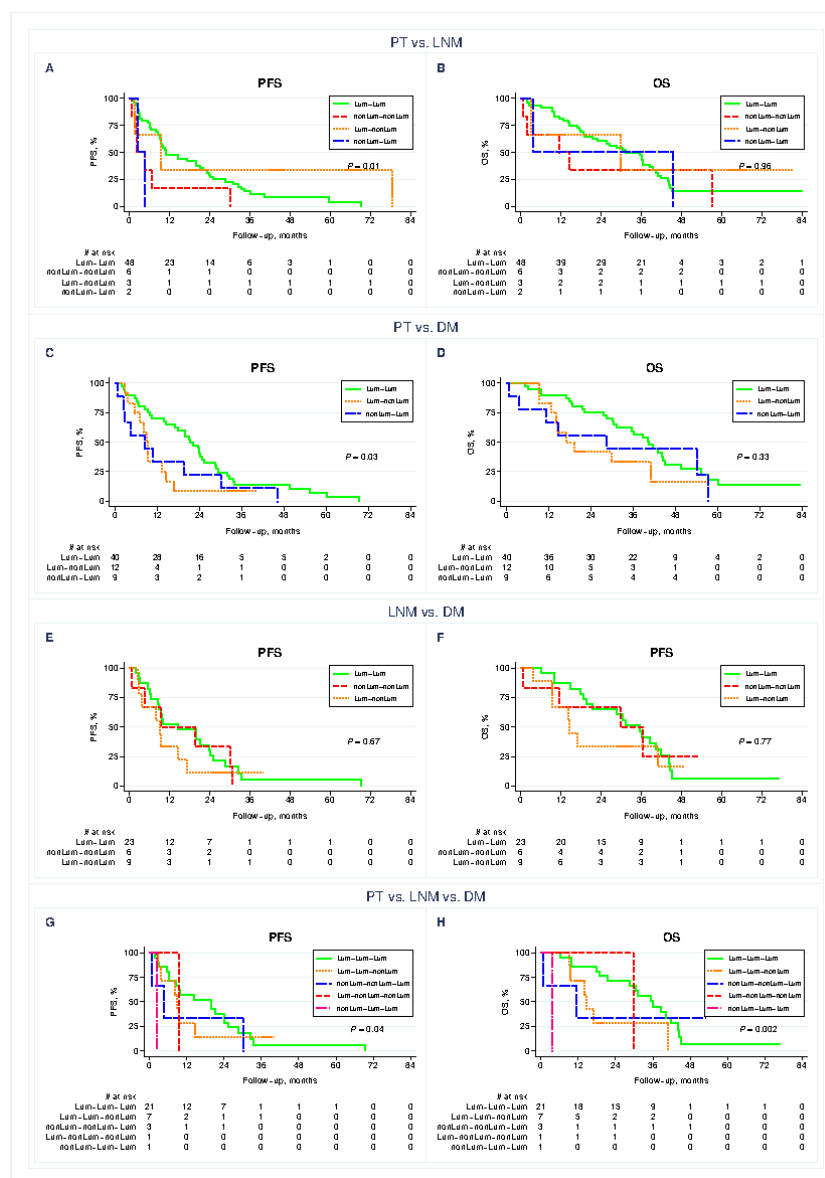


# Supplementary Materials: PAM50 Intrinsic Subtype Profiles in Primary and Metastatic Breast Cancer Show a Significant Shift toward More Aggressive Subtypes with Prognostic Implications

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**Figure S1:** Kaplan–Meier survival curves for progression-free survival and overall survival according to luminal versus non-luminal subtype subgroups in the primary tumor, lymph node metastasis, and distant metastasis. *p*-values were calculated with the log-rank test

**Table S1.** Patient demographics, disease characteristics, and prior therapy given for the entire CTC–MBC cohort and for patients included/excluded in the present study.

