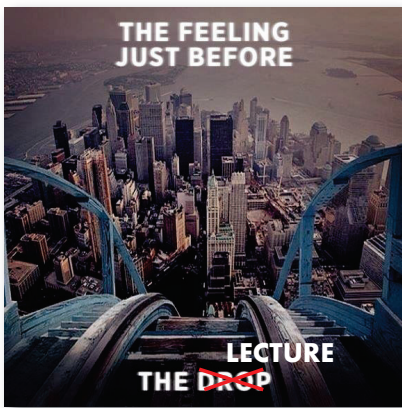


Breast Cancer Care Updates 2019

Jodi Winicour PT, CMT, CLT-LANA

What Will Be Covered?



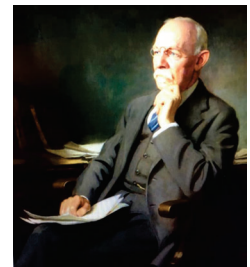
<https://edmidentity.com>

For More Than 100 Years

The extent of breast cancer surgery was based on the “Halstedian” concept of breast cancer:

- BrCA as a locoregional disease.
- Spread through lymphatic system.
- Cured by resection.

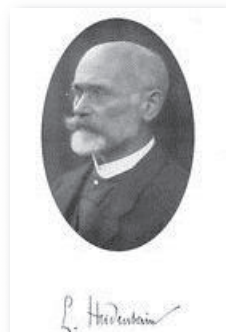
Giuliano 2017



William Stewart Halsted
Osborne 2007

Influenced by Lothar Heidenhain

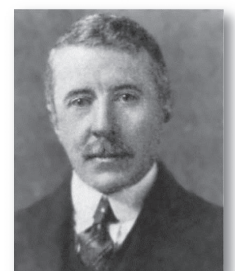
- Berlin, Germany
- Carefully documented the spread of cancer from within the breast to the pectoralis major muscle and the lymphatics.
- “...occasionally isolated embolic or a few free cancer cells are present in the lymph...”. (1889)



Osborne 2007

William Sampson Handley-London, England

- “continuous growth of cancer along the lymphatics...” which he termed lymphatic permeation. (1907)
- The hypothesis of lymphatic permeation was used to explain the spread of cancer, in a centrifugal manner, to more distant sites such as the lung, liver, and skeleton.

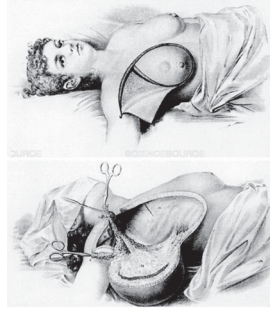


Osborne 2007

<https://aibolita.com>

The Notion of Centrifugal Spread...

- Led Halsted to devise a radical procedure for breast cancer, which he undertook in 1894.
- This procedure involved removal of the breast, the pectoral muscle, and the regional lymph nodes en bloc to ensure that no cancer was incised, which would have allowed contamination of the operative site or resulted in residual disease.



Osborne 2007

“The Gloves of Love”

- Scrub nurse Caroline Hampton.
- Considered abandoning the hospital.
- “I gave the matter my consideration, and one day in New York requested the Goodyear Rubber Company to make, as an experiment, two pairs of thin rubber gloves with gauntlets”.



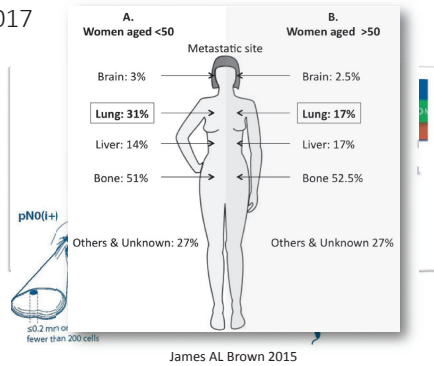
Caroline Hampton

William Stewart Halsted

Mikkic 2010

Staging Overview 1959-2017

- TNM system developed in 1959
- Developed for common nomenclature for disease prognosis across the U.S.
- 7 updates since 1959
- “In the past decade, there have been fundamental changes in our understanding of the biology of breast cancer.”



