

# Comparing MammaPrint and Blueprint results between core needle biopsy and surgical resection breast cancer specimens

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## Background

Pre-operative/neoadjuvant treatment utilization in early-stage breast cancer has been increasing, particularly during the COVID-19 pandemic. ESMO and ASCO guidelines note that genomic testing on diagnostic core needle biopsy (CNB) samples may be used to assist with the identification of patients with low-risk tumor biology who may be candidates for surgical delay.<sup>1,2</sup>

In addition, pre-operative genomic testing on CNB is typically utilized in more clinically high-risk tumors from patients who are candidates for neoadjuvant therapy, to obtain additional insight in the tumor biology. The interest in neoadjuvant treatment is increasing in Europe with 34 active neo-adjuvant trials in early breast cancer (89 worldwide). One-third (n=12) of the neo-adjuvant trials are initiated in Germany.

- MammaPrint (MP), a 70-gene risk of recurrence signature, and Blueprint (BP), an 80-gene molecular subtyping signature, have been routinely used in formalin-fixed paraffin embedded (FFPE) CNB and surgical resection (SR) samples since MammaPrint obtained FDA clearance for FFPE tissue in 2015<sup>3</sup>.
- In addition, over 1,750 CNB tumor samples from patients enrolled in prospective neoadjuvant treatment trials (NBREaST II [P088]<sup>4</sup>, NBRST<sup>5</sup> and ISPY-2<sup>6</sup>) have received successful MP and BP testing.

This study compares the gene expression results between CNB and SR specimens to better elucidate how these tests perform across specimen type.

## Methods

Routine diagnostic samples from outside the US submitted to Agendia between January 2017 and October 2020 (n=10,574) for MP and BP testing were processed according to standard FFPE microarray procedures. MP was used to stratify samples into UltraLow Risk (ULR), Low Risk (LR) and High Risk (HR). BP was used to classify samples into Basal, Luminal or HER2-type.

This study included 1,072 CNB and 9,502 SR specimens. About 70% of the samples also have a BP result in which most classified as BP Luminal-type amongst both specimen types (>97%), therefore we compared MP Index (MPI) distribution between CNB and SR samples for Luminal-type tumors.

In addition, comparative “logistics metrics” (average turnaround time [TAT] and success rate) were assessed between these specimen types. The percentage of CNB samples sent in the US<sup>7</sup> compared to those received from “rest of world” (RoW) were also compared.

## Conclusion

MammaPrint and Blueprint testing were successfully performed on both CNB and SR samples in approximately 97% of all eligible specimens with rapid TAT enabling use of genomic testing for pre-operative decision making. Among Luminal-type tumors, the frequency of each MP risk group as well as the distribution pattern of MP Index were essentially identical between CNB and SR, indicating comparable performance regardless of specimen type. These observations from samples received from mainly European countries are similar to those seen from samples originating from the US<sup>7</sup>.

Increased utilization of genomic testing on CNB to guide pre-operative management has been accelerated by recent COVID-19 pandemic guidelines, highlighting the importance of having reliable assay performance across specimen types. With no observed differences in MPI distribution, TAT or success rate between CNB and SR specimens, use of MammaPrint and Blueprint on CNB is reliable and could be a useful tool to pre-operatively triage early BC patients. Beyond the COVID-19 pandemic, MammaPrint and Blueprint have utility in tailoring pre- and post-operative treatment as well as determining the timing of surgery and should be incorporated into routine diagnostic work-up of early-stage breast cancer to enable more informed decision making.

## References

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## Results

### MammaPrint risk distributions were similar between CNB and surgical resection specimens

Of the 10,574 samples included in this analysis, 10% were CNB and 90% were SR. BP Basal, Luminal, and HER2-type distributions were 2%, 97%, and 1% respectively for CNB samples and 1%, 98.6%, and 0.4% respectively for SR samples.

- Overall, MP risk category distributions were similar between samples tested from CNB vs. SR (Table 1).
- Within BP defined Luminal-type tumors (Table 2), the frequency of UL, LR, and HR results were 14%, 61%, and 39% for CNB, and 13%, 58%, and 42% for SR, respectively.

Table 1: All Blueprint Subtypes

CNB	(n)	(%)	SR	(n)	(%)
<b>Total CNB</b>	1072	10%	<b>Total SR</b>	9502	90%
CNB <i>Ultralow*</i>	157	15%	SR <i>Ultralow</i>	1260	13%
CNB Low Risk	637	59%	SR Low Risk	5497	58%
CNB High Risk	435	41%	SR High Risk	4005	42%

\*Ultralow results are a subset of Low Risk

Table 2: Blueprint Luminal-type

CNB	(n)	(%)	SR	(n)	(%)
<b>Luminal CNB</b>	753	11%	<b>Luminal SR</b>	6252	89%
CNB <i>Ultralow*</i>	103	14%	SR <i>Ultralow</i>	804	13%
CNB Low Risk	459	61%	SR Low Risk	3637	58%
CNB High Risk	294	39%	SR High Risk	2615	42%

### Logistics metrics were similar between CNB and surgical resection specimens

- Average turn-around time between CNB and SR were 4.47 and 4.84 days, respectively. For specimens that met the minimum 30% invasive tumor threshold, successful testing rates for CNB and SR were 97.3% and 97.7%, respectively (Table 3).

