

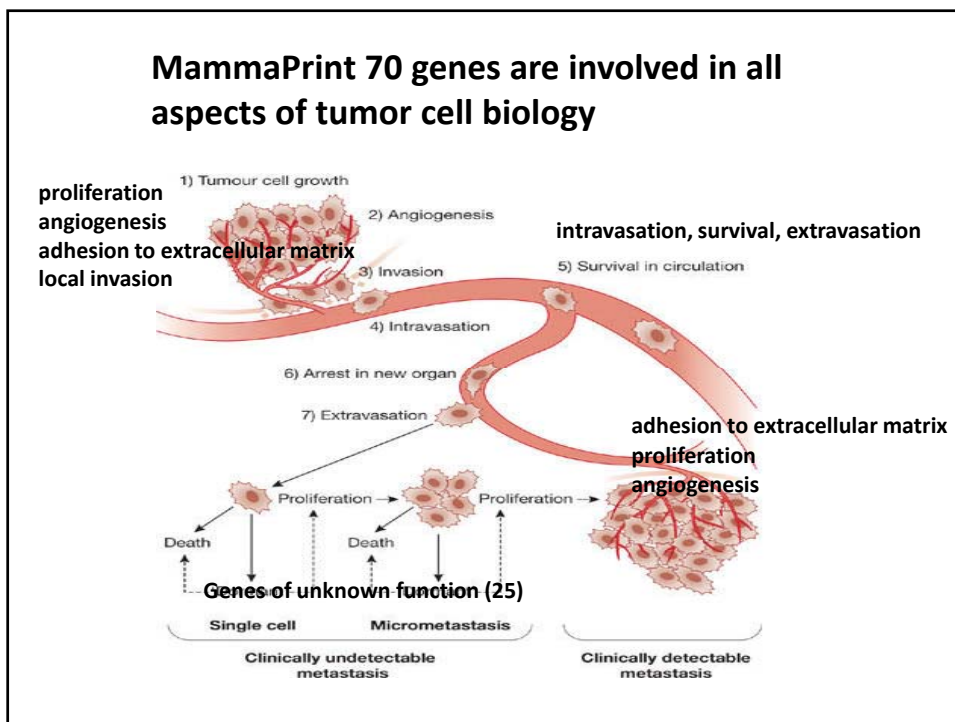
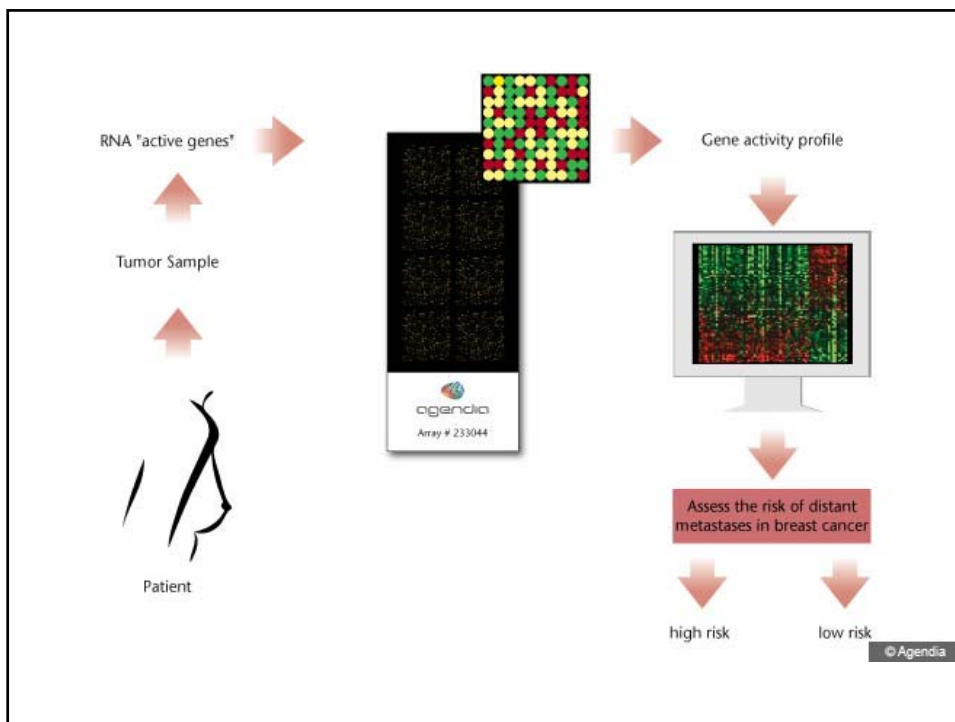


