SUPPLEMENTARY MATERIALS

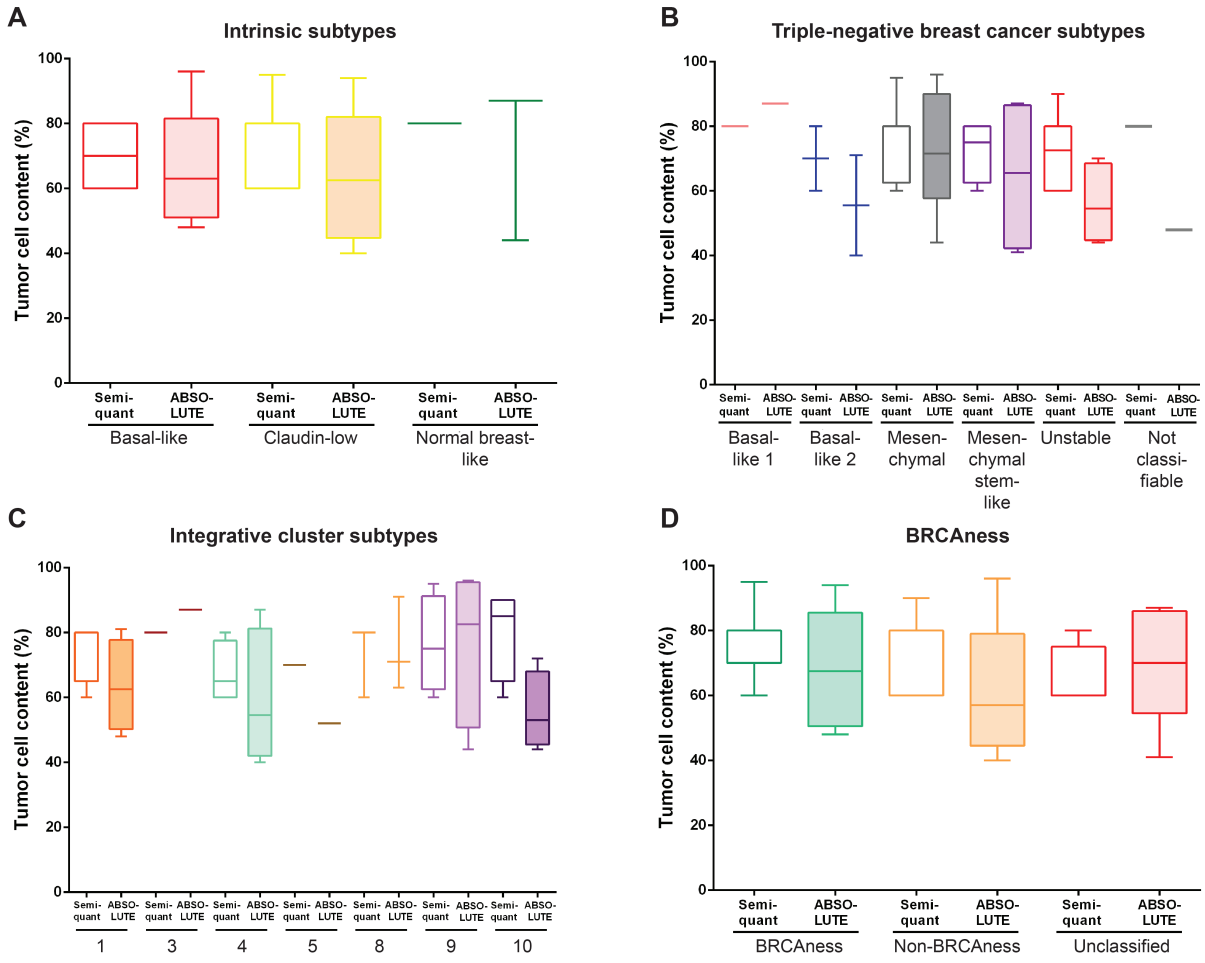
Metaplastic breast carcinomas display genomic and transcriptomic heterogeneity

Weigelt et al.