AJCC BrCA Staging 2017

Over the Succeeding Decades...Remarkable progress challenged the Halstedian view of tumor progression with the understanding of the potential for distant systemic spread of invasive cancers irrespective of nodal involvement ...

- This has led to:
- More limited surgical management.
- Reduction of axillary staging with SLNB becoming leading approach with clinically (-) axilla.
- Dramatic improvements in the safety of radiation delivery.
- Recognition that early adjuvant systemic treatment reduces the chances of recurrence and mortality.
- Increasing neoadjuvant systemic therapies for larger and locally advanced tumors.
- A better understanding of biologic markers of prognosis and prediction of response to categories of systemic therapy.

AJCC BrCA Staging 2017

The Seed and Soil Hypothesis

- Over the summer of 2011, the waters of Lake Michigan became crystal clear.
- Late 1980s from Ukraine.
- Zebra and Quagga mussels had devoured the plankton of the Great Lake.
- By 2012 950 trillion mussels in the lake.



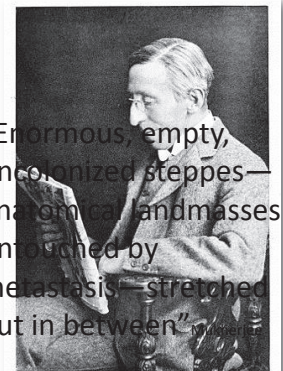
discovermagazine.com/2017/oct/the-great-takeover

Mukherjee 2017

The Seed & Soil Hypothesis

- 1889
- Set out to understand cancer’s “primary growth and the situation of the secondary growths derived from it.”
- Studied the files of 735 women who died of BrCA.
- Found their metastases did not appear to spread centrifugally.
- They appeared in discrete, anatomically distant sites.

“Enormous, empty, uncolonized steppes—ancient sandmasses untouched by metastasis—stretched out in between”



STEPHEN PAGET, M.A., F.R.C.S.
(Follower of the Research Defers Society)

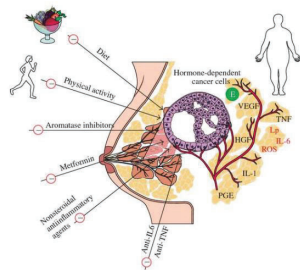
Mukherjee 2017

BrCA Staging Implemented January 2018

NOW:

- BrCA biology, rather than the extent of surgery, is a major risk determinant of systemic and locoregional recurrence.
- We now think as BrCA as a GROUP of diseases with different molecular characteristics.
- Originate in breast tissue but have varying prognosis, patterns of recurrence and responses to treatments.

AJCC BrCA Staging 2017

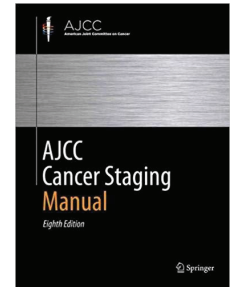


<https://www.eeletter.com/the-biology-of-breast-cancer/>

Updates in Staging 2017

- Biologic Factors
 - Hormone receptivity
 - HER2 overexpression
 - Tumor grade
 - Genomic panels
- Have become as or more important than the anatomical extent of disease to define prognosis & select systemic and locoregional treatments.

AJCC BrCA Staging 2017



Breast Cancer Subtypes

Luminal A:

- Most favorable prognosis.
- ER and/or PR (+) HER2 (-)
- Low Ki-67; Tumor grade 1-2.
- 30-74% of subtypes.

HER2 Type Enriched:

- ER (-) PR (-) HER2 (+)
- Tend to be LN (+); Tend to grow and spread more aggressively.
- More common in younger women.
- 5-15% of subtypes.