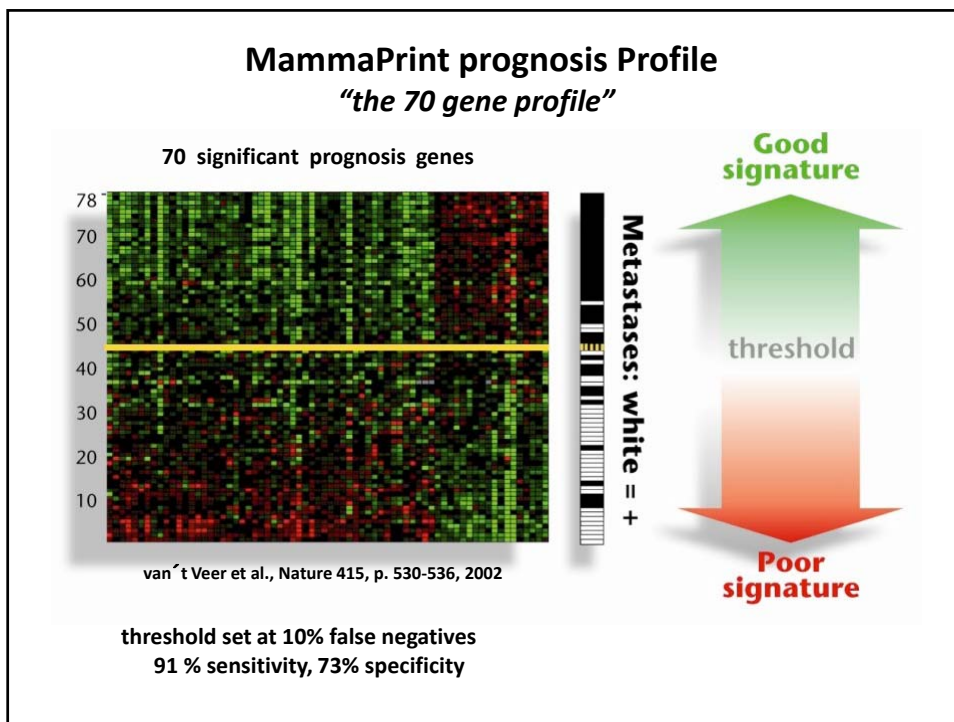
MammaPrintは手術によって切除された腫瘍の70遺伝子における活性を測定することにより、再発リスクの高低を調べる

MammaPrintは適切なテーラーメイドの治療計画を立てるための医師にとっての貴重な情報を提供することができる

従来の方と比べて、MammaPrintではハイリスクと判定される患者の数を大きく減らすことができるので、結果として不必要な化学療法を避けることができ、また、潜在的な副作用の危険を最小限にすることが可能

乳癌は、たとえ腫瘍自体が小さくても、しばしば悪性であることがあり、MammaPrintを用いれば、このようなケースは、ハイリスクと区分され、適切な治療計画を立てることが可能





MammaPrint®
Breast Cancer Prognosis Service

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www.agenda.com

ANALYSIS REPORT

Customer : Mrs. Dr. Sixt	Report number : 12345678
Location : Breast Cancer Hospital 99 Mammastreet 11 12345, Amsterdam Netherlands TEL: -	Analysis performed : MammaPrint™ service Sample received : October 26, 2007 Date analysis report : October 26, 2007 Your reference : 12345-ABC Our reference : 12345678

SERVICE DESCRIPTION

The tissue sample you submitted, labeled as 12345678, was analyzed with MammaPrint Breast Cancer Prognosis Service. The analysis was performed in duplicate. This comprises of independent labeling with two different color dyes and independent hybridisation on two different mini-arrays, that include 70 prognostic genes in triplicate.

ANALYSIS RESULT

The tissue sample you submitted, labeled as 12345678, was analyzed with MammaPrint Breast Cancer Prognosis Service. The analysis was performed in duplicate.