Supplementary Figures S1 and S2

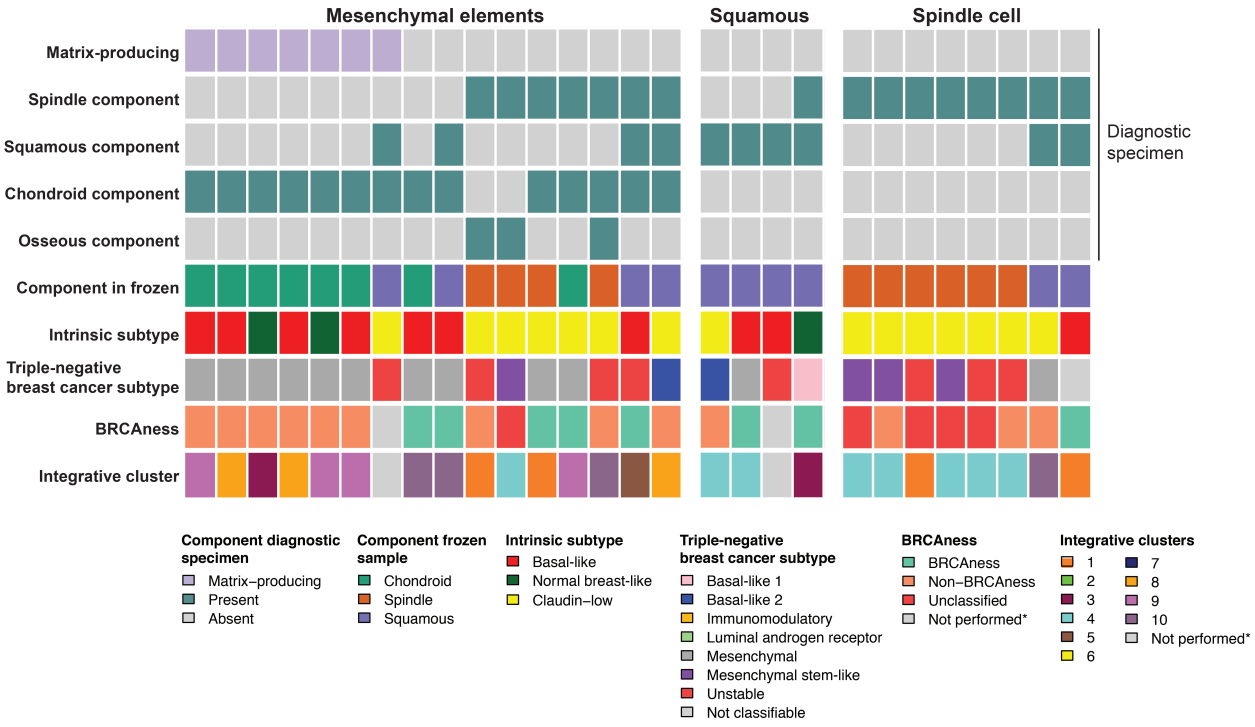
Supplementary Tables S1-S3

Supplementary Figure S1



Supplementary Figure S1. Tumor cellularity in distinct molecular subtypes of metaplastic breast cancers as determined by semi-quantitative histologic assessment and ABSOLUTE. (A) PAM50 intrinsic molecular subtypes, (B) Triple-negative breast cancer subtypes, (C) Integrative cluster subtypes, and (D) BRCAness subtypes.

Supplementary Figure S2



Supplementary Figure S2. Molecular subtypes of 28 metaplastic breast cancers according to the histologic assessment of the diagnostic material.

Classification of metaplastic breast cancers according to diagnosis and metaplastic components present in the frozen sample subjected to molecular profiling. The PAM50 intrinsic molecular subtype, triple-negative breast cancer subtype, BRCAness signature and integrative cluster for each case is shown. *For two cases, no SNP6 data were available; hence, integrative cluster and BRCAness analysis could not be performed.

Supplementary Table S1. Metaplastic breast cancers subjected to gene copy number and gene expression profiling and results of molecular subtyping.

Sample ID	Component in frozen sample	SNP6 gene copy number profiling	HT12 gene expression profiling	PAM50/ claudin-low subtype	Triple-negative breast cancer subtype	BRCAness	Integrative cluster
META30	Chondroid	Yes	Yes	Basal-like	Mesenchymal-like	Non-BRCAness	9
META31	Chondroid	Yes	Yes	Basal-like	Mesenchymal-like	Non-BRCAness	8
META32	Spindle	Yes	Yes	Claudin-low	Unstable	Non-BRCAness	1
META33	Chondroid	Yes	Yes	Basal-like	Mesenchymal-like	BRCAness	10
META34	Squamous	Yes	Yes	Claudin-low	Basal-like 2	Non-BRCAness	4
META36	Chondroid	Yes	Yes	Normal breast-like	Mesenchymal-like	Non-BRCAness	3
META37	Squamous	Yes	Yes	Normal breast-like	Basal-like 1	BRCAness	3
META39	Spindle	Yes	Yes	Claudin-low	Mesenchymal-like	BRCAness	1
META40	Squamous	Yes	Yes	Claudin-low	Mesenchymal-like	Non-BRCAness	10
META41	Squamous	Yes	Yes	Basal-like	Mesenchymal-like	BRCAness	10
META42	Squamous	Yes	Yes	Basal-like	Mesenchymal-like	BRCAness	4
META43	Squamous	Yes	Yes	Basal-like	Unstable	BRCAness	5
META44	Squamous	No	Yes	Claudin-low	Unstable	Not analyzed*	Not analyzed*
META45	Squamous	Yes	Yes	Basal-like	Not classifiable	BRCAness	1
META46	Squamous	No	Yes	Basal-like	Unstable	Not analyzed*	Not analyzed*
META47	Spindle	Yes	Yes	Claudin-low	Mesenchymal stem-like	Unclassified	4
META49	Spindle	Yes	Yes	Claudin-low	Mesenchymal stem-like	Non-BRCAness	4
META52	Chondroid	Yes	Yes	Claudin-low	Mesenchymal-like	BRCAness	9
META53	Chondroid	Yes	Yes	Basal-like	Mesenchymal-like	Non-BRCAness	8
META55	Chondroid	Yes	Yes	Normal breast-like	Mesenchymal-like	Non-BRCAness	9
META56	Spindle	Yes	Yes	Claudin-low	Unstable	Unclassified	1
META57	Spindle	Yes	Yes	Claudin-low	Mesenchymal stem-like	Unclassified	4
META58	Spindle	Yes	Yes	Claudin-low	Mesenchymal stem-like	Unclassified	4
META59	Spindle	Yes	Yes	Claudin-low	Unstable	Non-BRCAness	10
META60	Spindle	Yes	Yes	Claudin-low	Unstable	Unclassified	4
META62	Squamous	Yes	Yes	Claudin-low	Basal-like 2	Non-BRCAness	8
META64	Chondroid	Yes	Yes	Basal-like	Mesenchymal-like	Non-BRCAness	9
META65	Spindle	Yes	Yes	Claudin-low	Unstable	Non-BRCAness	4