Luminal B:

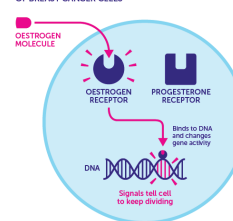
- ER and/or PR (+) HER2 (+) or HER2 (-) with high Ki-67
- Higher tumor grade; LN (+)
- More aggressive with larger tumor size.
- 10-20% of subtypes.

Triple (-)/Basal-like:

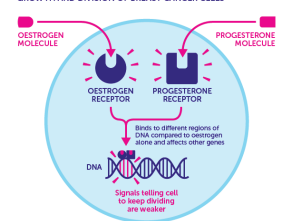
- ER (-) PR (-) HER2 (-)
- 75% of Triple (-) BrCAs are basal-like subtype.
- 2x > in black women than white women.
- More common pre-menopause & with BRCA1 gene.
- 15-20% of subtypes.

Estrogen and Progesterone Receptivity

ESTROGEN FUELS THE GROWTH AND DIVISION OF BREAST CANCER CELLS



PROGESTERONE PUTS A BRAKE ON ESTROGEN FUELLED GROWTH AND DIVISION OF BREAST CANCER CELLS



<https://scienceblog.cancerresearchuk.org/2015/07/08/solving-a-breast-cancer-mystery-why-do-double-positive-women-do-better/>

Genomic Assays

- **Mammaprint ©**
- Gene expression profiling of 70 genes
- High/Low risk over 10 years.
- Level II evidence
- Approved by ASCO 2017 to direct adjuvant chemotherapy with low risk profile.

AJCC BrCA Staging 2017

- **Oncotype DX©**
- Gene expression profiling of 21 genes
- Risk score 0-100.
- Levels of recurrence:
 - Low < 18
 - Intermediate 18-30
 - High >31
- Level I evidence

TailorX Trial of 2015 & 2018-Oncotype DX

- Chemotherapy may be avoided in 70% of women with BrCA if:
 - Hormone (+)
 - HER2 (-)
 - Node (-)
 - Taking anti-estrogen medications.
- **Old levels of risk:**
 - Low < 18
 - Intermediate 18-30
 - High >31
- **Redefined levels of risk:**
 - 0-10 Low risk
 - 11-25 Intermediate risk
- **Found that in this group, chemotherapy did not add to the benefits of the anti-estrogen medications.**

AJCC BrCA Staging 2017

The Details vs. the Big Picture

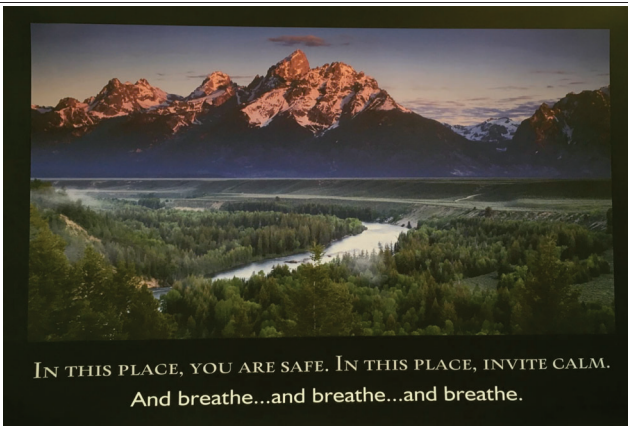


www.deceptology.com

Staging 2017

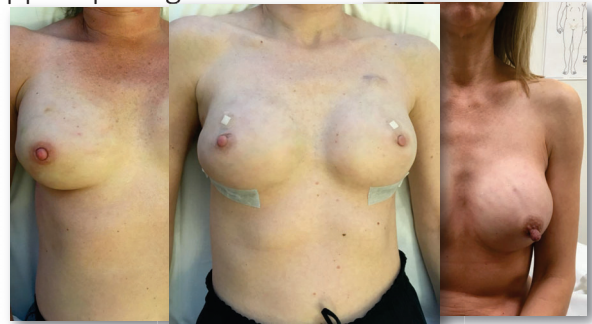
- **Clinical Prognostic Staging**
 - For ALL patients
 - Provides comparison between patients regardless of order sequence of treatments.
 - Primary staging for those receiving:
 - Neoadjuvant chemotherapy
 - Radiation before surgery
 - No surgery
 - Based on clinical information from Hx, exam, imaging, biopsy before treatment.
- **Pathological Prognostic Staging**
 - Not for those receiving neoadjuvant chemotherapy.
 - Applies to those receiving:
 - Surgical resection as initial treatment.
 - Includes Clinical Prognostic Stage
 - Information during surgery:
 - Tumor characteristics
 - Nodal status
 - Genomic Assays

