

WHAT'S NEW IN BREAST CANCER

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February 24, 2024



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OBJECTIVES

- Review historical approaches to surgical management of breast cancer
- Highlight modern therapeutics and current trends in multidisciplinary care
- Introduce “what’s new and next” in breast cancer care

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DISCLOSURES

***I have no relevant financial disclosures
related to this presentation***

*Thanks to Tim Schaefer MD, Mark Migliori MD, and their patients for
use of educational images*

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HISTORICAL APPROACH

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HISTORICAL APPROACH

Dr William S Halsted

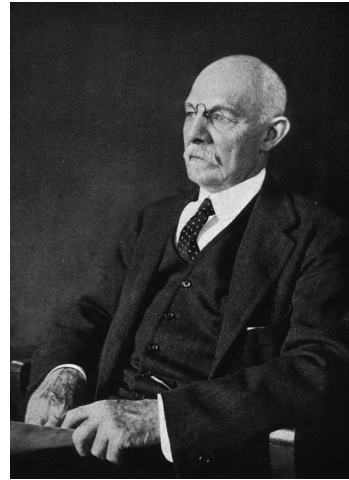
Considered the father of modern surgery

First described mastectomy for cancer treatment in 1882

Represented a milestone in treatment of breast cancer

No other options at that time

Belief that the more extensive the surgery, the less likely cancer would return



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HISTORICAL APPROACH



- Extremely disfiguring surgery
- Recurrence rates profoundly high
- Survival was dismal
- No chemotherapy, no endocrine therapy, no radiation therapy

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HISTORICAL APPROACH

NSABP - B06

- Randomized prospective trial
- Compared mastectomy to lumpectomy plus radiation to lumpectomy alone
- No difference in survival
- Modest decrease in local recurrence with mastectomy
- More contemporary data show equal rates of local recurrence in modern treatment era.

Fisher B et al, NEJM, 2002

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HISTORICAL APPROACH

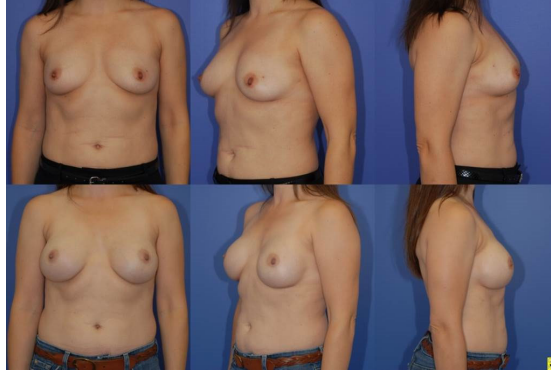
Breast conservation



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HISTORICAL APPROACH

NIPPLE SPARING MASTECTOMY AND CONTRALATERAL PROPHYLACTIC MASTECTOMY



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HISTORICAL APPROACH

Sentinel Node: NSABP - B32

- Randomized prospective trial
- 5611 patients
- Randomized to SLN plus ALND **versus** SLND with ALND only if SLN +
- No difference in survival
- No difference in local control
- **Significant change** in management of axilla

Positive SLN ACOSOG Z0011

- Known since NSABP B-04:
No survival advantage to CLND
- Randomized to SLN plus ALND if SLN + **versus** SLN plus radiation if SLN +
- No difference in survival
- No difference in local control
- **ANOTHER significant change** in management of axilla

Krag D et al, Lancet, 2010

Giuliano A et al, JAMA 2011

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HISTORICAL APPROACH

To summarize:

- De-escalation of surgical intervention
- Equivalent patient survival and recurrence rates
- Far less destructive

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CURRENT TRENDS AND MODERN THERAPEUTICS

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CURRENT TRENDS

- Better technology and precision medicine
- Whole person care
- Increasing exploration of diversity and oncologic outcomes

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CURRENT TRENDS

- Better technology and precision medicine
- Whole person care
- Increasing exploration of diversity and oncologic outcomes

