Breast Cancer and Radiation: Less is More, More or Less

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Some structure

- Radiation and Breast Cancer – A Brief History

- Current Practices in Early Breast Cancer
  – Description and Case

- Current Practices in Advanced Breast Cancer
  – Description and Case

- Summary Thoughts

Radiation and Breast Cancer – A Brief History

- 1984 - inaugural Susan G. Komen Race for the Cure

- 1985 – Lumpectomy and Radiation becomes a mainstream, supported alternative to total mastectomy in single, small, completely removed lesions- i.e. early breast cancer
  – Less is More!
Radiation and Breast Cancer – A Brief History

- Breast conservation in early breast cancer is supported in multiple trials before and since that time, including
  - NSABP B06, B17, British Columbia
  - NSABP-06, a randomized trial of > 1200 women
  - Compared to prior standard of mastectomy has been determined to provide equal local tumor control
  - Reduces risk in all tumor sizes
  - No change in overall survival

Radiation and Breast Cancer – A Brief History

- Early breast cancer and partial breast RT
  - Perhaps lumpectomy and radiation of the entire breast can be avoided in certain patients?
  - Less is More!
    - Kuske et al. A phase II trial of brachytherapy alone following lumpectomy for stages I and II breast cancer: Initial outcomes of RTOG 95-17.
  - Who qualifies?
    - Age over 60, less than 2cm tumor, (less than 3cm possible) invasive ductal or other favorable subtypes, ER+, lymph node neg, single site, neg margins, no neoadjuvant chemo
    - Obviously, a select group, but fortunately, not a rare one!

Radiation after mastectomy

- Post-mastectomy radiation recommended in all patients with
  - Four or more axillary lymph nodes involved
  - Locally invasive tumor characteristics & inflammatory cancer (T3 or T4)
  - Tumor cells within the deep margin of resection

Danish Trials, ECOG, British Columbia research
Radiation and Breast Cancer – A Brief History

- Some subtle factors that predispose us to post-mastectomy treatment, if multiple are present (MSK, UVA)
  - Lymphovascular invasion present
  - ER/PR negative status
  - Pre-menopausal (or age under 50, depending on who you ask)

Current Practices in Early Breast Cancer

- Radiation Techniques
  - Three Dimensional Conformal therapy
  - Intensity Modulated Radiation Therapy
  - Accelerated Partial Breast Irradiation (APBI)
    1. Brachytherapy
    2. External Beam technique (3D or IMRT)
    3. IORT (Intraoperative radiation therapy)

Current Practices in Early Breast Cancer

Case Study
- 58 yof, mammographically detected and biopsy proven invasive ductal cancer, 1.3cm in size, desiring breast conservation. No significant family history.
- What are her options?
  - All of the above, and since partial breast therapy is a possible option, seeing the Rad Onc prior to surgery is critical (can’t give partial breast without it)
Pathway One: Whole Breast

- 3D vs Intensity modulated therapy
  - IMRT useful in some situations (Left breast, heart in the way!), 3D in others (Right breast, Left breast prone)
- Prone vs supine

- Duration?
Pathway One: Whole Breast (prone)

- Prone (face down) Position
  - The heart and lung are effectively eliminated in this treatment.

- Left Lung
- Heart
- Treatment (planning)
- Volume
  - (area outlined in red)

Pathway One: Whole Breast

- Duration?
  - 5-5.5 weeks to whole breast, 1-1.5 weeks to tumor bed, 6 to 7 weeks total – Standard
  - START (Standardization of Radiation Trials) A and B, UK. Also Canadian and Italian research
    - Same radiation, just different, higher daily dose
    - 13-15 fractions, no boost, over 3 weeks.
    - NO difference in disease control in any study
    - Shorter course may have better cosmetic outcome!
  - Less is More!

Pathway Two: Partial Breast

- If she meets the many criteria, even less is more!
- Catheters – 1 week, twice daily
Pathway Two: Partial Breast

• IORT
  – Done during surgery.
  – No skin, chest wall dose
  – Duration of therapy: 20 minutes during surgery
  – Much less is much more!
Pathway Three: NO TREATMENT?
- Well, not in someone in their 50s, recurrence rates can be 20-30% or higher
- But what if she were over 70?
  - Lumpectomy plus tamoxifen with or without irradiation in women age 70 years or older with early breast cancer: long-term follow-up of CALGB 9343
- 70 or over, ER+, small, single, completely removed tumors using Tamoxifen
  - Recurrence with RT 2%, without 10% at 10 years, but OS the same
  - Statistically significant, but clinically less so
  - My opinion: IORT might be excellent low impact option

Current Practices in Advanced Breast Cancer
- I must admit to a lie:
  - Less is not always more.