AJCC BrCA Staging 2017



IN THIS PLACE, YOU ARE SAFE. IN THIS PLACE, INVITE CALM.
And breathe...and breathe...and breathe.

What's New in Surgery? Nipple Sparing Mastectomies



Breast reconstruction and risk of arm lymphedema development: A meta-analysis 2018

- 19 studies reviewed from 2001-2016.
- N=7 prospective
- N=6 retrospective
- N=3 case controlled
- N=3 cross sectional (LOE IV)
- 7 studies LOE II; 9 studies LOE III
- Duration of studies:
 - 21 months-123 months
- Diagnostic criteria for objective measures of lymphedema:
 - Arm circumference
 - Clinical records
- Subjective data (e.g., interviews, questionnaires)
- We coded lymphedema as a dichotomous outcome (present/absent).

Siotos 2018 Department of Plastic and Reconstructive Surgery, Johns Hopkins Hospital

Reconstruction & Lymphedema Risk

- 16 studies
- 7501 women had surgery for breast cancer.
- 2069 had breast reconstruction
 - 325 (15.7%) developed UE lymphedema.
- 5434 did not (some had conserving surgery)
 - 1565 (28.8%) developed UE lymphedema.
- 1 of these studies reported outcomes per breasts receiving mastectomies:
 - 35 cases of lymphedema in
 - 681 mastectomies with reconstruction (5.14%)
 - 56 cases of lymphedema in
 - 210 mastectomies without reconstruction (26.67%)
- Another comparison found no statistical difference in UE lymphedema with TE vs. autologous only reconstruction.

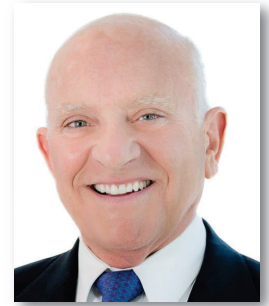
Siotos 2018

Post Halloween Stroll



ALND to SLND...the Long Transition

- Between 1998 and 2004
 - Use of ALND declined from 94% to 36% in women with no axillary nodal metastases.
- In 2004
 - 68% of Pts with SLN mets underwent ALND.
- But...is it necessary?
- Significant risk of:
 - Lymphedema
 - AWS
 - Scarring with decreased ROM and function of the shoulder.

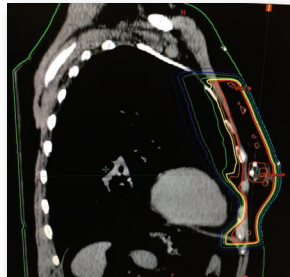


Armando Giuliano, MD
www.giantsforcancer.com

Giuliano 2017

ACOSOG Z0011 November 2017

- Enrolled Pts from May 1999-December 2004 at 115 sites.
- T1-T2 invasive BrCA
- No palpable axillary adenopathy
- 1-2 SLN with metastases
- All patients had planned:
 - Lumpectomy
 - Whole breast radiation
 - Adjuvant systemic therapy
 - Third field radiation was prohibited



Giuliano 2017

ACOSOG Z0011 2017

- 856 women completed the trial
 - 446 in SLNB alone
 - 445 in completion ALND group
- Median follow up 9.3 years
- 10-year overall survival
 - 86.3% for SLND alone
 - 83.6% for completion ALND group
- 10-year disease-free survival
 - 80.2% for SLND alone
 - 78.2% in completion ALND group
- 10-year regional recurrence did not differ significantly between the 2 groups.

