Genomic classifiers and focal therapy: Small series conclusions

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INTRODUCTION AND OVERALL GOAL

Therapy planning and prognosis for prostate cancer are currently based primarily on Gleason Score and TNM staging[1]. Risk stratification of prostate cancer and treatment response may be influenced by predictive modeling based upon genomic profile of a tumor.

SPECIFIC AIMS

This HIPAA-compliant, IRB-exempt retrospective series illustrates the clinical utility of genomic classifiers for potential risk stratification in prostate cancer patients seeking laser focal therapy for organ-confined Gleason 3+3, 3+4 or 4+3 cancer.

RATIONALE AND BACKGROUND

ERG and PTEN are well-established for predicting tumor behavior and immunosuppressive ability of the patient[2]. Newer classifiers have evolved, that render high, intermediate and low-risk results from tissue samples. Our goal was to look at men in our laser focal therapy clinical trial to determine if the genomic status of their pre-treatment MRI-guided biopsy specimens could yield reliable prognostic information. Random, systematic biopsy specimens were not used because of their inherent lack of precision[3].

METHODS AND MATERIALS

30 men were identified from a Phase I clinical trial (NCT #02243033) who underwent laser focal therapy and had 6 month biopsy follow-up after treatment. All pre-treatment biopsy tissue underwent ERG and PTEN testing to obtain risk level. The pre-treatment ERG and PTEN risk levels were then correlated with 6-month biopsy results.

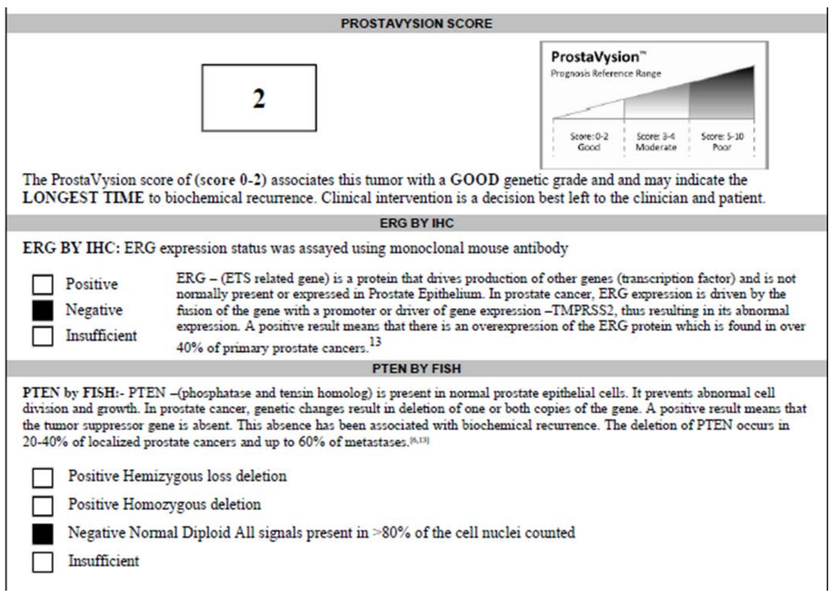
RESULTS

10 of 22 men with negative 6-month biopsy at the treatment area had normal ERG and PTEN status. Only 2 of the 8 men with positive 6-month biopsy had normal genomic status. The only other small cluster of note was that 3 of the 8 men with positive six month biopsy had ERG overexpression and hemizygous deletion of PTEN. In this group 33% were 3+3, 50% were 3+4 and 17% were 4+3.

DISCUSSION AND CONCLUSION

Our trend suggests that normal ERG and PTEN may be predictive of treatment response for laser focal therapy, and one can use this information to clinically assess suitability as to whether undergoing active surveillance or laser focal therapy would be a preferred decision.

Fig. a – Negative ERG and PTEN intact


PROSTAVYSION SCORE

2

ProstaVysion™ Prognosis Reference Range — Score: 0-2 Good | Score: 3-4 Moderate | Score: 5-10 Poor

The ProstaVysion score of (score 0-2) associates this tumor with a GOOD genetic grade and and may indicate the LONGEST TIME to biochemical recurrence. Clinical intervention is a decision best left to the clinician and patient.