| Characteristics              | Entire CTC-MBC Cohort | Included in PAM50 Cohort | PAM50 Subtype Available |
|------------------------------|-----------------------|--------------------------|-------------------------|
|                              | <i>n</i> (%)          | <i>n</i> (%)             | <i>n</i> (%)            |
|                              | 156 (100)             | 140 (90)                 | 123 (79)                |
| Age at MBC diagnosis (years) |                       |                          |                         |
| <65                          | 75 (48)               | 70 (50)                  | 63 (51)                 |
| ≥65                          | 81 (52)               | 70 (50)                  | 60 (49)                 |
| ECOG (baseline)              |                       |                          |                         |
| 0                            | 91 (60)               | 82 (60)                  | 70 (58)                 |
| 1                            | 37 (25)               | 35 (25)                  | 31 (26)                 |
| 2                            | 22 (15)               | 20 (15)                  | 19 (16)                 |
| Missing                      | 6                     | 3                        | 3                       |
| Primary tumor size           |                       |                          |                         |
| T1                           | 57 (39)               | 47 (36)                  | 38 (33)                 |
| T2                           | 51 (35)               | 48 (36)                  | 43 (37)                 |
| T3                           | 20 (13)               | 20 (15)                  | 19 (16)                 |
| T4                           | 19 (13)               | 17 (13)                  | 17 (14)                 |
| Missing                      | 9                     | 8                        | 6                       |
| Nodal status <sup>a</sup>    |                       |                          |                         |
| Negative                     | 44 (32)               | 36 (30)                  | 31 (29)                 |
| Positive                     | 92 (68)               | 87 (70)                  | 77 (71)                 |
| Missing                      | 20                    | 17                       | 15                      |
| NHG (PT)                     |                       |                          |                         |
| I                            | 13 (11)               | 11 (10)                  | 8 (8)                   |
| II                           | 65 (52)               | 59 (53)                  | 50 (51)                 |
| III                          | 46 (37)               | 42 (37)                  | 40 (41)                 |
| Missing                      | 32                    | 28                       | 25                      |
| ER (PT)                      |                       |                          |                         |
| Negative                     | 24 (16)               | 22 (17)                  | 20 (17)                 |
| Positive                     | 123 (84)              | 110 (83)                 | 99 (83)                 |
| Missing                      | 9                     | 8                        | 4                       |
| PR (PT)                      |                       |                          |                         |
| Negative                     | 45 (31)               | 42 (32)                  | 37 (32)                 |
| Positive                     | 100 (69)              | 88 (68)                  | 80 (68)                 |
| Missing                      | 11                    | 10                       | 6                       |
| HER2 (PT)                    |                       |                          |                         |
| Negative                     | 109 (86)              | 96 (85)                  | 89 (86)                 |
| Positive                     | 18 (14)               | 17 (15)                  | 14 (14)                 |
| Missing                      | 29                    | 27                       | 20                      |
| BC subtype (PT)              |                       |                          |                         |
| ER+ HER2-                    | 92 (73)               | 81 (72)                  | 75 (73)                 |
| HER2+                        | 17 (13.5)             | 16 (14)                  | 13 (13)                 |
| ER- HER2-                    | 17 (13.5)             | 15 (14)                  | 14 (14)                 |
| Missing                      | 30                    | 28                       | 21                      |
| BC subtype (REC/distant met) |                       |                          |                         |
| ER+ HER2-                    | 80 (70)               | 73 (70)                  | 64 (72)                 |
| HER2+                        | 16 (14)               | 16 (15)                  | 12 (13)                 |
| ER- HER2-                    | 18 (16)               | 16 (15)                  | 13 (15)                 |
| Missing                      | 42                    | 35                       | 34                      |
| MFI (years)                  |                       |                          |                         |
| 0                            | 31 (20)               | 29 (21)                  | 26 (21)                 |
| >0-3                         | 28 (18)               | 25 (18)                  | 23 (19)                 |
| >3                           | 97 (62)               | 86 (61)                  | 74 (60)                 |

|                            |          |         |         |
|----------------------------|----------|---------|---------|
| Number of metastatic sites |          |         |         |
| 1–2                        | 109 (70) | 96 (69) | 82 (67) |
| ≥3                         | 47 (30)  | 44 (31) | 41 (33) |
| Metastatic site            |          |         |         |
| Non-visceral               | 65 (42)  | 58 (41) | 51 (42) |
| Visceral                   | 91 (58)  | 82 (59) | 72 (58) |
| Number of CTCs (BL)        |          |         |         |
| <5                         | 73 (48)  | 66 (48) | 57 (46) |
| ≥5                         | 79 (52)  | 73 (52) | 66 (54) |
| Missing                    | 4        | 1       | 0       |
| Prior Therapy <sup>b</sup> |          |         |         |
| Neoadjuvant chemo          | 27 (17)  | 26 (19) | 25 (20) |
| Adjuvant chemo             | 71 (46)  | 66 (47) | 57 (46) |
| Adjuvant endocrine         | 96 (62)  | 85 (61) | 75 (61) |
| Adjuvant HER2-targeted     | 5 (3)    | 4 (3)   | 2 (2)   |