Right treatment, right patient, right time

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CURRENT TRENDS

Genomic testing (somatic)

- Allow for more precise diagnosis of tumor type
- Identify best treatment options
- Identify what drugs more likely to work or not work
- Find common genetic mutations linked to cancer: *EGFR*, *KRAS*, *BRAF*, and *PIK3CA*



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CURRENT TRENDS

• Genetic testing (germline)

- Virtual visits
- Guide decision making, treatment, risk reduction

• Screening and guidelines

- USPTF changed breast cancer screening guidelines to 40
- 3-D mammograms

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CURRENT TRENDS

Whole person care

- Safety and quality
- Improve patient and family experience
- Improve health of the broader community
- Improve access and coordination
- Make care more affordable / reduce financial toxicity

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CURRENT TRENDS

- Safety and quality
 - Reduce mortality
 - Reduce hospital stay
- Improve patient and family experience
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CURRENT TRENDS

- Safety and quality
 - Reduce mortality
 - Reduce hospital stay
- Improve patient and family experience
 - Nurse navigation
 - Cancer nutrition, integrative health
 - Cancer rehabilitation, palliative care partnerships
- Improve health of the broader community
- Improve access and coordination
- Make care more affordable / reduce financial toxicity

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- Safety and quality
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 - Cancer nutrition, integrative health
 - Cancer rehabilitation, palliative care partnerships
- Improve health of the broader community
 - Increase cancer screening
 - Targeting underserved communities
- Improve access and coordination
- Make care more affordable / reduce financial toxicity

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CURRENT TRENDS

- Safety and quality
 - Reduce mortality
 - Reduce hospital stay
- Improve patient and family experience
 - Nurse navigation
 - Cancer nutrition, integrative health
 - Cancer rehabilitation, palliative care partnerships
- Improve health of the broader community
 - Increase cancer screening
 - Diversity / Equality / Inclusion
- Improve access and coordination
 - Advances in digital footprint, patient education, follow up calls
- Make care more affordable / reduce financial toxicity

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CURRENT TRENDS

- Safety and quality
 - Reduce mortality
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- Improve patient and family experience
 - Nurse navigation
 - Cancer nutrition, integrative health
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- Improve health of the broader community
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CURRENT TRENDS

- Treatment costs
 - Newly approved cancer drugs cost a average of \$10,000 a month and cost as high as \$50,000 a month with costs rising
- Loss of wages, productivity and financial security
 - 80% of patients exhaust all life savings
 - 45% of survivors experienced job-related income loss
 - Leading cause of bankruptcy, 2X national average
- Continued cost of care following treatment
 - Radiation and surgical course of treatment costs
 - Imaging, medications, visits and overall well being

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CURRENT TRENDS

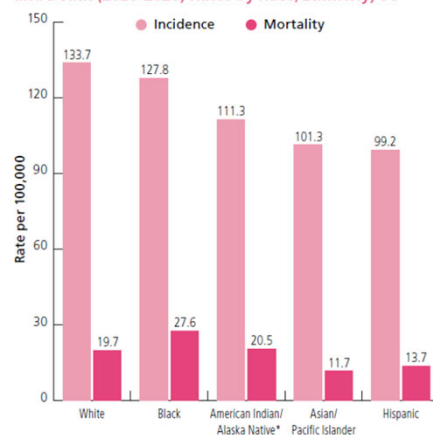
Diversity: Scary statistics

- Black Americans have lower rates of breast cancer, higher death rates and shorter survival
- Black people are more likely to be diagnosed at later stage, experience treatment delays, and less likely to receive comprehensive treatment

American Cancer Society: www.cancer.org

Cancer Disparities and Health Equity: A Policy Statement From
The American Society of Clinical Oncology *JCO* 2020 Oct

Figure 3. Female Breast Cancer Incidence (2015-2019) and Death (2016-2020) Rates by Race/Ethnicity, US



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CURRENT TRENDS

But Why?