ERG BY IHC

ERG BY IHC: ERG expression status was assayed using monoclonal mouse antibody

☐ Positive
■ Negative
☐ Insufficient

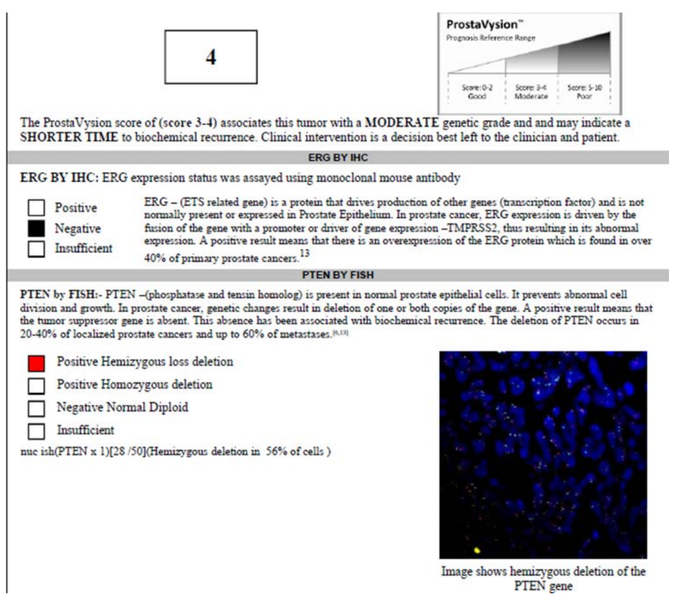
ERG – (ETS related gene) is a protein that drives production of other genes (transcription factor) and is not normally present or expressed in Prostate Epithelium. In prostate cancer, ERG expression is driven by the fusion of the gene with a promoter or driver of gene expression –TMPRSS2, thus resulting in its abnormal expression. A positive result means that there is an overexpression of the ERG protein which is found in over 40% of primary prostate cancers.[13]

PTEN BY FISH

PTEN by FISH:- PTEN –(phosphatase and tensin homolog) is present in normal prostate epithelial cells. It prevents abnormal cell division and growth. In prostate cancer, genetic changes result in deletion of one or both copies of the gene. A positive result means that the tumor suppressor gene is absent. This absence has been associated with biochemical recurrence. The deletion of PTEN occurs in 20-40% of localized prostate cancers and up to 60% of metastases.[6,13]

☐ Positive Hemizygous loss deletion
☐ Positive Homozygous deletion
■ Negative Normal Diploid All signals present in >80% of the cell nuclei counted
☐ Insufficient

Fig. b – Hemizyous PTEN deletion


4

ProstaVysion™ Prognosis Reference Range — Score: 0-2 Good | Score: 3-4 Moderate | Score: 5-10 Poor

The ProstaVysion score of (score 3-4) associates this tumor with a MODERATE genetic grade and and may indicate a SHORTER TIME to biochemical recurrence. Clinical intervention is a decision best left to the clinician and patient.

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ERG BY IHC: ERG expression status was assayed using monoclonal mouse antibody

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☐ Positive Homozygous deletion
☐ Negative Normal Diploid
☐ Insufficient

nuc ish(PTEN x 1)[28 /50](Hemizygous deletion in 56% of cells)

Image shows hemizygous deletion of the PTEN gene

Fig. c – ERG+ (overexpression)

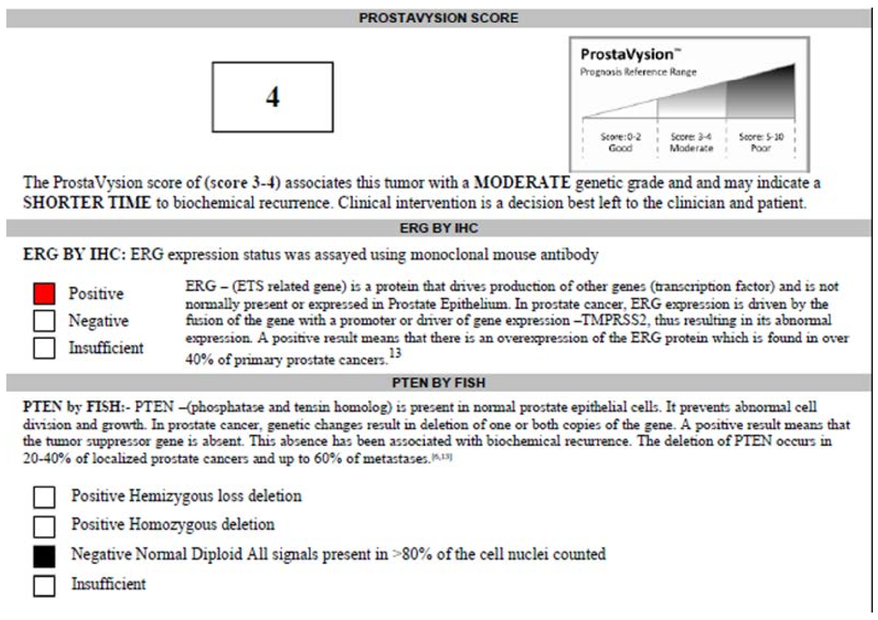
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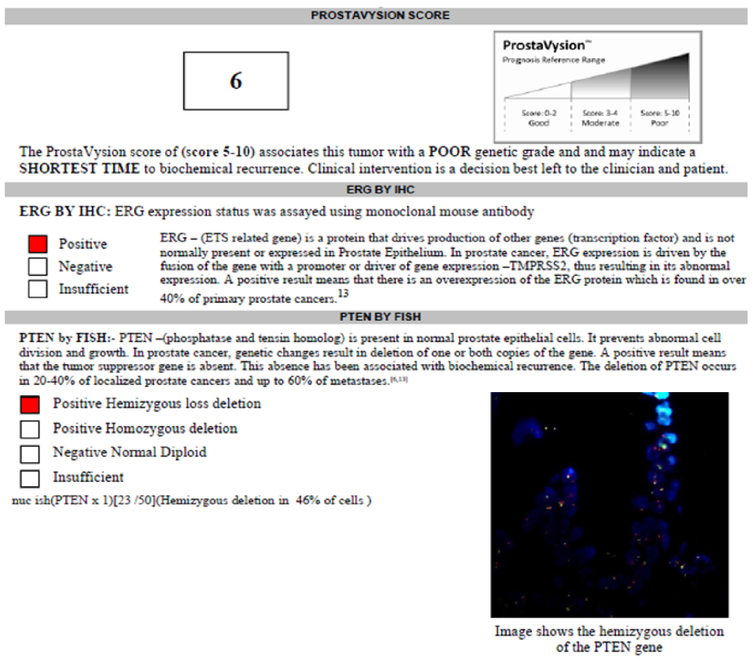
Fig. d – ERG+ and hemizygous PTEN deletion