Abbreviations: BL, baseline; BC, breast cancer; CTC, circulating tumor cell; ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; MBC, metastatic breast cancer; MFI, metastasis-free interval; *n*, number; NHG, Nottingham Histological Grade; PR, progesterone receptor; PT, primary tumor; REC, recurrence; <sup>a</sup>At primary diagnosis; <sup>b</sup>Some patients were given more than one type of therapy, hence the percentages in parentheses sum up to more than 100.

**Table S2.** Patient and tumor characteristics for the lymph node metastases in the PAM50 cohort with subtypes available and subdivided into the different breast cancer intrinsic subtypes.

| Characteristics              | Subtype Available<br><i>n</i> (%) | Lum A<br><i>n</i> (%) | Lum B<br><i>n</i> (%) | HER2-E<br><i>n</i> (%) | Basal-Like <i>n</i> (%) | <i>P</i> <sup>a</sup> |
|------------------------------|-----------------------------------|-----------------------|-----------------------|------------------------|-------------------------|-----------------------|
|                              | 68                                | 18                    | 37                    | 9                      | 4                       |                       |
| Age at MBC diagnosis (years) |                                   |                       |                       |                        |                         | 0.96                  |
| <65                          | 27 (40)                           | 7 (39)                | 14 (38)               | 4 (44)                 | 2 (50)                  |                       |
| ≥65                          | 41 (60)                           | 11 (61)               | 23 (62)               | 5 (56)                 | 2 (50)                  |                       |
| ECOG (BL)                    |                                   |                       |                       |                        |                         | 0.16                  |
| 0                            | 43 (65)                           | 15 (88)               | 22 (61)               | 4 (44)                 | 2 (50)                  |                       |
| 1                            | 16 (24)                           | 1 (6)                 | 10 (28)               | 4 (44)                 | 1 (25)                  |                       |
| 2                            | 7 (11)                            | 1 (6)                 | 4 (11)                | 1 (12)                 | 1 (25)                  |                       |
| Missing                      | 2                                 | 1                     | 1                     | 0                      | 0                       |                       |
| Size (PT)                    |                                   |                       |                       |                        |                         | 0.16                  |
| T1                           | 16 (25)                           | 4 (24)                | 9 (25)                | 2 (22)                 | 1 (33)                  |                       |
| T2                           | 28 (43)                           | 3 (17)                | 19 (53)               | 5 (56)                 | 1 (33)                  |                       |
| T3                           | 13 (20)                           | 6 (35)                | 6 (17)                | 1 (11)                 | 0                       |                       |
| T4                           | 8 (12)                            | 4 (24)                | 2 (5)                 | 1 (11)                 | 1 (33)                  |                       |
| Missing                      | 3                                 | 1                     | 1                     | 0                      | 1                       |                       |
| Nodal status <sup>b</sup>    |                                   |                       |                       |                        |                         |                       |
| Negative                     | 0                                 |                       |                       |                        |                         |                       |
| Positive                     | 65 (100)                          | 18 (100)              | 35 (100)              | 9 (100)                | 3 (100)                 |                       |
| Missing                      | 3                                 | 0                     | 2                     | 0                      | 1                       |                       |
| NHG (PT)                     |                                   |                       |                       |                        |                         | 0.45                  |
| I                            | 5 (8)                             | 2 (13)                | 3 (9)                 | 0                      | 0                       |                       |
| II                           | 37 (61)                           | 11 (74)               | 20 (59)               | 5 (56)                 | 1 (33)                  |                       |
| III                          | 19 (31)                           | 2 (13)                | 11 (32)               | 4 (44)                 | 2 (67)                  |                       |
| Missing                      | 7                                 | 3                     | 3                     | 0                      | 1                       |                       |
| ER (PT)                      |                                   |                       |                       |                        |                         | 0.003                 |
| Negative                     | 7 (11)                            | 0                     | 2 (6)                 | 3 (33)                 | 2 (67)                  |                       |
| Positive                     | 57 (89)                           | 16 (100)              | 34 (94)               | 6 (67)                 | 1 (33)                  |                       |
| Missing                      | 4                                 | 2                     | 1                     | 0                      | 1                       |                       |

