MammaPrint accurately identifies good prognosis group within clinically indeterminate risk patients.

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mammaprint™
decoding breast cancer.

Abstract

Background: A 70-gene tumor expression profile was established as a powerful predictor of disease outcome in patients with breast cancer[1,2]. The test, known as "MammaPrint," was recently validated in independent cohorts, and implementation was shown to be feasible in community hospitals[3-7]. We have shown that MammaPrint predicts risk of recurrence in T1, T2 N0 and N1-3+ breast cancer patients, ER independent.

Clinicopathological guidelines give indeterminate risk assessment in patients with ER positive LN0 grade 2 early-stage breast cancer. Here we have focused on this specific subgroup to determine MammaPrint performance.

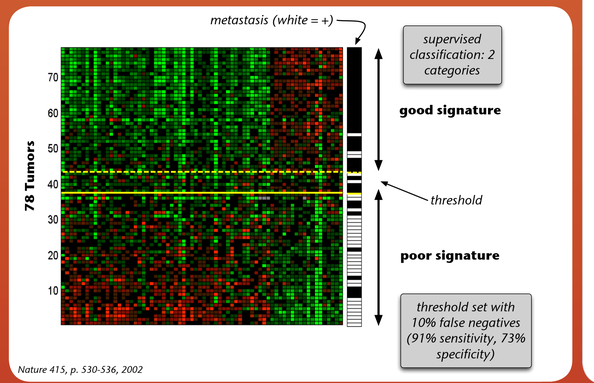
Methods: Patients with ER positive LN0 grade2 early stage breast cancer from the original validation series (van de Vijver et al, NEJM 2002) were analyzed for MammaPrint outcome and further divided by histological grade.

Results: Among the 40 ER positive LN0 grade 2 patients, 23 samples (58%) had a good prognosis signature according to MammaPrint and had a 10 year overall survival of 100%. Seventeen patients (42%) had a poor prognosis signature and a 10 year survival of 51% . At ten years the probability of remaining free of distant metastasis was 89% in the group with the good prognosis signature and 42% in the group with the poor prognosis signature.

Conclusions: Clinical guidance in patients with ER+ LN0 grade 2 breast cancer is problematic using clinical pathological guidelines. MammaPrint provides a significant separation in recurrence risk and overall survival in these indeterminate tumors thereby improving guidance for the requirement of adjuvant therapy.

Development of the 70-gene MammaPrint profile

A gene expression signature that is predictive for the development of breast cancer metastases, was discovered using an initial cohort of 78 patients who did or did not develop distant metastases[1]. This profile forms the basis of the MammaPrint breast cancer prognostic test. The profile was validated in multiple independent series[2,4-7], translated into a diagnostic test[3] and was shown to be feasible to be implemented in clinical practice[5].