*: No SNP6 data available.

Supplementary Table S2. Assignment of 997 breast cancers of the METABRIC discovery cohort to the PAM50 molecular and integrative cluster subtypes using the methods described in this manuscript, and agreement with PAM50 molecular and integrative cluster subtypes of the same cases as published by Curtis et al, Nature 2012.

		Applied approach for PAM50 molecular subtyping of METABRIC discovery set in current study				
		Basal-like	**HER2**	**Luminal A**	**Luminal B**	**Normal breast-like**
PAM50 molecular subtypes of METABRIC discovery set published by Curtis et al, Nature 2012	**Basal-like**	115	2	0	0	1
	HER2	0	87	0	0	0
	Luminal A	0	0	451	14	1
	Luminal B	0	4	8	256	0
	Normal breast-like	0	2	8	0	48
						997

Rand index=0.955
Kappa=0.941

		Integrative cluster (IntClust) subtypes of METABRIC discovery set published by Curtis et al, Nature 2012									
		IntClust 1	**IntClust 2**	**IntClust 3**	**IntClust 4**	**IntClust 5**	**IntClust 6**	**IntClust 7**	**IntClust 8**	**IntClust 9**	**IntClust 10**
Applied approach for integrative cluster subtyping of METABRIC discovery set in current study	**IntClust 1**	68	3	3	5	1	0	3	0	2	1
	IntClust 2	0	37	3	2	0	0	0	0	0	0
	IntClust 3	1	0	115	4	1	0	2	13	0	1
	IntClust 4	0	2	2	120	1	0	0	0	1	0
	IntClust 5	1	0	0	4	78	0	1	0	1	0
	IntClust 6	0	0	1	4	0	39	2	0	0	0
	IntClust 7	1	2	0	11	0	0	93	2	2	0
	IntClust 8	0	0	26	0	1	1	2	126	0	0
	IntClust 9	1	1	2	5	5	4	4	1	54	0
	IntClust 10	4	0	4	12	7	0	2	1	7	94
											997

Rand index=0.93
Kappa=0.804

Supplementary Table S3. Results of the classification of 28 metaplastic breast cancers into intrinsic molecular subtypes, triple-negative breast cancer subtypes, integrative clusters and BRCAness.

		Integrative cluster							Triple-negative breast cancer subtype						BRCAness signature		
		1	3	4	5	8	9	10	Basal-like 1	Basal-like 2	Mesenchymal-like	Mesenchymal stem-like	Unstable	Not classifiable	BRCAness	Non-BRCAness	Unclassified
PAM50/ claudin-low	Basal-like	1		1	1	2	2	2			7		2	1	5	4	
	Normal		2				1		1		2				1	2	
	Claudin-low	3		7		1	1	2		2	3	4	6		2	7	5

		Integrative cluster							Triple-negative breast cancer subtype					
		1	3	4	5	8	9	10	Basal-like 1	Basal-like 2	Mesenchymal-like	Mesenchymal stem-like	Unstable	N/A
BRCA-ness signature	BRCAness	2	1	1	1		1	2	1		5		1	1
	Non-BRCAness	1	1	3		3	3	2		2	7	1	3	
	Unclassified	1		4								3	2	

		Integrative cluster						
		1	3	4	5	8	9	10
Triple-negative breast cancer subtype	Basal-like 1		1					
	Basal-like 2			1		1		
	Mesenchymal-like	1	1	1		2	4	3
	Mesenchymal stem-like			4				
	Unstable	2		2	1			1
	Not classifiable	1						