

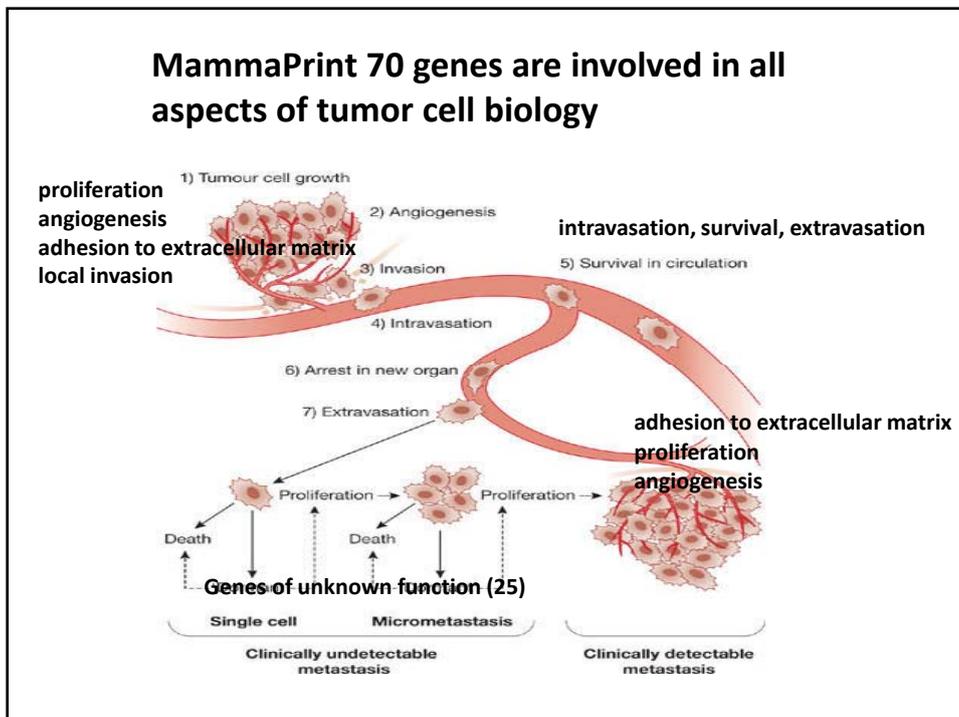
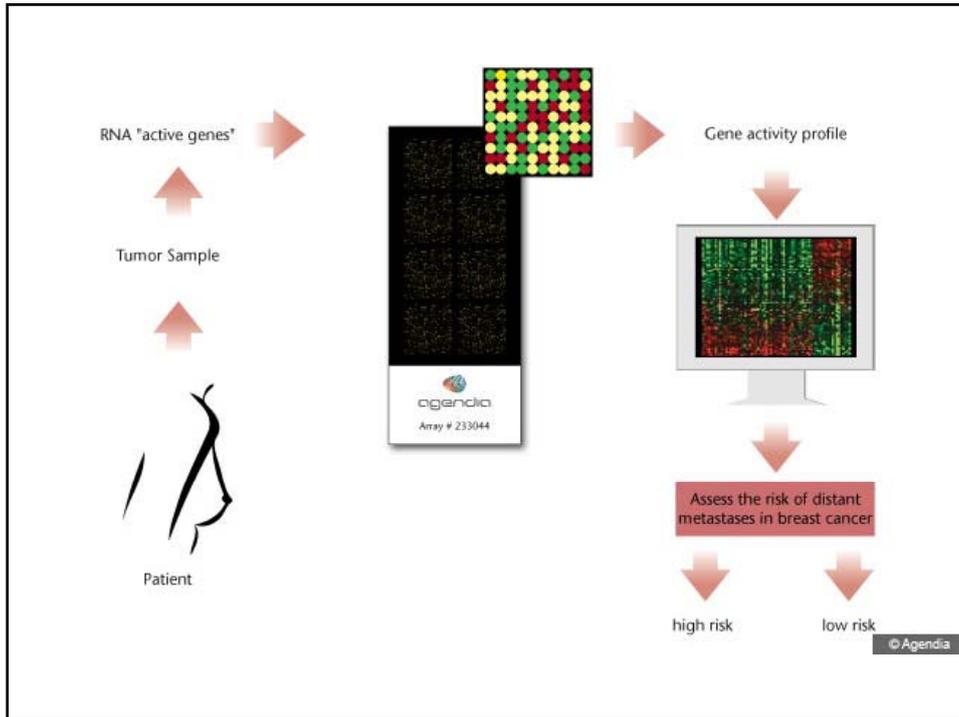