The sample is classified as: **LOW RISK**

ANALYSIS EXPLANATION

The analysis result is correlated with previously published results of the 70 gene prognostic profile in breast tumors of patients with good outcome (i.e. no metastases within 10 years) in the reference group as published^[1], patients classified as LOW RISK had a 97% chance of survival after 10 years and 87% chance to be metastasis free after 10 years, without adjuvant treatment.

The patients classified^[1] as HIGH RISK, patients had less than 50% chance of survival after 10 years and less than 44% chance to be metastasis free after 10 years, without adjuvant treatment.

ANALYSIS INFORMATION

General information about Agenda and the MammaPrint Breast Cancer Prognosis Service can be found at www.agenda.com.

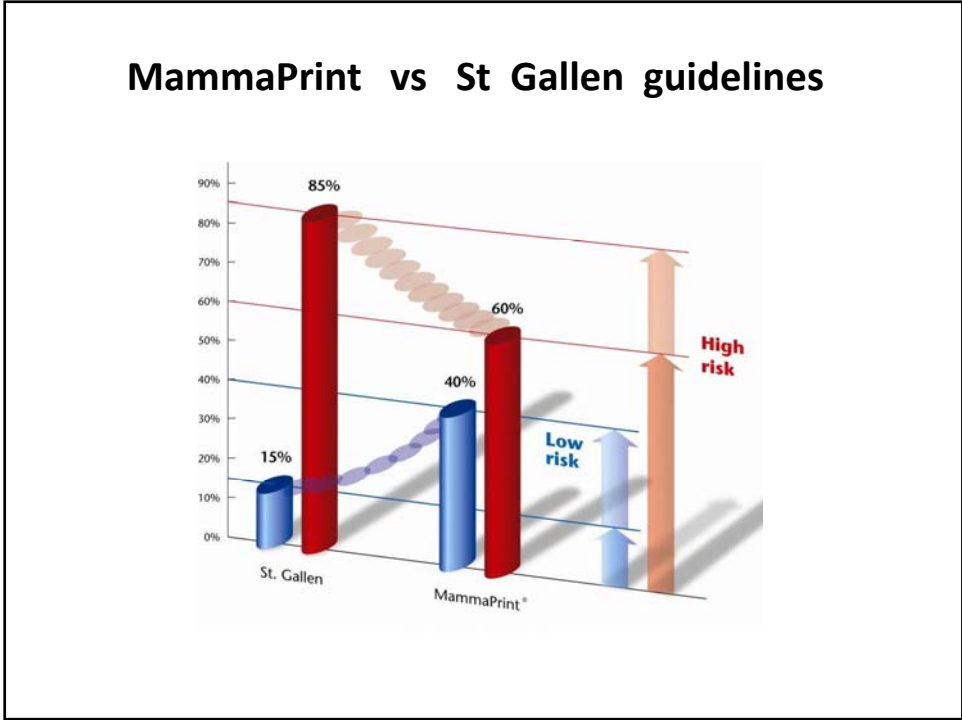
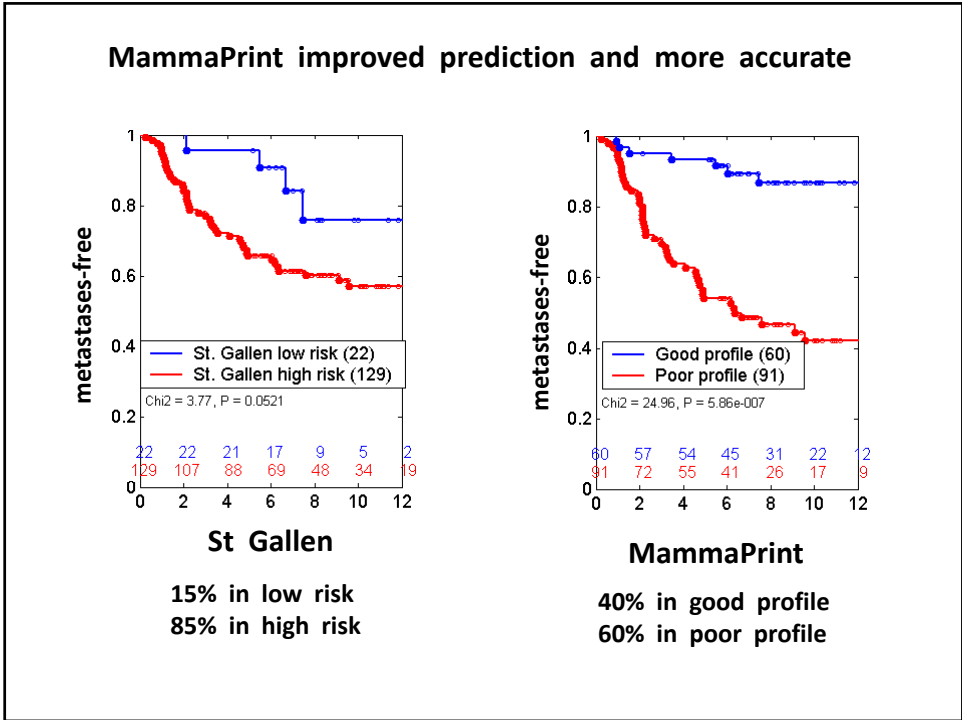
If you have any questions regarding this report please do not hesitate to contact us at +31 20 462 1510