|                            |         |          |         |        |        |        |
|----------------------------|---------|----------|---------|--------|--------|--------|
| PR (PT)                    |         |          |         |        |        | 0.08   |
| Negative                   | 19 (31) | 2 (13)   | 10 (29) | 5 (56) | 2 (67) |        |
| Positive                   | 43 (69) | 13 (87)  | 25 (71) | 4 (44) | 1 (33) |        |
| Missing                    | 6       | 3        | 2       | 0      | 1      |        |
| HER2 (PT)                  |         |          |         |        |        | 0.02   |
| Negative                   | 44 (85) | 11 (100) | 27 (90) | 5 (56) | 1 (50) |        |
| Positive                   | 8 (15)  | 0        | 3 (10)  | 4 (44) | 1 (50) |        |
| Missing                    | 16      | 7        | 7       | 0      | 2      |        |
| BC subtype PT              |         |          |         |        |        | <0.001 |
| ER+ HER2-                  | 39 (75) | 11 (100) | 26 (87) | 2 (22) | 0      |        |
| HER2+                      | 8 (15)  | 0        | 3 (10)  | 4 (45) | 1 (50) |        |
| ER- HER2-                  | 5 (10)  | 0        | 1 (3)   | 3 (33) | 1 (50) |        |
| Missing                    | 16      | 7        | 7       | 0      | 2      |        |
| MFI (years)                |         |          |         |        |        | 0.03   |
| 0                          | 6 (9)   | 1 (5)    | 4 (11)  | 0      | 1 (25) |        |
| >0-3                       | 14 (20) | 3 (17)   | 4 (11)  | 5 (56) | 2 (50) |        |
| >3                         | 48 (71) | 14 (78)  | 29 (78) | 4 (44) | 1 (25) |        |
| Number of metastatic sites |         |          |         |        |        | 0.71   |
| 1–2                        | 46 (68) | 11 (61)  | 27 (73) | 6 (67) | 2 (50) |        |
| ≥3                         | 22 (32) | 7 (39)   | 10 (27) | 3 (33) | 2 (50) |        |
| Metastatic site            |         |          |         |        |        | 0.67   |
| Non-visceral               | 27 (40) | 6 (33)   | 14 (38) | 5 (56) | 2 (50) |        |
| Visceral                   | 41 (60) | 12 (67)  | 23 (62) | 4 (44) | 2 (50) |        |
| Number of CTCs (BL)        |         |          |         |        |        | 0.41   |
| <5                         | 28 (42) | 10 (56)  | 15 (41) | 2 (22) | 1 (33) |        |
| ≥5                         | 39 (58) | 8 (44)   | 22 (59) | 7 (78) | 2 (67) |        |
| Missing                    | 1       | 0        | 0       | 0      | 1      |        |

Abbreviations: BL, baseline; CTCs, circulating tumor cell; ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HER2-E, human epidermal growth factor receptor 2 enriched; MBC, metastatic breast cancer; MFI, metastasis-free interval; NHG, Nottingham Histological Grade; *n*, number; PT, primary tumor PR, progesterone receptor. <sup>a</sup>*P*-value from Fisher's exact test; <sup>b</sup>At primary diagnosis

**Table S3.** Patient and tumor characteristics for the distant metastases in the PAM50 cohort with subtype available and subdivided into the different breast cancer intrinsic subtypes.