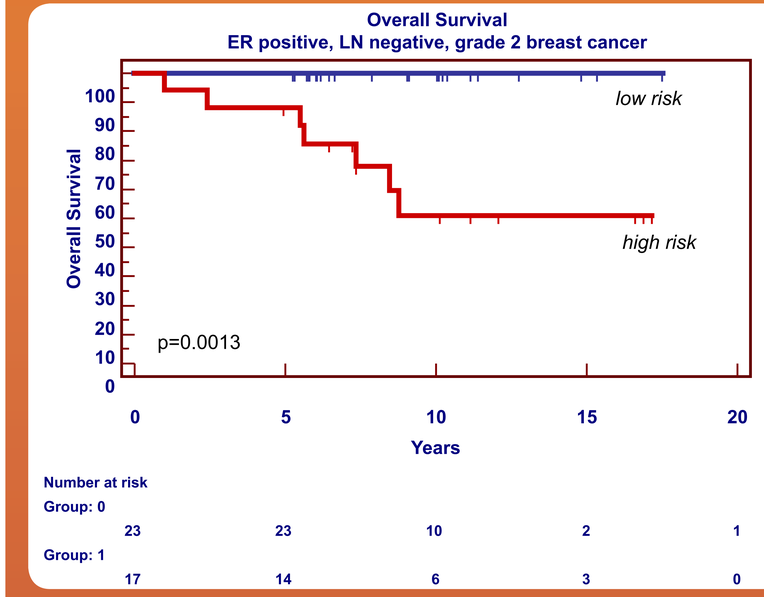


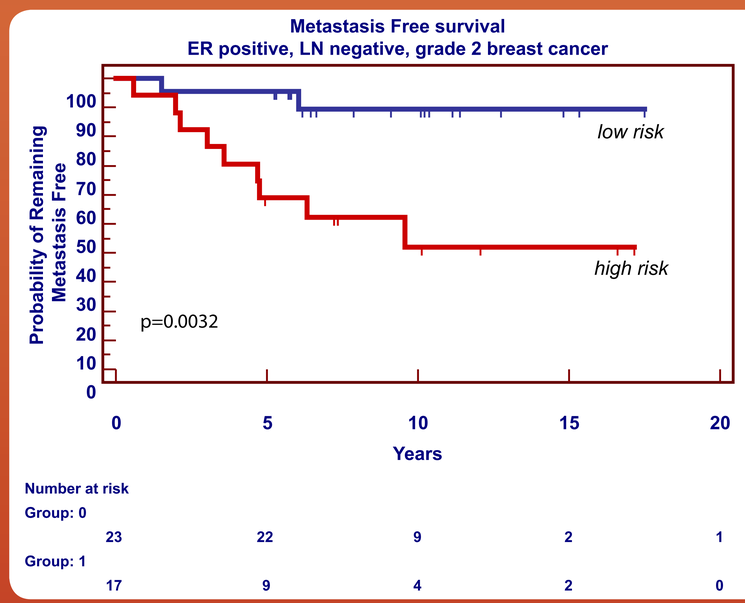
Nature 415, p. 530-536, 2002

References: (1) van 't Veer LJ et al. Nature 2002; (2) van de Vijver MJ et al. N Engl J Med 2002; (3) Glas AM et al. BMC Genomics 2006; (4) Buyse et al. JNCI 2006; (5) Bueno-de-Mesquita et al. Lancet Oncol 2007;(6) Wittner et al. Clin Can Res 2008; (7) Mook, S et al. Breast Can Res Treat, 2008

Clinically Indeterminate Risk Groups

Women with ER positive LN0 grade 2 early stage breast cancer are generally considered to have indetermined risk by clinico pathological guidelines. MammaPrint can significantly identify patients who will develop distant metastases, but also those whose risk is minimal.



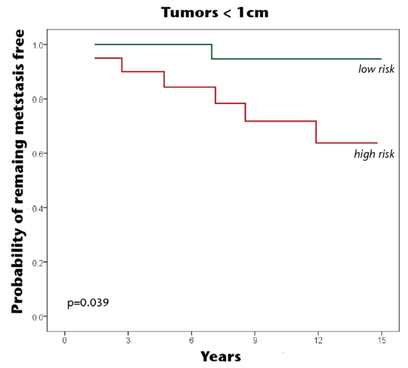


Kaplan -Meier Analysis of overall survival and the probablity that patients woud remain free of distant metastasis by MammaPrint among ER positive LN0 grade 2 early stage breast cancer patients*.

* only 4of 40 patients received adjuvant hormonal and/or chemotherapy

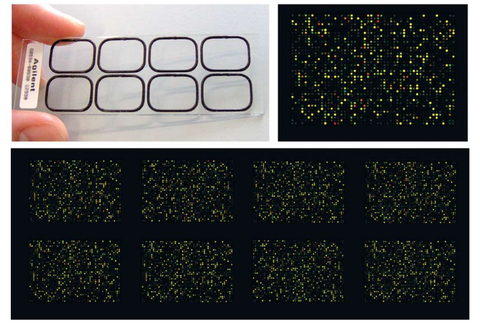
Small tumors

To underscore MammaPrint adds information to all risk categories, we have also perfomed a sub analysis in patients with tumors generally considered to be of low risk; tumors smaller than 1 cm. (from the Van de Vijver and Buyse data sets[2,4]). n=39, 19 (49%) good prognosis signature, 20 (51%) poor prognosis signature.



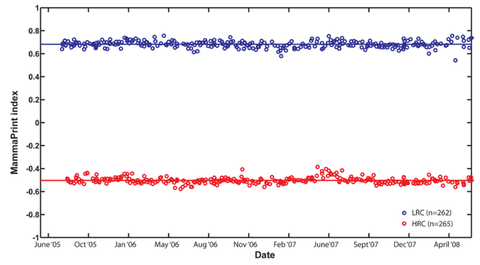
Diagnostic Microarray

A diagnostic '8-pack' array is a single 1"x3" slide with eight subarrays each containing the MammaPrint probes, normalization and control features. This allows simultaneous analysis of up to 8 samples.



Robust

To ensure that the outcome of the test is stable time, two control samples were amplified and hybridized repeatedly over a period of 3 years. MammaPrint shows extreme stability over time.



Conclusion

MammaPrint provides a significant separation in recurrence risk and overall survival in patients clinically regarded as having indeterminate risk (patients with ER positive LN0 grade 2 early stage breast cancer).

Moreover, in a subgroup generally considered to be of low risk (tumors <1cm), MammaPrint identifies a substantial proportion of patients with a poor prognosis profile.

MammaPrint can improve guidance over clinical pathological guidelines for the requirement of adjuvant therapy. MammaPrint is an extremely robust test and cleared by FDA for clinical practice.

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