Feasibility of using core-needle biopsies for the 70-gene prognosis signature

mammaprint™
decoding breast cancer.

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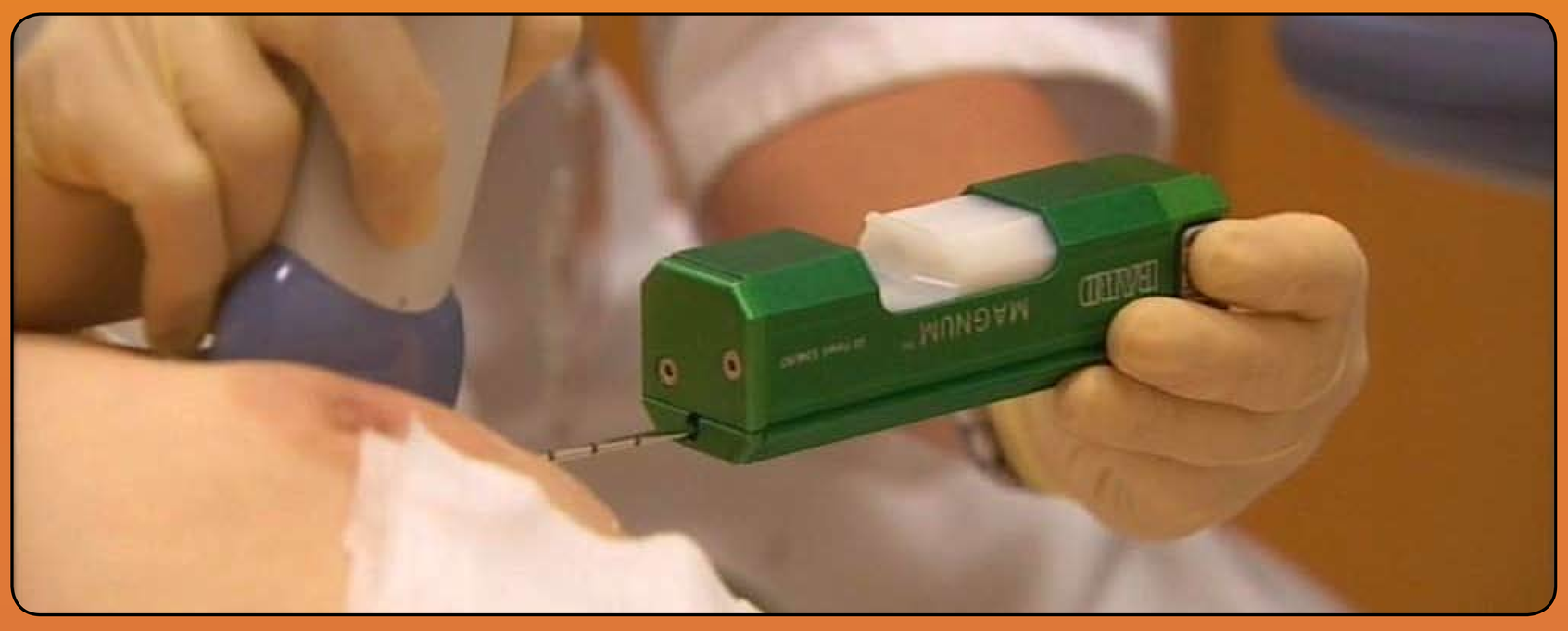
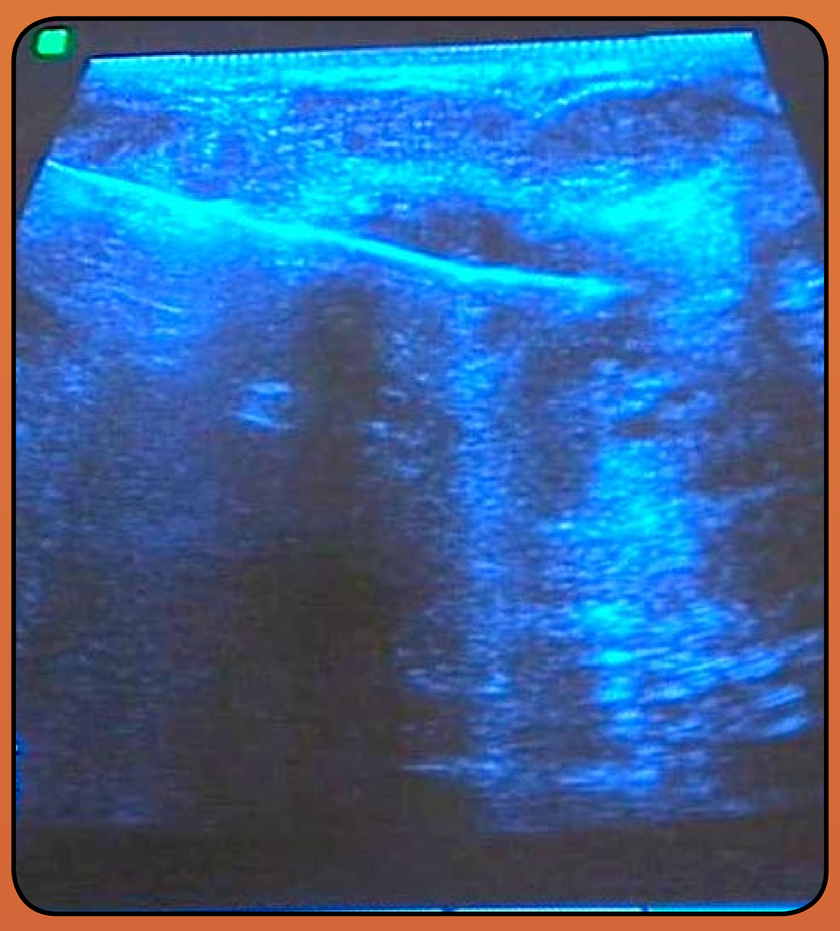
Background

