



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
 - $T (4), N (4), M (2) = 4 \times 4 \times 2 = 32$
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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): = $4 \times 4 \times 2 \times 3 \times 2 \times 2 \times 2 = 768$ bins
 - Adding 3 new factors with binary definitions: $768 \times 2 \times 2 \times 2 = 3,072$ bins
 - Adding 10 new factors = 393,216 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
 - Kattan et al. CA Can J Clin 2016; 66:370-4.
- Systematic application of guidelines to all existing tools
- Results published in 8th Edition Breast Chapter

AJCC Endorsed Prognostication Tools

- 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.