| Characteristics              | Subtype Available<br><i>n</i> (%) | Lum A<br><i>n</i> (%) | Lum B<br><i>n</i> (%) | HER2-E<br><i>n</i> (%) | Basal-Like <i>n</i> (%) | <i>P</i> <sup>a</sup> |
|------------------------------|-----------------------------------|-----------------------|-----------------------|------------------------|-------------------------|-----------------------|
| Age at MBC diagnosis (years) | 74                                | 7                     | 41                    | 19                     | 7                       | 0.41                  |
| <65                          | 34 (46)                           | 3 (43)                | 16 (39)               | 10 (53)                | 5 (71)                  |                       |
| ≥65                          | 40 (54)                           | 4 (57)                | 25 (61)               | 9 (47)                 | 2 (29)                  |                       |
| ECOG (BL)                    |                                   |                       |                       |                        |                         | 0.41                  |
| 0                            | 38 (53)                           | 2 (29)                | 18 (46)               | 13 (68)                | 5 (71)                  |                       |
| 1                            | 21 (29)                           | 4 (57)                | 12 (31)               | 4 (21)                 | 1 (14.5)                |                       |
| 2                            | 13 (18)                           | 1 (14)                | 9 (23)                | 2 (11)                 | 1 (14.5)                |                       |
| Missing                      | 2                                 | 0                     | 2                     | 0                      | 0                       |                       |
| Size (PT)                    |                                   |                       |                       |                        |                         | 0.31                  |
| T1                           | 29 (41)                           | 1 (14)                | 17 (42)               | 8 (47)                 | 3 (43)                  |                       |
| T2                           | 30 (42)                           | 3 (43)                | 18 (45)               | 7 (41)                 | 2 (29)                  |                       |
| T3                           | 8 (11)                            | 1 (14)                | 4 (10)                | 2 (12)                 | 1 (14)                  |                       |

|                            |         |         |          |         |          |
|----------------------------|---------|---------|----------|---------|----------|
| T4                         | 4 (6)   | 2 (29)  | 1 (3)    | 0       | 1 (14)   |
| Missing                    | 3       | 0       | 1        | 2       | 0        |
| Nodal status <sup>b</sup>  |         |         |          |         | 0.80     |
| Negative                   | 21 (30) | 1 (17)  | 12 (30)  | 5 (31)  | 3 (43)   |
| Positive                   | 48 (70) | 5 (83)  | 28 (70)  | 11 (69) | 4 (57)   |
| Missing                    | 5       | 1       | 1        | 3       | 0        |
| NHG (PT)                   |         |         |          |         | 1.00     |
| I                          | 6 (9)   | 0       | 4 (11)   | 2 (12)  | 0        |
| II                         | 41 (64) | 4 (80)  | 23 (62)  | 10 (59) | 4 (80)   |