Giuliano 2017

Sentinel

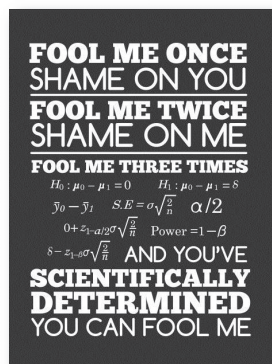
- A soldier or guard whose job is to stand and keep watch.
- In Medicine-
- An indicator of the presence of disease.

The Oxford Dictionary

ACOSOG Z0011 2017

- After initial trial results in 2005
- National Cancer Database study of 74,309 Pts
- Yao et al observed SLND in Pts meeting ACOSOG Z0011 criteria-
 - Increased from 23%-56%
 - 2009-2011
- However-
 - < 50 years & triple (-) BrCA predicted > use of ALND despite not being supported with ACOSOG Z0011 findings in 2005. (or in 2017)
 - Age was not significantly associated with locoregional recurrence after controlling for other factors.

Giuliano 2017



<https://www.teepublic.com>

Routine Use of ALND for 1-2 (+) SLNs is No Longer Justified

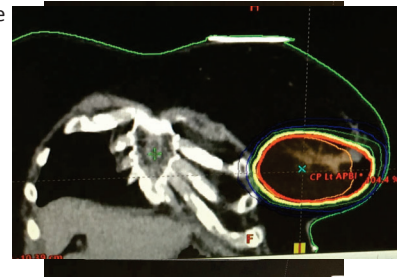
- If meeting Z0011 eligibility.
- Should not be extrapolated to:
 - Palpable axillary nodes
 - Mets to > 2 SLNs
 - Pts forgoing whole-breast radiation.
 - Mastectomy without radiation
 - Neoadjuvant chemotherapy
- Positive Sentinel Node-Adjuvant Therapy alone vs Adjuvant Therapy Plus Clearance or Axillary Radiotherapy trial
 - Expected to complete accrual in 2018.
 - Women with mets in 1-2 SLNs
 - Breast conserving OR mastectomy

Giuliano 2017



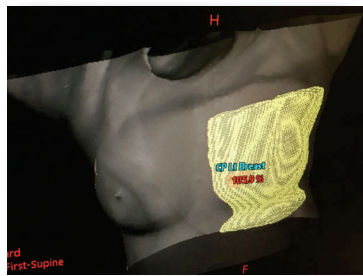
Accelerated Partial Breast Radiation Executive Summary: ASTRO Guidelines 2017

- APBI is localized radiation to the lumpectomy site after tumor removal.
- Compared to whole breast radiation:
 - Less time to deliver the dose
 - Less tissues irradiated
 - Heart/lungs
 - Ribs
 - Intercostals
 - Fascia
 - Lymphatics

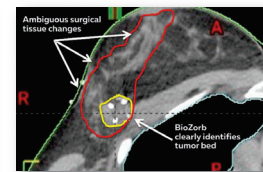
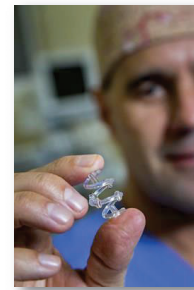


Accelerated Partial Breast Radiation Executive Summary: ASTRO Guidelines 2017

- Suitability group
 - Changed from 60 to 50 yrs
- Cautionary group
 - Changed from 50 to 40 yrs
- Qualifiers:
 - Early stage
 - (-) Margins - < 2mm margin
 - T1-T2
 - DCIS \leq 3 cm
 - etc, etc...



BioZorb® for Early BrCA & Partial Breast Radiation Therapy



<http://www.nzms.co.nz/229/biozorb%E2%84%A2-3d-bioabsorbable-marker/>



BioZorb 3D Bioabsorbable Marker

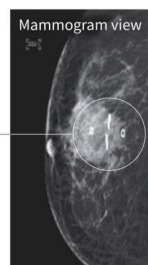
Dissolves over time

As the breast heals, the body slowly resorbs the material over the course of a year or more.