Table 3: Logistics Metrics †

	CNB		SR
CNB Avg TAT	4.47 days	SR Avg TAT	4.84 days
CNB Success %	97.3%	SR Success %	97.7%

†Definitions: *Turnaround Time (TAT)* is calculated from the time a specimen is received at the laboratory to the time a result is available. *Success %* excludes test failures due to insufficient RNA yield % and sub-optimal RNA quality, and evaluates the total number of specimens that have met the pre-requisite 30% minimum invasive tumor requirement that have a valid result

### MammaPrint Index result distribution from CNB and surgical resection samples were highly comparable

- MammaPrint Index distributions between CNB and SR samples were essentially identical (Figure 1).

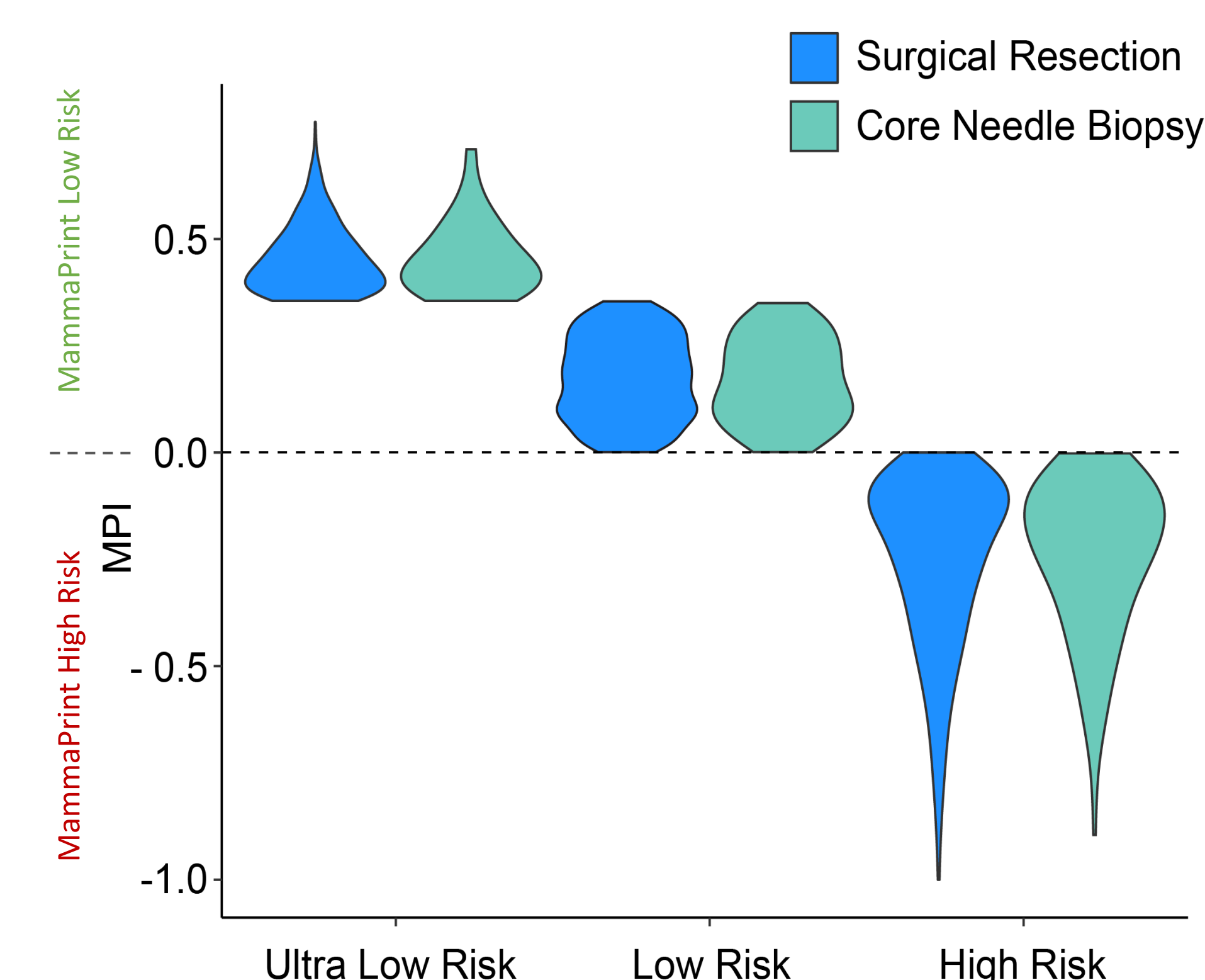


Figure 1: CNB vs SR: MammaPrint Index (MPI) Result Distribution MPI distribution between CNB and SR samples were highly comparable amongst Blueprint Luminal-Type classified samples.

### Comparison between RoW and US Sample type

- A clear difference between the percentage of CNB samples in the RoW versus the US is observed (Table 4). In the RoW 10% of the samples are CNB, while in the US 35% of the samples are CNB. Of the samples from RoW with a molecular subtyping result by Blueprint, the samples were mainly luminal-type samples (>97%), compared to 85% for the US.

Table 4: Comparison between RoW and US samples

	CNB (%)	SR (%)	Luminal-type (%)
RoW	10%	90%	>97%
US	35%	65%	>85%