AJCC Session
Panel Discussion: Breast Cancer

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Staging and Precision Medicine/Prognostication Tools

• Prognostication: estimation of outcome
  – AJCC - survival at 5 years

• Anatomic stage is the strongest prognostic factor for solid tumors

• Many other factors modify outcome
Breast Cancer Prognostic Factors

- Critical for current practice and meaningful classification of patients
- Prognostic stage groupings with non-anatomical factors incorporated into bins with TNM to describe all possible combinations
- 7th Edition describes 32 unique bins (permutations of T,N,M parameters) within which to classify patients
  - $T (4), N (4), M (2) = 4 \times 4 \times 2 = 32$
Breast Cancer 8th Edition vs. 7th Edition: Evolution of Practice

- 8th Edition describes 768 unique bins
  - $T(4), N(4), M(2), G(3), H(2), E(2), P(2): = 4 \times 4 \times 2 \times 3 \times 2 \times 2 \times 2 = 768\text{ bins}$
  - Adding 3 new factors with binary definitions: $768 \times 2 \times 2 \times 2 = 3,072\text{ bins}$
  - Adding 10 new factors $= 393,216\text{ bins}$

- Bin model relatively inflexible: a calculator becomes a necessity

- The 8th Edition of the AJCC Cancer Staging Manual represents a significant step towards individualization of treatment

- The Personalized Medicine Core offers an additional perspective: individualized prognosis using computational approaches
Classifier vs. Calculator: Roles in Precision Medicine

• Classifiers group patients into ordered risk strata with probability estimate cut-points.
  – TNM system is a classifier with ordered strata (I, II, III, IV) of increasingly poor prognosis.
  – Classifiers are constrained by the number of categories that are manageable.
  – Classifiers are limited by the variability of prognosis of patients within a given risk class.

• Prognostication tools are risk calculators with individualized probability estimates.
  – Algorithms are designed to deliver more precise estimates of outcome for an individual patient through computational integration of a variety of patient-specific data elements.

• AJCC regards both as necessary
Analysis of Prognostication Tools: State of the Science

- Intensive search to locate all exiting prognostication tools
- Initial observations: wide variation in quality, consistency, outcome assessed, included elements and validations (internal or external)
- Development and publication of guidelines for prognostication tool quality
- Systematic application of guidelines to all existing tools
- Results published in 8th Edition Breast Chapter
30 prognostication models/tools were identified and reviewed. Only two were found to have met all predefined AJCC inclusion and none of the exclusion criteria, and both have been externally validated.

- Adjuvant! Online (currently unavailable)
- PREDICT-Plus

Adjuvant! Online: developed to assist decision-making about adjuvant therapy in early-stage disease

- Probability estimates made according to a proprietary system

PREDICT-Plus developed to predict outcome in women treated for early breast cancer in the United Kingdom

- Open system
Going Forward

- AJCC encourages the development of high-quality prognostication tools by the community.
- Tools are needed for all patients, not just those with early stage disease.
- AJCC published quality criteria will serve as a guideline for tool development.
- AJCC PMC will continue to review and report of quality of newly generated tools as a service to the community.