A 70-gene microarray prognosis signature was previously discovered to improve the selection of patients with breast cancer for adjuvant therapy[1,2]. This diagnostic test known as "MammaPrint" was recently validated in an independent cohort and implementation was shown to be feasible in community hospitals[3-7]. MammaPrint was originally established on surgical resection specimens. Since most breast cancer patients will undergo core needle biopsies, we investigated whether the MammaPrint prognosis signature could be assessed in core needle biopsies.



Patients and Methods

We determined MammaPrint outcome in patients with breast cancer stage II-IV who had core needle biopsies (14-gauge) and subsequent neo-adjuvant treatment. These patients presented to 4 ONCAMI hospitals from November 2006 up to present and participated in the TAXCET trial. The average age of these patients was 53 years (ranging from 30 to 78 years). Core needle biopsies from 50 patients before treatment were subjected to microarray expression analysis using MammaPrint, the 70-gene prognosis signature, and were classified as being at either low or high risk for distant metastasis.



Overview of patients

Stage	number of patients
IIa	5
IIb	9
IIIa	20
IIIb	14
IV	2
total	50

Chemotherapy response

All but one patient (received TEC) received AT, usually 6 cycles. Most therapies ended late 2007, beginning 2008. Tumor diameter was assessed by physical examination and mammography.

High risk patients	
unknown	3
progressive disease	0
stable disease	1
partial response	24
complete response*	3
total	31

Low risk patients	
unknown	1
progressive disease	0
stable disease	0
partial response	3
complete response*	0
total	4

*pathological complete response

Results

Thirty five signatures were obtained in this study. In this neo-adjuvant data set four of the 35 cases were assigned low risk for recurrence and thirty-one cases were predicted to be high risk. The high percentage of high risk MammaPrint outcome can be ascribed to the inclusion criteria of the trial, including breast cancer patients with stages III and IV. MammaPrint is originally designed for early stage breast cancer patients (stage I and II).

Twelve samples were rejected on the grounds of low tumor percentage, three samples because of insufficient RNA quality. Ninety two percent (92%) of samples with sufficient tumor cell precentage received a MammaPrint result.

Core Needle Biopsies

The workup for breast cancer usually includes an ultrasound-guided or stereotactic core biopsy, allowing the pathologist to microscopically examine the tissue. A MammaPrint prognosis signature can be obtained from a core needle biopsy. The core needle biopsy tissue is added to the RNA stabilizing fluid (RNA Retain), in which RNA is stable for 1 week at room temperature.

Microarray based receptor read-out

Roepman et al.[8] recently showed microarray read-out of hormone and HER2 receptor status to be strongly correlated with IHC assessment, especially for ER and HER2. Here we show the ER data for the current study:

		IHC		
	ER	pos	neg	unknown
Microarray	pos	17	4	1
	neg	0	8	1

Conclusion

The MammaPrint assay was originally designed for tumor tissue from surgical specimens. We show here that MammaPrint prognosis signatures can be obtained in the majority of core needle biopsies. In addition the same biopsy can be used for ER, PR and HER2 gene expression read-out. The results of this study have broadened the clinical applicability of the MammaPrint prognosis signature.

Diagnostic Microarray

A diagnostic '8-pack' is a single 1"x3" slide with eight sub-arrays each containing ER, PR and HER2 probes and normalization features. This allows simultaneous analysis of up to 8 samples.

References
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