Clips remain

The small marker clips remain permanently at the surgical site for follow-up imaging.



<https://www.focalrx.com/patients/>

American Society for Radiation Oncology (ASTRO) March 2018

- New clinical guidelines for hypofractionated whole breast radiation therapy.
- Replaces guidelines from 2011.
- Most women with BrCA should be treated with hypofractionated whole breast radiation as standard of care.
- **Hypofractionated Dose:**
 - 4,000 cGy in 15 fractions (2.67 Gy/day) or
 - 4,250 cGy in 16 fractions (2.66 Gy/day)
 - May or may not receive boost of 10-12.5 Gy in 4-5 fractions.
- **Conventional Dose:**
 - 5000 cGy in 25 fractions (2 Gy/day)
 - Boost of 10-14 Gy in 5-7 fractions.

Smith 2018

Hypofractionated Whole Breast XRT

- Regardless of:
 - Age
 - Tumor stage with or without tx of low axilla.
 - Whether they have received chemotherapy.
 - Breast size (homogenous dose)
 - Herceptin or endocrine therapy
- Boost may or may not be given depending on findings and age.
- Prior to 2018 accelerated treatments:
 - Older patients
 - Those with less advanced disease.
 - No nodal involvement.
 - No chemotherapy.
- Recent long-term results from several large trials strongly support the safety and efficacy of accelerated treatment for most breast cancer patients.
- Conventional therapy vs. hypofractionation (whole breast):
 - No benefit in tumor control or side effects.

Pen Amnesty



Hypofractionated Whole Breast Radiation



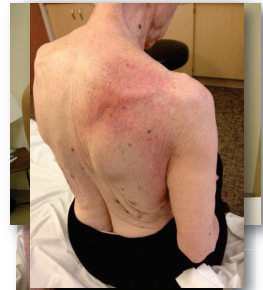
9 Treatments of Radiation



4 Months Post Radiation

ASTRO Guidelines for Post Mastectomy Radiation Therapy (PMRT) 2016

- Panel unanimously agrees:
- In patients with:
 - T1-2 breast cancer
 - One to three positive axillary nodes.
- PMRT Reduces the risks of-
 - Local regional failure
 - Any recurrence
 - Breast cancer mortality
- Panel generally recommends treatment of:
 - Internal mammary nodes
 - Supraclavicular-axillary apical nodes



Recht et al 2016

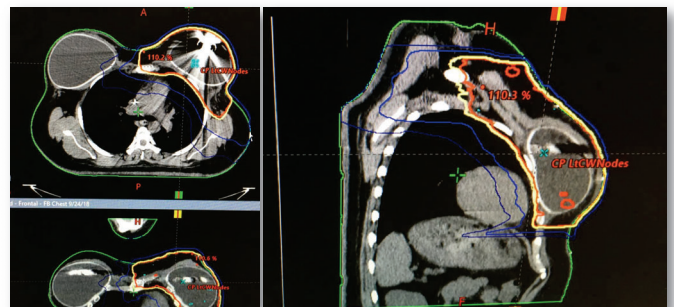
PMRT Early Effects



Late Effects



PMRT with Expanders Including SCF



PMRT with SCF Simulation 9/2018; Picture 2/2019



Subclavius & Anterior Intercostal Mobility



Pectoralis Major Bending



Side-Lying Chicken Wing with a Twist At Your Desk Stretch



Hands Behind Head Side-Bends Side-Lying PNF D2 Flexion



I Like To Keep My Referring Plastic Surgeons Happy...Not Angry.



Spinal Mobilization and Manipulation with Expanders?



Sara P Piva @www.
Researchgate.net

Seated Thrust

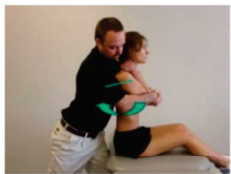


Figure 1. Seated thoracic spine distraction thrust manipulation used in this study. The therapist uses his or her thumbs as a fulcrum on the subject's midthoracic spine and applies a high-velocity distraction thrust in an upward direction.