- For advanced breast cancer:
  - More is more, less isn’t enough

Current practices in advanced breast cancer
- Breast conserving or not, if they have 4 or more lymph nodes, large tumor, they need 6-7 weeks RT, likely via IMRT technique
- They may need it even if 1-3 lymph nodes, or if they have multiple subtler bad features on pathology (see slide 7)
- 1-3 lymph nodes undergoing evaluation by NSABP, but meta-analysis of older studies hints that it may be appropriate, esp in higher risk pts (e.g. pre-menopausal, ER-)
Current practices in Advanced Breast Cancer

• Inflammatory Breast Cancer—Much more is more
  – Both distant and local recurrence is very common
  – Local recurrence with standard chest/node RT is 40% (MD Anderson data)
  – Hyperfractionating (Twice daily radiation) over 5 weeks results in local recurrence of 15%

Current practices in Advanced Breast Cancer

• Recurrent disease
  – Thorny issue, often prior surgery, chemotherapy and radiation can limit treatment options, including less additional radiation.
  – Can be painful, can be messy (open wounds), often deteriorates quality of life as much as distant recurrences
  – It is still treatable, however!

Recurrent Cancer

• No large trials, all treatment is case by case

• Any treatment must be integrated, and any treatment center must have every available option for advanced therapy for advanced recurrence

• So a Case Study as an example, then
Case Study: Terry

- 54 y.o. female seen initially on 10/4/10
- Erythematous rash on left upper outer quadrant of breast seen in August 2009
- Biopsied and determined to be IBC, Triple negative
- Negative met w/u. Under chemotherapy until 1/10
- s/p MRM and axillary dissection
- Path revealed persistent inflammatory carcinoma with extensive dermal invasion, LV+; 7/7 LN +. Stage IIIC.
- Post-op radiation to 50.0 with 10.0 gY boost to scar completed 4/2010

Case Study: Terry

- In 6/10, erythema recurred, eventually biopsied and shown to be recurrent cancer
- PET/CT confirmed no evidence of distant disease
- Patient placed on Xeloda
- Seen 10/10. Exam at that time was unremarkable except for "the left chest wall which showed erythema and some chronic radiation skin changes. The disease does extend to the lower abdomen and also to the back. The right breast has no obvious masses." and moderate chronic left arm lymphedema

Case study: Terry

- On Xeloda prior to CTCA patient had apparent progression by comparison of outside description and patient observation
- Given prior radiation, patient was initiated on hyperthermia to all affected areas twice weekly while on Xeloda.
- Wait, what’s hyperthermia? It’s More for those who can only get Less (Radiation, that is)!
Hyperthermia - Heat Kills Cancer, With Help

How it works
- Location
  - Clinically set and determined
  - Non-invasive temperature monitors placed

- Length: Typically one hour per site

- Timing: Typically twice weekly per site

Hyperthermia in action

Does it work? Does it hurt?

- Numerous studies showed in recurrent breast cancer, superficial hyperthermia could up to double response rates in previously treated cancers receiving re-irradiation
- More recent work also shows efficacy with chemotherapy

- Side effects of pain in treatment site and blister are minor, and uncommon (10%)
Case Study: Terry

• Patient was seen on treatment, and in follow-up

• Follow-up Note from 1/11: “She has had excellent clinical response on the left chest wall with complete disappearance of erythematous areas

• PET/CT 1/11 without obvious disease

• Note from 2/28/11: “Skin erythema over left chest wall has recurred”

• Disease now extending onto arm and across back in addition to extensive disease on chest wall/abdomen
Case Study: Terry

• Given extensive recurrence, decision was made to proceed with Tomotherapy IMRT radiation with hyperthermia and sensitizing chemotherapy (Xeloda). (Hyperfractionated IMRT radiation, hyperthermia, chemotherapy together. *More!*)

• Radiation planned was 1.5gy/fx BID for 30fx to 45.0gy over three weeks to clinically wired out disease extent:
Terry, f/u 5/24/11

- PET/CT negative for metastatic disease.
- Exam: "Examination of the skin of the chest wall and the arm that was treated showed some mild dryness and mild erythema consistent with radiation with essentially resolution of the prior seen metastatic disease within that area. No new disease was seen."

Terry, 2015

- Patient did recur outside treated field, and is currently being treated with Gemzaar and hyperthermia with successful control in 2015!

Summary Thoughts

- Early breast cancer: Less treatment, in both volume and time, continues to show similar disease control with better side effect outcomes.
- Advanced breast cancer: More treatment, but with multiple modalities, advanced equipment and treatment schemes to minimize side effects while maximizing tumor effects.