PROSTAVYSION SCORE

6

ProstaVysion™ Prognosis Reference Range — Score: 0-2 Good | Score: 3-4 Moderate | Score: 5-10 Poor

The ProstaVysion score of (score 5-10) associates this tumor with a POOR genetic grade and and may indicate a SHORTEST TIME to biochemical recurrence. Clinical intervention is a decision best left to the clinician and patient.

ERG BY IHC

ERG BY IHC: ERG expression status was assayed using monoclonal mouse antibody

■ Positive
☐ Negative
☐ Insufficient

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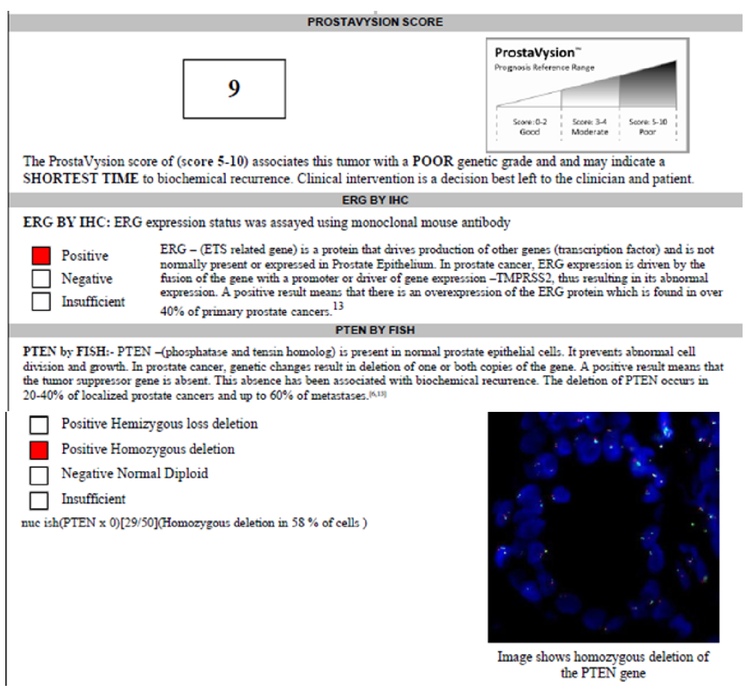
■ Positive Hemizygous loss deletion
☐ Positive Homozygous deletion
☐ Negative Normal Diploid
☐ Insufficient

nuc ish(PTEN x 1)[23 /50](Hemizygous deletion in 46% of cells)

Image shows the hemizygous deletion of the PTEN gene

Fig. e – ERG+ and homozygous PTEN del.


PROSTAVYSION SCORE

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☐ Positive Hemizygous loss deletion
■ Positive Homozygous deletion
☐ Negative Normal Diploid
☐ Insufficient

nuc ish(PTEN x 0)[29/50](Homozygous deletion in 58 % of cells)

Image shows homozygous deletion of the PTEN gene

Fig. f – Patients relate to bicyclist analogy

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