Yours sincerely,

Dr. L. van 't Veer
Chief Operating Officer

Agenda

^[1]The classification is described in "A Gene-Expression Signature as a Predictor of Survival in Breast Cancer", Marc J. van de Vijver, M.D., Ph.D. et. al. N Engl J Med. 2002 Dec 19;347(25):1999-2009
^[2]Validation and Clinical Utility of a 70-Gene Prognostic Signature for Women With Node-Negative Breast Cancer. Marc Buyse et al., Journal of the National Cancer Institute, Vol. 98, No. 11, September 8, 2006



St Gallen 2007

		Endocrine responsiveness		
		Highly responsive	incompletely responsive	non-responsive
HER2/neu gene overexpressed and/or amplified	no	ET (リスクに応じてCTの追加を考慮)	ET (リスクに応じてCTの追加を考慮)	CT
	yes	ET+ trastuzumab +CT	ET+ trastuzumab +CT	trastuzumab+CT

ET: endocrine therapy
CT: chemotherapy

化学療法を追加すべきかどうかのジレンマ

本パネルでは、Oncotype Dx™などの分子レベルのツールや MammaPrint™による遺伝子発現プロファイリングはリスク分類法として十分に確立されていないとみなした。これらの2つの方法は、プロスペクティブな臨床試験において現在検証中である。

		HER2 ⇒	過剰発現・増幅なし					過剰発現・増幅あり							
		内分泌反応性 ⇒	高度		不完全		なし	高度		不完全		なし			
		閉経状況 ⇒	前	後	前	後	前・後	前	後	前	後	前・後			
リスクカテゴリー	低	n = 0	HR + and HER2 -	E 1	E 2	E 3	E 4								
	中	n = 0		E C⇒E 5	E C⇒E 6	C⇒E E 7	C⇒E E 8	C 9	C⇒E +H 10	C⇒E +H 11	C⇒E +H 12	C⇒E +H 13	C +H 14		
		n = 1-3	HR+ and HER2 -												
	高	n = 1-3	HR - or HER2 +					C 19	C⇒E +H 20	C⇒E +H 21	C⇒E +H 22	C⇒E +H 23	C +H 24		
		n ≥ 4		C⇒E 15	C⇒E 16	C⇒E 17	C⇒E 18								

乳癌手術症例304例の24病型分布

ホルモン陽性率: 75% HER2陽性率: 21.4%

		HER2 ⇒	過剰発現・増幅なし					過剰発現・増幅あり				
		内分泌反応性 ⇒	高度		不完全		なし	高度		不完全		なし
		閉経状況 ⇒	前	後	前	後	前・後	前	後	前	後	前・後
リスクカテゴリー	低	n = 0 HR + and HER2 -	E 13	E 16	E 0	E 3						
	中	n = 0	E C⇒E 41 (13)	E C⇒E 81 (28)	C⇒E E 6 (2)	C⇒E E 21 (3)	C 39	C⇒E +H 7	C⇒E +H 4	C⇒E +H 2	C⇒E +H 6	C +H 21
		n = 1-3	HR+ and HER2 -									
	高	n = 1-3	HR - or HER2 +					C 8	C⇒E +H 5	C⇒E +H 6	C⇒E +H 1	C⇒E +H 4
n ≥ 4			C⇒E 2	C⇒E 6	C⇒E 0	C⇒E 3						