- Less access to health care
- Lower levels of comprehensive insurance
- Differences in cultural or religious beliefs
- Lack of ethnically diverse workforce
 - In oncology 2% workforce is black or Hispanic, vs 13% of population

Cancer Disparities and Health Equity: A Policy Statement From the American Society of Clinical Oncology
JCO 2020 Oct

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CURRENT TRENDS

Solutions

- National awareness: ASCO Strategic Plan for Increasing Racial and Ethnic Diversity in the Oncology Workforce
- Improvements in language translation
- Community outreach and local care
- Improvements in medical financing

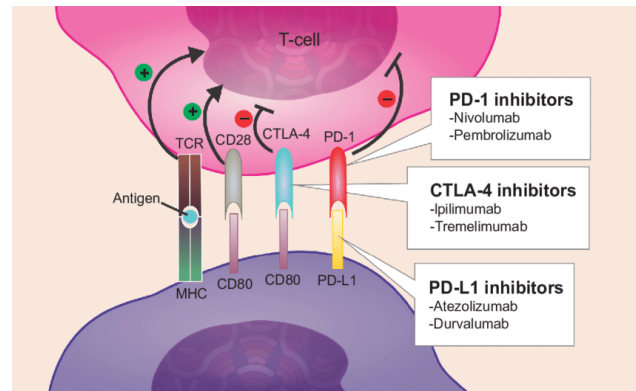
Cancer Disparities and Health Equity: A Policy Statement From the American Society of Clinical Oncology
JCO 2020 Oct

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MODERN THERAPEUTICS

Immune checkpoint inhibitor

- Block channels on T-cells so checkpoint proteins (from cancer) can't bind
- Prevents cancer cells from sending "off" signal
- Allows T-cells to kill cancer cells



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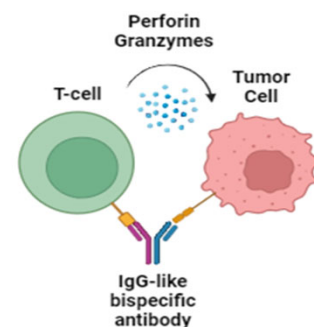
MODERN THERAPEUTICS

Bispecific Antibodies (BsAbs)

Bind to target antigen expressed on B-cells and CD3 expressed on T-cells, bringing them in close proximity and mediating the cytotoxic activity of T cells

Toxicity

- Cytokine release syndrome and neurotoxicity
- Financial Toxicity: \$25-50k per month (\$285-650k total)
- Infection: Pancytopenia & hypogammaglobulinemia



Slide courtesy of Justine Preedit

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MODERN THERAPEUTICS

Breast surgery:

- Superparamagnetic Iron Oxide (SPIO)
 - Delayed nodal staging
- Understanding the role axillary surgery
 - Nodal status less predictive of outcomes or treatment plan
- Same day mastectomy programs
 - Improved patient satisfaction, less IV narcotic use, reduced medical costs

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CURRENT TRENDS AND MODERN THERAPEUTICS

To summarize:

- Cancer care continues to evolve, both from a medical approach as well as a psychosocial approach
- Advanced therapeutics are being developed to target cancer-specific biology

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WHAT'S NEW AND NEXT

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WHAT'S NEW AND NEXT: SURGICAL ONCOLOGY