| III                        | 17 (27) | 1 (20)  | 10 (27)  | 5 (29)  | 1 (20)   |
| Missing                    | 10      | 2       | 4        | 2       | 2        |
| ER (PT)                    |         |         |          |         | <0.001   |
| Negative                   | 11 (16) | 0       | 0        | 5 (26)  | 6 (86)   |
| Positive                   | 57 (84) | 7 (100) | 35 (100) | 14 (74) | 1 (14)   |
| Missing                    | 6       | 0       | 6        | 0       | 0        |
| PR (PT)                    |         |         |          |         | 0.009    |
| Negative                   | 20 (30) | 0       | 7 (21)   | 8 (42)  | 5 (71)   |
| Positive                   | 47 (70) | 7 (100) | 27 (79)  | 11 (58) | 2 (29)   |
| Missing                    | 7       | 0       | 7        | 0       | 0        |
| HER2 (PT)                  |         |         |          |         | 0.05     |
| Negative                   | 53 (89) | 7 (100) | 28 (97)  | 13 (72) | 5 (83)   |
| Positive                   | 7 (11)  | 0       | 1 (3)    | 5 (28)  | 1 (17)   |
| Missing                    | 14      | 0       | 12       | 1       | 1        |
| BC subtype PT              |         |         |          |         | <0.001   |
| ER+ HER2-                  | 45 (76) | 7 (100) | 28 (100) | 9 (50)  | 1 (17)   |
| HER2+                      | 6 (10)  | 0       | 0        | 5 (28)  | 1 (17)   |
| ER- HER2-                  | 8 (14)  | 0       | 0        | 4 (22)  | 4 (66)   |
| Missing                    | 15      | 0       | 13       | 1       | 1        |
| MFI (years)                |         |         |          |         | 0.37     |
| 0                          | 11 (15) | 3 (43)  | 4 (10)   | 3 (16)  | 1 (14.5) |
| >0-3                       | 8 (11)  | 0       | 4 (10)   | 3 (16)  | 1 (14.5) |
| >3                         | 55 (74) | 4 (57)  | 33 (80)  | 13 (68) | 5 (71)   |
| Number of metastatic sites |         |         |          |         | 0.92     |
| 1–2                        | 56 (76) | 5 (71)  | 30 (73)  | 15 (79) | 6 (86)   |
| ≥3                         | 18 (24) | 2 (29)  | 11 (27)  | 4 (21)  | 1 (14)   |
| Metastatic site            |         |         |          |         | 0.18     |
| Non-visceral               | 39 (53) | 5 (71)  | 20 (49)  | 8 (42)  | 6 (86)   |
| Visceral                   | 35 (47) | 2 (29)  | 21 (51)  | 11 (58) | 1 (14)   |
| ER (DM)                    |         |         |          |         | <0.001   |
| Negative                   | 12 (16) | 0 (0)   | 0 (0)    | 7 (37)  | 5 (71)   |
| Positive                   | 61 (84) | 6 (100) | 41 (100) | 12 (63) | 2 (29)   |
| Missing                    | 1       | 1       | 0        | 0       | 0        |
| PR (DM)                    |         |         |          |         | 0.017    |
| Negative                   | 42 (58) | 4 (67)  | 17 (43)  | 15 (79) | 6 (86)   |
| Positive                   | 30 (42) | 2 (33)  | 23 (57)  | 4 (21)  | 1 (14)   |
| Missing                    | 2       | 1       | 1        | 0       | 0        |
| HER2 (DM)                  |         |         |          |         | 0.006    |
| Negative                   | 61 (88) | 5 (100) | 39 (97)  | 12 (67) | 5 (83)   |
| Positive                   | 8 (12)  | 0 (0)   | 1 (3)    | 6 (33)  | 1 (17)   |
| Missing                    | 5       | 2       | 1        | 1       | 1        |
| Number of CTCs (BL)        |         |         |          |         | 0.24     |
| <5                         | 29 (39) | 4 (57)  | 12 (29)  | 9 (47)  | 4 (57)   |
| ≥5                         | 45 (61) | 3 (43)  | 29 (71)  | 10 (53) | 3 (43)   |

