IMAGING

MRI and molecular profiles: improving prediction

Prostate cancer is one of the most common malignancies diagnosed in American men. Selection of the most appropriate treatment regimen and prediction of prognosis, however, depend on various clinical parameters such as tumor stage, serum prostate-specific antigen (PSA) levels and biopsy Gleason score. Of these parameters, biopsy Gleason score and PSA levels are important predictors of prostate cancer progression and recurrence. A study published in *Clinical Cancer Research* has shown that pretreatment MRI findings correlate well with molecular markers in surgical prostate cancer specimens and clinical parameters such as biopsy Gleason score. Moreover, the study demonstrated that findings from MRI and molecular marker analyses are a powerful tool for the prediction of prostate cancer recurrence.

Prediction of prognosis and risk of recurrence prior to treatment is crucial in the selection of appropriate treatment for patients with prostate cancer, and several algorithms and nomograms have been devised for these purposes. MRI and magnetic resonance spectroscopic imaging (MRSI) have also been shown to aid in the pretreatment evaluation of prostate cancer. MRI and MRSI could, therefore, be useful for tumor detection and staging and for post-treatment follow-up in patients with prostate cancer. Studies of endorectal MRI in patients with biopsy Gleason score 7 and PSA levels of <10 ng/ml, have shown that local therapy was effective for those with stage T2 disease, whereas more-aggressive therapy was required for patients with stage T3 prostate cancer. Models that incorporate preoperative clinical variables and MRI data have been generated to predict prostate cancer recurrence following surgery. Molecular profiles from tumor tissue samples obtained at biopsy or surgery might also help elucidate tumor biology and treatment outcome.

Researchers have developed a 'systems pathology' approach for the prediction of prostate cancer recurrence in patients who

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had undergone radical prostatectomy. This model is highly accurate and incorporates clinicopathologic measures along with quantified biomarkers. The combination of MRI with systems pathology could be useful in the prediction of prostate cancer recurrence. Shukla-Dave *et al.* evaluated whether pretreatment MRI and MRSI along with molecular markers of tumor progression correlated with each other and with preoperative clinical measures in patients with prostate cancer. Moreover, they determined whether molecular markers and MRI findings provided additional pretreatment clinical value in predicting prostate cancer recurrence.

The study included 88 patients with prostate cancer who had MRI and MRSI prior to undergoing radical prostatectomy. Patients were between 46–79 years of age with a PSA range of 2.6–76.8 ng/ml and a biopsy Gleason score range of 6–9. A score of 1–7 (from no tumor detected to tumors with lymph-node metastasis) was assigned for the imaging results. Immunohistochemistry was used to assess the expression of proliferation marker Ki-67, the serine/threonine kinase phospho-Akt, and the androgen receptor in biopsy or surgical tumor samples. These three markers were assessed as they are

associated with high Gleason score and prostate cancer progression.

The researchers found that all of the assessed markers (Ki-67, phospho-Akt and androgen receptor) demonstrated an important prognostic value for prostate cancer recurrence, and correlated significantly with MRI and MRSI score. Moreover, these molecular markers and MRI and MRSI score were highly associated with clinical stage and biopsy Gleason score but not with PSA levels. Prostate cancer recurrence was observed in 31% of patients at the time of last follow-up and Ki-67, phospho-Akt and androgen-receptor expression indices were higher in these patients than those without recurrence. MRI and MRSI score was also associated with time to recurrence.

In conclusion, MRI and MRSI findings correlated well with molecular markers and provide additional value to the already established clinical parameters used in the prediction of prostate cancer recurrence.

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Original article Shukla-Dave, A. *et al.* Prediction of prostate cancer recurrence using magnetic resonance imaging and molecular profiles. *Clin. Cancer Res.* 15, 3842–3849 (2009).