

Quantitative Digital Image Analysis Accurately Identifies Bone Metastatic Prostate Tumors Based Upon Histomorphometric and Nuclear Features of Diagnostic Prostate Needle Biopsies

Isla Garraway^{1,2*}, Eric Miller¹, Arkadiusz Gertych³, Beatrice Knudsen³

¹Department of Urology, Jonsson Comprehensive Cancer Center, David Geffen School of Medicine at UCLA, ²Division of Urology, Greater Los Angeles VA Healthcare System, ³Department of Pathology, Cedars-Sinai Medical Center

Background:

Clinical stage M1 prostate cancer (PC), associated with de novo bone metastases at diagnosis, is almost always fatal, with a 5-year survival of 28%. Interestingly, pathologic features of primary tumors from M1 cases are generally indistinguishable from those of M0 cases, where 5-year survival approaches 100%. We hypothesize that the amalgamation of histomorphometric and nuclear features present in diagnostic prostate needle biopsies (PNBX) of M1 cases significantly differ from M0 cases. Furthermore, we hypothesize that integrating "QI signatures" into the interpretation of PNBX could improve prognostication and identify patients at highest risk of micrometastases and subsequent disease progression. We have applied novel quantitative digital imaging (QI) technology and validated machine learning software tools to extract more than 160 QI features from PNBX in order to develop an algorithm capable of distinguishing tumor image tiles based upon M-stage.

Methods:

We created a diverse, annotated PC biorepository, which includes diagnostic PNBX and prostate tumor specimens from nearly 2200 patients diagnosed and treated at the Greater Los Angeles VA Healthcare System between 2000 and 2016. Retrospective analysis identified cohorts matched for age, race, and Gleason grade that were either clinical stage M0 (n=48) or M1 (n=35) at diagnosis. Archival hematoxylin and eosin (H&E) stained PNBX slides were reviewed and annotated for Gleason grade and pathological features, including neuroendocrine differentiation, in a blinded fashion by two GU pathologists. Slides were then digitally scanned at 40X magnification for image analysis. Approximately fifteen image tiles were collected from each slide. QI analysis was used to refine a set of parameters, including Fractal Dimensions [FD], Lacunarity [LA], and Nuclear Features [NF] that differed in M0 and M1 PC.

Results:

Image tiles from M0 (n=1200) and M1 (n=2018) cases were converted to nuclear masks. Using 60 Gabor and 45 segmentation-based fractal analysis (STFA) features, M1 and M0 could be distinguished with an accuracy of 71.8%. When nuclear features were applied (8 CP and 44 GLRL), accuracy increased to 80%. A trained classifier that merged all features achieved 85.5% accuracy in distinguishing images from M1 and M0 cases.

Conclusions: This rare cohort of patients that display disparate PC outcomes provides a unique opportunity to generate, test, and validate the performance of novel QI algorithms. Continued validation of this "computer vision" approach to routine diagnostic biopsies in larger cohorts with known outcomes may identify tumors with high-risk of dissemination, prompting consideration of upfront combination therapy.

Conflict of Interests: None to disclose.

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