149例

Agendia 社(アムステルダム) からの受託研究

- 細胞診、組織診で乳癌と診断された症例
- 年齢75歳以下、PS 0-1
- St.Gallen 2007 24病型分類で推奨される治療が
 - 内分泌療法単独
 - 抗がん剤治療後内分泌療法
 のいずれかが推奨される症例
- Mammaprint検討用の検体提供および検査結果を本人に知らせ、その情報を抗がん剤を追加するかどうかの判断根拠としては参考にしないことを同意した症例

Case 1 38 F premenopausal

Scirrhou ca 1cm NG2 ly- v- n0/6
ER(AS 8) PgR(AS 8) HER2 negative

highly endocrine responsive
Intermediate risk

Case 1 38 F premenopausal

Scirrhou ca 1cm NG2 ly- v- n0/6
ER(AS 8) PgR(AS 8) HER2 negative

highly endocrine responsive
Intermediate risk

Zoladex + tamoxifen

Case 1 38 F premenopausal

Scirrhou ca 1cm NG2 ly- v- n0/6
ER(AS 8) PgR(AS 8) HER2 negative

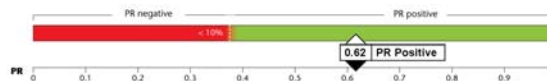
highly endocrine responsive
Intermediate risk

MammaPrint: **LOW RISK**

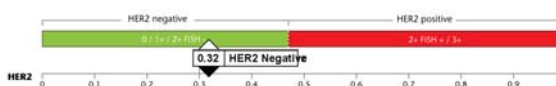
Estrogen Receptor
ER Positive



Progesterone Receptor
PR Positive



HER2/neu
HER2 Negative



Case 2 45 F premenopausal

Scirrhou ca 1.6cm NG2 ly+ v+ n1/9
ER (AS 7) PgR (AS 8) HER2 negative

highly endocrine responsive
Intermediate risk

Case 2 45 F premenopausal

Scirrhou ca 1.6cm NG2 ly+ v+ n1/9
 ER (AS 7) PgR (AS 8) HER2 negative

highly endocrine responsive
 Intermediate risk

AC x 4 → Zoladex + tamoxifen

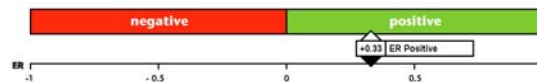
Case 2 45 F premenopausal

Scirrhou ca 1.6cm NG2 ly+ v+ n1/9
 ER (AS 7) PgR (AS 8) HER2 negative

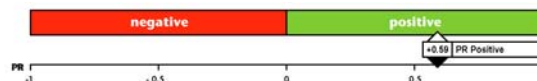
highly endocrine responsive
 Intermediate risk

MammaPrint: **HIGH RISK**

Estrogen Receptor
 ER Positive



Progesterone Receptor
 PR Positive



HER2/neu
 HER2 Negative



Case 3 64 F postmenopausal

Scirrhou ca 1.7cm NG3 ly+ v+ n0/3
ER(AS 8) PgR(AS 7) HER2 negative

highly endocrine responsive
Intermediate risk

Case 3 64 F postmenopausal

Scirrhou ca 1.7cm NG3 ly+ v+ n0/3
ER(AS 8) PgR(AS 7) HER2 negative

highly endocrine responsive
Intermediate risk

AC x 4 → AI

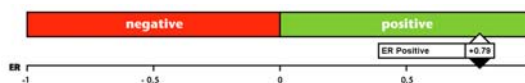
Case 3 64 F postmenopausal

Scirrhus ca 1.7cm NG3 ly+ v+ n0/3
ER(AS 8) PgR(AS 7) HER2 negative

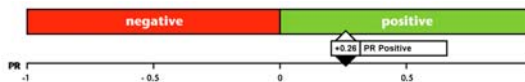
highly endocrine responsive
Intermediate risk

MammaPrint: **HIGH RISK**

Estrogen Receptor
ER Positive



Progesterone Receptor
PR Positive



HER2/neu
HER2 Negative



MINDACT trial

Microarray In Node-negative and 1 to 3 positive lymph node Disease
may Avoid ChemoTherapy