Missing 0

Abbreviations: BL, baseline; CTCs, circulating tumor cell; DM, distant metastasis; ECOG, Eastern Cooperative Oncology Group; ER, estrogen receptor; HER2, human epidermal growth factor receptor 2; HER2-E, human epidermal growth factor receptor 2 enriched; MBC, metastatic breast cancer; MFI, metastasis-free interval; NHG, Nottingham Histological Grade; *n*, number; PT, primary tumor PR, progesterone receptor. <sup>a</sup>*P*-value from Fisher's exact test; <sup>b</sup>At primary diagnosis.

**Table S4.** Changes in PAM50 breast cancer intrinsic subtype between PT, LNM, and DM.

| PT     | LNM        | DM         | <i>n</i> |
|--------|------------|------------|----------|
| Lum A  | Lum A      | Lum A      | 2        |
| Lum A  | Lum A      | Lum B      | 5        |
| Lum A  | Lum A      | HER2-E     | 0        |
| Lum A  | Lum A      | Basal-like | 0        |
| Lum A  | Lum B      | Lum A      | 1        |
| Lum A  | Lum B      | Lum B      | 6        |
| Lum A  | Lum B      | HER2-E     | 4        |
| Lum A  | Lum B      | Basal-like | 2        |
| Lum A  | HER2-E     | Lum A      | 0        |
| Lum A  | HER2-E     | Lum B      | 0        |
| Lum A  | HER2-E     | HER2-E     | 0        |
| Lum A  | HER2-E     | Basal-like | 0        |
| Lum A  | Basal-like | Lum A      | 0        |
| Lum A  | Basal-like | Lum B      | 0        |
| Lum A  | Basal-like | HER2-E     | 0        |
| Lum A  | Basal-like | Basal-like | 0        |
| Lum B  | Lum A      | Lum A      | 0        |
| Lum B  | Lum A      | Lum B      | 0        |
| Lum B  | Lum A      | HER2-E     | 0        |
| Lum B  | Lum A      | Basal-like | 0        |
| Lum B  | Lum B      | Lum A      | 0        |
| Lum B  | Lum B      | Lum B      | 7        |
| Lum B  | Lum B      | HER2-E     | 1        |
| Lum B  | Lum B      | Basal-like | 0        |
| Lum B  | HER2-E     | Lum A      | 0        |
| Lum B  | HER2-E     | Lum B      | 0        |
| Lum B  | HER2-E     | HER2-E     | 0        |
| Lum B  | HER2-E     | Basal-like | 0        |
| Lum B  | Basal-like | Lum A      | 0        |
| Lum B  | Basal-like | Lum B      | 0        |
| Lum B  | Basal-like | HER2-E     | 1        |
| Lum B  | Basal-like | Basal-like | 0        |
| HER2-E | Lum A      | Lum A      | 0        |
| HER2-E | Lum A      | Lum B      | 0        |
| HER2-E | Lum A      | HER2-E     | 0        |
| HER2-E | Lum A      | Basal-like | 0        |
| HER2-E | Lum B      | Lum A      | 0        |
| HER2-E | Lum B      | Lum B      | 0        |
| HER2-E | Lum B      | HER2-E     | 0        |
| HER2-E | Lum B      | Basal-like | 0        |
| HER2-E | HER2-E     | Lum A      | 0        |
| HER2-E | HER2-E     | Lum B      | 0        |
| HER2-E | HER2-E     | HER2-E     | 2        |
| HER2-E | HER2-E     | Basal-like | 0        |
| HER2-E | Basal-like | Lum A      | 0        |
| HER2-E | Basal-like | Lum B      | 0        |

|            |            |            |   |
|------------|------------|------------|---|
| HER2-E     | Basal-like | HER2-E     | 0 |
| HER2-E     | Basal-like | Basal-like | 0 |
| Basal-like | Lum A      | Lum A      | 0 |
| Basal-like | Lum A      | Lum B      | 0 |
| Basal-like | Lum A      | HER2-E     | 0 |
| Basal-like | Lum A      | Basal-like | 0 |
| Basal-like | Lum B      | Lum A      | 0 |
| Basal-like | Lum B      | Lum B      | 0 |
| Basal-like | Lum B      | HER2-      | 0 |
| Basal-like | Lum B      | Basal-like | 1 |
| Basal-like | HER2-E     | Lum A      | 0 |
| Basal-like | HER2-E     | Lum B      | 0 |
| Basal-like | HER2-E     | HER2-E     | 0 |
| Basal-like | HER2-E     | Basal-like | 0 |
| Basal-like | Basal-like | Lum A      | 0 |
| Basal-like | Basal-like | Lum B      | 0 |
| Basal-like | Basal-like | HER2-E     | 0 |
| Basal-like | Basal-like | Basal-like | 1 |

Abbreviations: DM, distant metastasis; HER2-E, human epidermal growth factor receptor 2 enriched; LNM, lymph node metastasis; n, number; PT, primary tumor

**Table S5.** Overall PAM50 breast cancer intrinsic subtype shifts from primary tumors to distant metastases in relation to adjuvant therapy given.

| Adjuvant Therapy                                     |     | <i>n</i> | Subtype Stable <i>n</i> (%) | Subtype Shift<br><i>n</i> (%) | <i>p</i> |
|------------------------------------------------------|-----|----------|-----------------------------|-------------------------------|----------|
| Chemotherapy                                         | Yes | 27       | 12(44)                      | 15 (56)                       | 0.61     |
|                                                      | No  | 34       | 18 (53)                     | 16 (47)                       |          |
| Endocrine therapy                                    | Yes | 44       | 17 (39)                     | 27 (61)                       | 0.01     |
|                                                      | No  | 17       | 13 (76)                     | 4 (24)                        |          |
| Endocrine therapy (in<br>PT luminal subtype<br>only) | Yes | 40       | 29 (73)                     | 11 (27)                       | 0.25     |
|                                                      | No  | 12       | 11 (92)                     | 1 (8)                         |          |

Abbreviations: *n*, number; PT, primary tumor