Prone Thrust



FIGURE 3. Multithoracic spine thrust manipulation.

<https://www.slideshare.net/JeffTurnerSPTCSCS/thoracic-spine-manipulation>

Overhead Moose Stretch



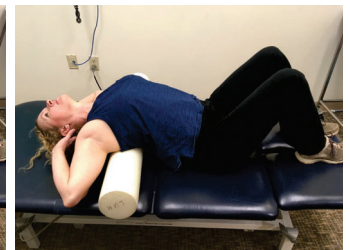
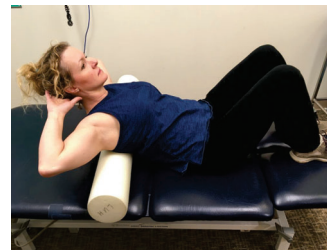
Ball Lean



Mobilization with Movement to Spine and Ribs



Thoracic Extension on Foam Roller



Take Home Message

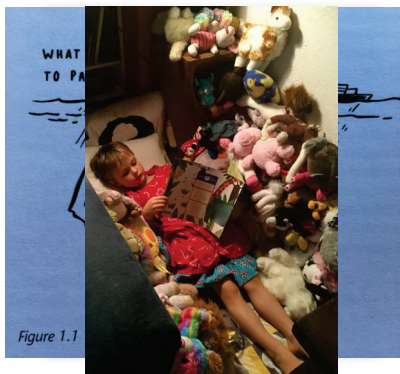


Figure 1.1



KeepCalmAndPosters.com

References

- Brunt AM, Haviland J, Sydenham M. LBA2 FAST Phase III RCT of Radiotherapy Hypofractionation for Treatment of Early Breast Cancer: 10-Year Results (CRUKE/04/015). 2018 ASTRO Annual Meeting Late-breaking Abstract Selection; International Journal of Radiation Oncology.
- Correa C, Harris EE, Cristina M, et al. Accelerated Partial Breast Irradiation: Executive summary for the update of an ASTRO EvidenceBased Consensus Statement. Practical Radiation Oncology (2017) 7, 73-79.
- The Fast Trialists group. First results of the randomized UK FAST Trial of radiotherapy hypofractionation for treatment of early breast cancer (CRUKE/04/015). Radiotherapy and Oncology 100(2011)93-100.
- Giuliano AE, Ballman KV, McCall L, et al. Effect of Axillary Dissection vs No Axillary Dissection on 10-Year Overall Survival Among Women With Invasive Breast Cancer and Sentinel Node Metastasis: The ACOSOG Z0011 (Alliance) Randomized Clinical Trial. JAMA. 2017. 12;318(10):918-926.
- Koulis TA, Phan T, Olivetto IA. Hypofractionated whole breast radiotherapy: current perspectives. Breast Cancer(Dove Med Press). 2015; 7: 363–370.
- Langley RR, Fidler IJ. The seed and soil hypothesis revisited—The role of tumor stroma interactions in metastasis to different organs. Int. J. Cancer. (2011) 128, 2527–2535.
- Mikic Z. The Gloves of Love. Med Pregl. 2010 Jan-Feb;63(1-2):133-7.
- Mukherjee, Siddhartha. Cancer's Invasion Equation. The New Yorker. Annals of Medicine. September, 2017.
- Osborne, MP. William Stewart Halsted: his life and contributions to surgery. Lancet Oncol 2007; 8: 256–65.
- Sotos C, Sebai ME, Wan EL. Breast reconstruction and risk of arm lymphedema development: A meta-analysis Journal of Plastic, Reconstructive & Aesthetic Surgery (2018) 71, 807–818.
- Smith BD, Bellon JR, Blitzblau, R, et al. Radiation therapy for the whole breast: Executive summary of an American Society for Radiation Oncology (ASTRO) evidence-based guideline. Practical Radiation Oncology (2018) 8, 145-152.