking
- Vascular integrity
- Low body mass index
- Prior pelvic RT

Viswanathian, et al. 2014
Bone complications

- Pathologic fracture = insufficiency fracture
  - Sacrum 75-85%
  - Pubic bone 10-20%
  - Acetabulum 5%
- Osteonecrosis
  - Hip
  - Pubic bone
  - Second malignancy

Bone Complication Treatment

- NSAIDs
- Pelvic rest
- Physical therapy
- Referral to Orthopedics – surgery?
- Refer to Endocrine
Skin Complications

- Risk factors
  - Diabetes
  - Vascular disease
  - Smoking
  - Age
  - Poor nutrition
  - High BMI (skin folds)

Skin Complications

- Short term
  - 2-3 weeks post RT start, peaks 1-2 weeks post tx and heals in another 3-4 weeks
  - Folliculitis, faint redness, dry desquamation
  - Decreased sweating
Skin Complications

- Long term
  - Hyperpigmentation
  - Telangiectasias
  - Texture changes
  - Skin thinning
  - Chronic folliculitis
  - Subcutaneous fibrosis
  - Cellulitis (recurrent)
  - Edema

Skin Complications

- Treatment
  - Topical moisturizers
  - Sitz bathes
  - Treat infections
  - Desquamation – silver clear nylon, hydrogel, Vaseline gauze
  - Silvadene
  - Compression stockings/massage
  - Dermatology referral
  - Hyperbaric therapy
Lumbosacral Plexy

- Rare complication
- L1-S4 Nerve Roots
- SSx:
  - Drop foot
  - Neuropathy
  - Pain (mild)
- Treatment:
  - Supportive care

Current Techniques to reduce Pelvic Radiation Toxicity

- Diet modifications and nutrient optimization
- Radiation field design, radiation type and site specific techniques (ie, bowel, skin)
- Smoking cessation
Future Techniques to Reduce Pelvic Radiation Toxicity

- Stem cell therapy
- Antibodies
- Pre-biotics +/- probiotics
- Radiosensitizers, protectors and mitigators
- Statins
- ACE Inhibitors
- Bowel Mesh
- Tissue expanders
- Nanotechnology


Before Hydrogel Spacer
Dosimetrist’s Role to Improve Patient Outcomes

- Educate - yourself
- Educate - patients
- Educate - providers
- Advocate, advocate and advocate
- Support groups
- Be an example of healthy living:
  - Eat and drink in moderation
  - Exercise
  - Screenings
Review of Objectives

1. Current treatment modalities which cause long-term complications in pelvic radiation therapy patients:
   a. Pelvic radiation techniques
   b. Brachytherapy
   c. Radio-sensitizing chemotherapies

2. Complications which affect quality of life of pelvic radiation therapy patients:
   a. Radiation enteritis
   b. Bladder dysfunction
   c. Sexual dysfunction
   d. Pelvic bone changes
   e. Skin changes
   f. Lumbosacral plexopathy

3. Known techniques which reduce long-term post-pelvic radiation therapy complications:
   a. Diet modifications and nutrient optimization
   b. Radiation field design and bowel displacement
   c. Smoking cessation
   d. Bladder filling

4. Research focusing on reduction of post-pelvis radiation long-term complications:
   a. Nutrition therapies
   b. Medications for short and long term control
   c. Hyperbaric therapy
   d. Stem cell therapy

5. Specific strategies radiation therapist can use to help patients reduce long-term side effects from pelvic radiation therapy:
   a. Education
   b. Advocacy

Thank you!

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References

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