Multi-modal AI models for intermediate- to high-risk localized prostate cancer

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NRG Oncology investigators analyzed clinical and digital histopathology data from five Phase III prostate cancer trials (NRG/RTOG 9202, 9408, 9413, 9910, and 0126) to develop and validate multi-modal intelligence

models (MMAI) that could outperform the National Comprehensive Cancer Network (NCCN) in the prediction of distant metastasis (DM) and other outcomes.

MMAI models could, in fact, stratify patients into risk groups that more accurately reflected their prognosis in comparison to NCCN risk groups. These results were presented during the Plenary Session of the American Society for Radiation Oncology's (ASTRO) Annual Meeting in October 2022, and related research was published in the *International Journal of Radiation Oncology*Biology*Physics*.

"Patients with localized prostate cancer are known to exhibit highly variable prognoses. Based on the NCCN risk stratification system, treatment guidelines result in overtreatment for many men. Conversely, it also understates the risk in some men who would benefit from treatment intensification. We are thrilled to have developed a risk stratification tool that offers this patient population a more accurate prognosis. As a result, patients and their physicians can tailor the intensity of their treatment to meet the patients' goals better and improve outcomes," stated Jonathan D. Tward, MD, Ph.D., of the University of Utah and lead author of the NRG abstract.

In the analysis, the previously locked MMAI 5-year metastasis model was applied across 5,569 patients, and deciles with similar DM rates were binned into three tiers: favorable (1–6th decile), moderate (7–9th), and unfavorable (10th) risk. Patients unable to be classified into NCCN risk groups were excluded. The Fine-Gray competing risk method was used to estimate the cumulative incidence of metastasis. The three-tier MMAI model was compared to standard prognostic factors such as PSA, Grade Group (GG), and 3-tier NCCN.

"The MMAI model identified six-fold more patients with a lower risk of distant metastasis than NCCN risk groups. Conversely, patients in the

MMAI unfavorable-risk group had a substantially greater risk of distant metastasis than the NCCN high-risk group. Men in the lower risk group could routinely consider radiation therapy alone sufficient and avoid the added toxicity of using androgen deprivation therapy combined with radiation. The degree of prognostic improvement seen in the three-tier MMAI stratification is striking and strongly points toward the MMAI models becoming a new standard supported by level 1 evidence for personalized risk assessment in newly diagnosed men contemplating their treatment options," added Dr. Tward.

At a median follow-up for censored patients of 11.4 years, the median (interquartile range) PSA was 8.4 (5.8–12), 14 (8.8–25), and 32 (16–63) ng/mL for MMAI favorable, moderate, and unfavorable risks. Of the 3,829 patients with GG1/2, 71%, 25%, and 4% were stratified as MMAI favorable, moderate, and unfavorable risk, respectively. Similarly, the 867 GG3 patients were stratified as 63%, 30%, and 7%, respectively, and the 716 GG4/5 patients were stratified as 7%, 50%, and 43%, respectively. NCCN classified 584 (10%) patients as low-, 3,060 (55%), as intermediate-, and 1,925 (35%) as high-risk, with estimated 5-year DM rates (DM5, 95% confidence intervals [CI]) of 1% (0%–2%), 3% (3%–4%), and 10% (9%–12%) respectively.

In contrast, the MMAI model grouped 3,342 (60%) patients as favorable, 1,671 (30%) as moderate, and 556 (10%) as unfavorable risk, with estimated DM5 rates of 1% (1–2%), 6% (5–7%), and 28% (25–32%). The estimated 10-year DM rates (DM10, 95%CI) were 3% (1%–4%), 6% (5%–7%), and 17% (15%–18%) for NCCN low-, intermediate-, and high-, respectively, and were 3% (3%–4%), 12% (10%–14%), and 37% (33%–41%) for MMAI risk groups. Within NCCN intermediate-risk, MMAI identified 83% favorable-risk patients with 4% DM10, and within NCCN high-risk, MMAI identified 13% favorable-risk patients with only 4% DM10.

More information: Prostate Cancer Risk Stratification in NRG Oncology Phase III Randomized Trials Using Multi-modal Deep Learning with Digital Histopathology. Paper presented at the annual meeting of the American Society for Radiation Oncology. San Antonio, TX. plan.core-apps.com/myastroapp2 … 88-b75e-c2879cdb59f3

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