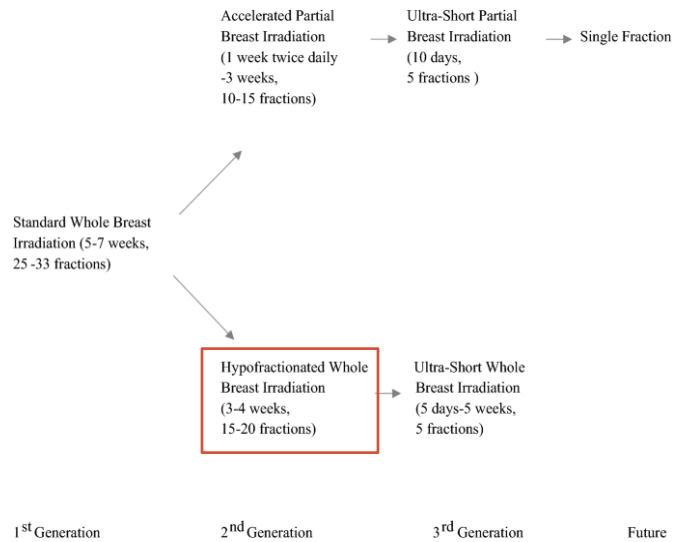
- **Observation of DCIS**
COMET trial
- **Non-operative ablation**
Radiofrequency, cryoablation
- **Observation after neoadjuvant therapy**
- **Oncoplastics**
Larger lumpectomy with breast reconstructions
- **Further minimization of axillary surgery**

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WHAT'S NEW AND NEXT : RADIATION ONCOLOGY

Evolution of post-surgical radiation

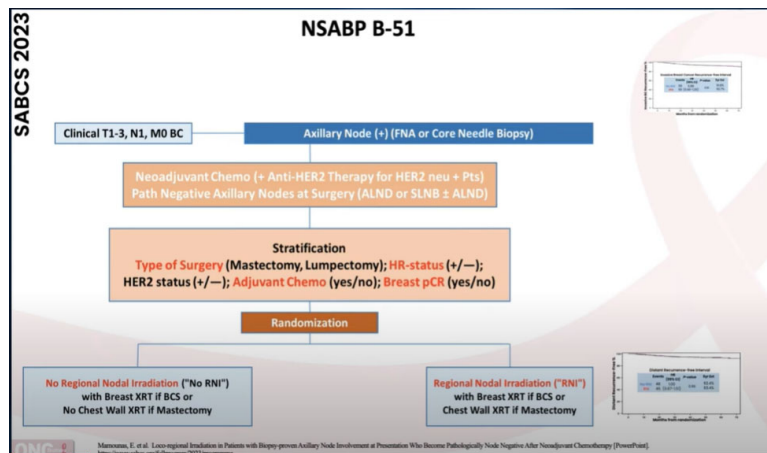
- Larger doses given per fraction, lower total dose
- Equal long-term efficacy in terms of recurrence
- Equal or less chronic treatment-related toxicity



Shah et al *Ann Surg Oncol* 2021 Sept

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WHAT'S NEW AND NEXT : RADIATION ONCOLOGY

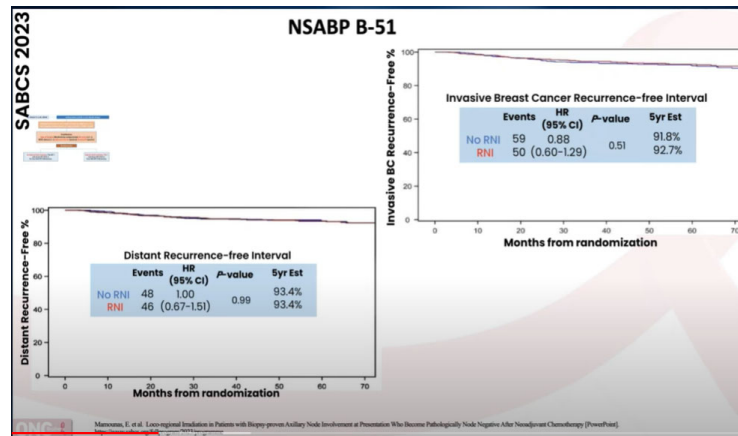


San Antonio Breast Cancer Symposium 2023

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WHAT'S NEW AND NEXT : RADIATION ONCOLOGY

Patients with upfront nodal metastases who achieve pCR after neoadjuvant chemotherapy do not benefit from post-operative nodal irradiation.