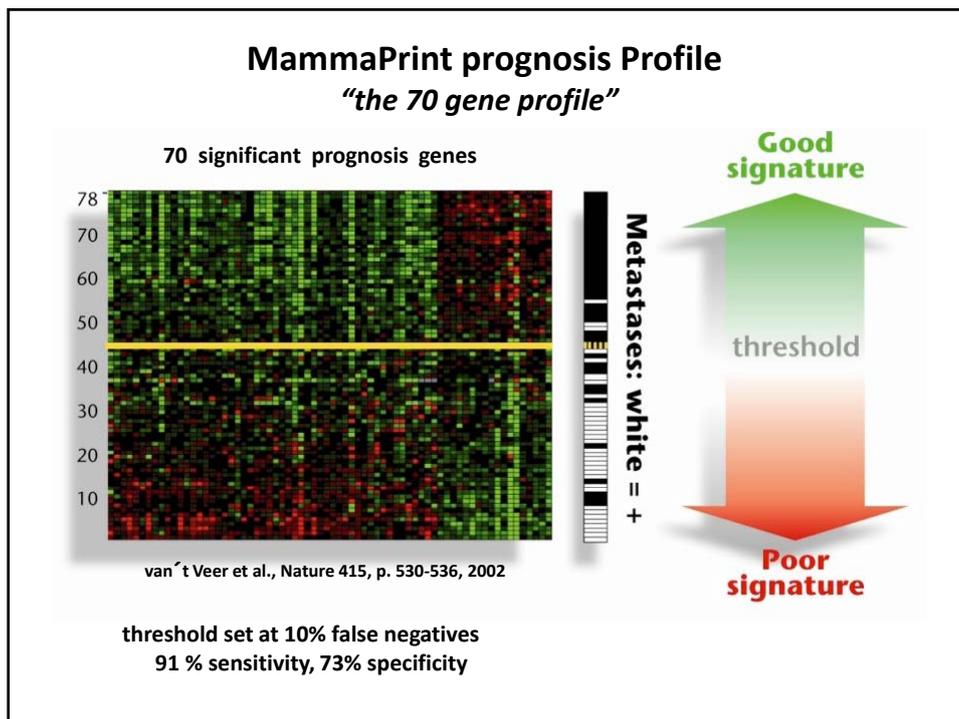
**MammaPrintは手術によって切除された腫瘍の70遺伝子における活性を測定することにより、再発リスクの高低を調べる**

**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

Agenda BV  
Postbus 406  
1096 SM Amsterdam  
The Netherlands  
Tel +31 20 462 1510  
info@agenda.com  
www.agenda.com

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**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

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**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.

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**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**

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**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<sup>(1)</sup>, 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<sup>(1)</sup> 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.

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**ANALYSIS INFORMATION**

General information about Agenda and the MammaPrint Breast Cancer Prognosis Service can be found at [www.agenda.com](http://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



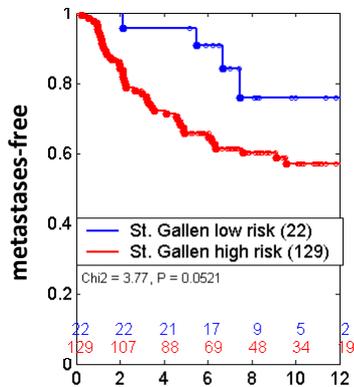
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<sup>(1)</sup>The classification is described in "A Gene-Expression Signature as a Predictor of Survival in Breast Cancer", Marc J. van de Vijver, M.D., Ph.D. et. al. N Engl J Med. 2002 Dec 19;347(25):1999-2009  
<sup>(2)</sup>Validation and Clinical 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

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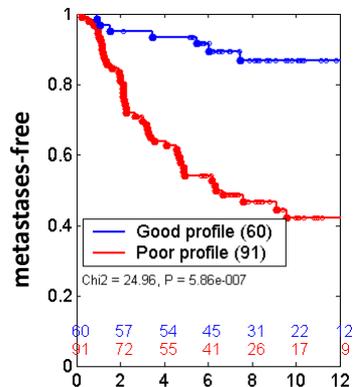


**MammaPrint improved prediction and more accurate**



**St Gallen**

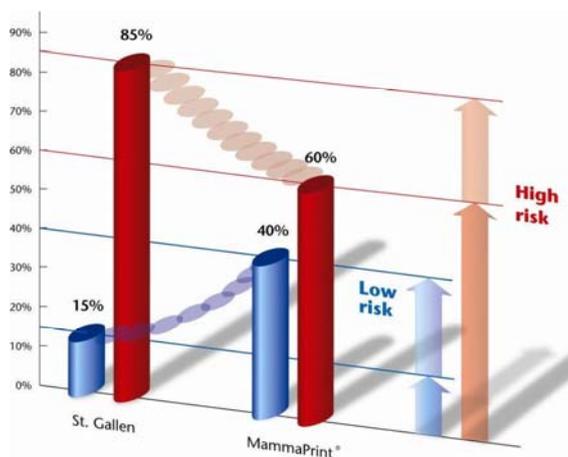
15% in low risk  
85% in high risk



**MammaPrint**

40% in good profile  
60% in poor profile

**MammaPrint vs St Gallen guidelines**



### 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	C +H 9
		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

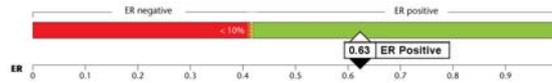
**Case 1 38 F premenopausal**

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

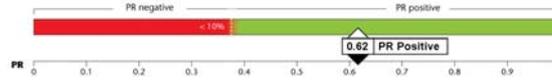
highly endocrine responsive  
Intermediate risk

MammaPrint: **LOW RISK**

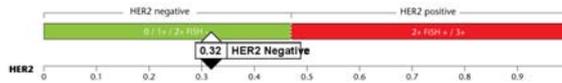
Estrogen Receptor  
ER Positive



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

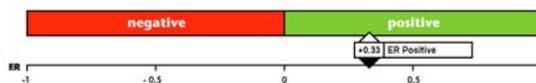
**Case 2 45 F premenopausal**

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**

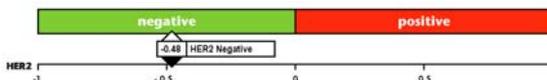
Estrogen Receptor  
 ER Positive



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

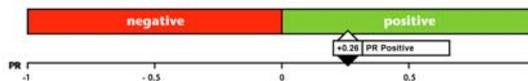
**highly endocrine responsive  
Intermediate risk**

**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**