San Antonio Breast Cancer Symposium 2023

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WHAT'S NEW AND NEXT : MEDICAL ONCOLOGY

IDEA Trial

- Omission of radiation therapy for low risk (node negative, ER+, HER-2 non-amplified, low grade, Oncotype < 11 margin negative) stage I tumors for patients aged 50-69 (postmenopausal).
- Patients had a high rate of compliance with endocrine therapy
- No local recurrences with 5-year outcomes in patients who did not receive radiation

KEYNOTE-522 Update:

- Benefit to adjuvant pembrolizumab for patients who received neoadjuvant chemotherapy plus pembrolizumab (T1cN1-2 or T2-4N0 TNBC)
- Whether node negative or node positive, the 5-year event free survival increased by nearly 10% with the addition of pembrolizumab in adjuvant setting
- This improvement was seen even in patients who demonstrated pCR

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WHAT'S NEW AND NEXT : MEDICAL ONCOLOGY

CheckMate 7FL and KEYNOTE-756:

Neoadjuvant chemotherapy plus immunotherapy significantly pCR rate in patients with ER+ HER-2 negative cancer

ALEXANDRA/IMpassion-030:

Adjuvant chemotherapy plus immunotherapy provides no additional benefit to chemo alone

*take home point: immunotherapy plays a bigger role up front,
when primary tumor is still intact*

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WHAT'S NEW AND NEXT : MEDICAL ONCOLOGY

Neoadjuvant

AZ Destiny D967RC00001: Phase 3, randomized, neoadjuvant study of T-DXd or T-DXd followed by THP compared to ddAC-THP in participants with high-risk HER2+ early-stage breast cancer (PI Perez).

Adjuvant

Gilead GS-US-595-6184: *Now open* A randomized, open-label, phase 3 study of adjuvant sacituzumab govitecan and pembrolizumab vs treatment of physician's choice in patients with TNBC who have residual disease after surgery and neoadjuvant therapy (PI Krie).

Eli Lilly EMBER-4 J2J-MC-JZLH: A randomized, open-label, phase 3 study of adjuvant imlunestrant vs standard adjuvant endocrine therapy in patients who have previously received 2 to 5 years of adjuvant endocrine therapy for ER+, HER2- early breast cancer with an increased risk of recurrence (PI Krie).

Unresectable LA/mTNBC

Gilead GS-US-586-6144: Phase 2 (Cohort 1): randomized, 2-arm open-label study of magrolimab in combination with nab-paclitaxel or paclitaxel versus nab-paclitaxel or paclitaxel in previously untreated unresectable, locally advanced or mTNBC or (Cohort 2): single-arm, open-label study of magrolimab in combination with sacituzumab govitecan in patients who have received

AstraZeneca's TROPION-Breast04. A Phase III, Open-label, Randomized Study of Neoadjuvant Datopotamab Deruxtecan (Dato-DXd) Plus Durvalumab Followed by Adjuvant Durvalumab With or Without Chemotherapy Versus Neoadjuvant Pembrolizumab Plus Chemotherapy Followed by Adjuvant Pembrolizumab With or Without Chemotherapy for the Treatment of Adult Patients With Previously Untreated Triple-Negative or Hormone Receptor-low/HER2-negative Breast Cancer

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SUMMARY

- The current and future of cancer care will focus not only on the surgical / medical / radiation modalities, but will increasingly address the psychosocial component
- For surgery and radiation: “Doing More” isn’t always the right thing
- This is probably because systemic therapy is increasingly sophisticated, targeted, and provides for improvements in outcomes

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THANK YOU



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Questions for panel

1. If you could summarize in a sentence, what do you see as the overriding theme of how we treat breast cancer now and in the coming years?
2. How do you approach or counsel patients who are skeptical of change or modern recommendations?