

**Supplemental Table S1.** Age- and body mass index-adjusted partial Spearman's rank correlation coefficients (rho) for progesterone, progesterone metabolites and unconjugated estradiol.

| <b>Luteal phase premenopausal women (N=65)</b>     | Pregnenolone      | 17 $\alpha$ -hydroxy pregnenolone | Progesterone      | 17 $\alpha$ -hydroxy progesterone | 3 $\alpha$ HP     | 5 $\alpha$ P      | 20 $\alpha$ HP | E2   |
|----------------------------------------------------|-------------------|-----------------------------------|-------------------|-----------------------------------|-------------------|-------------------|----------------|------|
| Pregnenolone                                       | 1.00              |                                   |                   |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxypregnenolone                   | 0.62 <sup>1</sup> | 1.00                              |                   |                                   |                   |                   |                |      |
| Progesterone                                       | 0.30              | -0.02                             | 1.00              |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxyprogesterone                   | 0.39              | 0.12                              | 0.56 <sup>1</sup> | 1.00                              |                   |                   |                |      |
| 3 $\alpha$ -dihydroprogesterone (3 $\alpha$ HP)    | 0.29              | 0.10                              | 0.51 <sup>1</sup> | 0.17                              | 1.00              |                   |                |      |
| 5 $\alpha$ -dihydroprogesterone (5 $\alpha$ P)     | 0.27              | -0.02                             | 0.72 <sup>1</sup> | 0.50 <sup>1</sup>                 | 0.45              | 1.00              |                |      |
| 20 $\alpha$ -Dihydroprogesterone (20 $\alpha$ HP)  | 0.35              | 0.08                              | 0.89 <sup>1</sup> | 0.40                              | 0.57 <sup>1</sup> | 0.65 <sup>1</sup> | 1.00           |      |
| Unconjugated estradiol (E2)                        | 0.34              | 0.12                              | 0.05              | 0.64 <sup>1</sup>                 | -0.14             | 0.16              | 0.03           | 1.00 |
| <b>Follicular phase premenopausal women (N=88)</b> | Pregnenolone      | 17 $\alpha$ -hydroxy pregnenolone | Progesterone      | 17 $\alpha$ -hydroxy progesterone | 3 $\alpha$ HP     | 5 $\alpha$ P      | 20 $\alpha$ HP | E2   |
| Pregnenolone                                       | 1.00              |                                   |                   |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxypregnenolone                   | 0.50 <sup>1</sup> | 1.00                              |                   |                                   |                   |                   |                |      |
| Progesterone                                       | 0.37              | 0.24                              | 1.00              |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxyprogesterone                   | 0.32              | 0.51 <sup>1</sup>                 | 0.57 <sup>1</sup> | 1.00                              |                   |                   |                |      |
| 3 $\alpha$ HP                                      | 0.05              | -0.01                             | 0.09              | 0.11                              | 1.00              |                   |                |      |
| 5 $\alpha$ P                                       | 0.22              | 0.21                              | 0.02              | -0.06                             | -0.09             | 1.00              |                |      |
| 20 $\alpha$ HP                                     | 0.43 <sup>1</sup> | 0.22                              | 0.76 <sup>1</sup> | 0.19                              | 0.001             | 0.10              | 1.00           |      |
| E2                                                 | -0.01             | 0.12                              | 0.09              | 0.48                              | 0.19              | 0.39              | -0.07          | 1.00 |
| <b>Postmenopausal women (N=103)</b>                | Pregnenolone      | 17 $\alpha$ -hydroxy pregnenolone | Progesterone      | 17 $\alpha$ -hydroxy progesterone | 3 $\alpha$ HP     | 5 $\alpha$ P      | 20 $\alpha$ HP | E2   |
| Pregnenolone                                       | 1.00              |                                   |                   |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxypregnenolone                   | 0.54 <sup>1</sup> | 1.00                              |                   |                                   |                   |                   |                |      |
| Progesterone                                       | 0.62 <sup>1</sup> | 0.47 <sup>1</sup>                 | 1.00              |                                   |                   |                   |                |      |
| 17 $\alpha$ -hydroxyprogesterone                   | 0.37 <sup>1</sup> | 0.59 <sup>1</sup>                 | 0.69 <sup>1</sup> | 1.00                              |                   |                   |                |      |
| 3 $\alpha$ HP                                      | 0.001             | 0.05                              | 0.04              | -0.02                             | 1.00              |                   |                |      |
| 5 $\alpha$ P                                       | 0.09              | 0.07                              | -0.01             | -0.04                             | -0.15             | 1.00              |                |      |
| 20 $\alpha$ HP                                     | 0.53 <sup>1</sup> | 0.21                              | 0.64 <sup>1</sup> | 0.14                              | 0.04              | 0.12              | 1.00           |      |
| E2                                                 | -0.03             | 0.01                              | 0.07              | 0.15                              | -0.04             | 0.10              | 0.04           | 1.00 |

<sup>1</sup> P-value < 0.0001

**Supplemental Table S2.** Distribution of progesterone, progesterone metabolites, unconjugated estradiol, MBD measures and TDLU measures, stratified by menopausal status and menstrual cycle phase, among BREAST Stamp Project participants with benign biopsy diagnoses.

|                                                   | Luteal (N=58) |            | Follicular (N=76) |            | Postmenopausal (N=78) |            |
|---------------------------------------------------|---------------|------------|-------------------|------------|-----------------------|------------|
|                                                   | Median        | (IDR)      | Median            | (IDR)      | Median                | (IDR)      |
| Hormones (pmol/L)                                 |               |            |                   |            |                       |            |
| Pregnenolone                                      | 3898          | 2310-7419  | 2780              | 1375-6017  | 1776                  | 853-3291   |
| 17 $\alpha$ -hydroxypregnenolone                  | 3586          | 2353-8492  | 3497              | 1878-10482 | 2545                  | 1508-6534  |
| Progesterone                                      | 14333         | 1961-40437 | 278               | 122-1547   | 108                   | 76.8-198.2 |
| 17 $\alpha$ -hydroxyprogesterone                  | 2112          | 786-3701   | 565               | 306-1675   | 325                   | 195-909    |
| 3 $\alpha$ -dihydroprogesterone (3 $\alpha$ HP)   | 81.7          | 30.0-208.5 | 42.5              | 24.8-93.2  | 44.8                  | 24.3-85.4  |
| 5 $\alpha$ -dihydroprogesterone (5 $\alpha$ P)    | 1969          | 713-5172   | 807               | 285-1821   | 832                   | 283-2007   |
| 20 $\alpha$ -Dihydroprogesterone (20 $\alpha$ HP) | 4095          | 540-11338  | 218               | 114-559    | 112                   | 64.6-186.0 |
| 5 $\alpha$ P/3 $\alpha$ HP Ratio                  | 23.4          | 8.3-54.8   | 17.7              | 5.0-52.8   | 17.5                  | 4.9-72.5   |
| Unconjugated estradiol (E2)                       | 243           | 96-746     | 220               | 22.5-602.1 | 8.1                   | 2.2-40.5   |
| Progesterone/E2 Ratio                             | 81.4          | 3.6-187.5  | 1.8               | 0.4-17.4   | 13.5                  | 2.8-57.5   |

Abbreviation: IDR Interdecile Range

**Supplemental Table S3.** Relationships of MBD and TDLU measures with circulating geometric mean concentrations of progesterone and progesterone metabolites (pmol/L) in luteal phase women with benign biopsy diagnoses.

|                                            | Pregnenolone              | 17 $\alpha$ -hydroxy<br>pregnenolone | Progesterone              | 17 $\alpha$ -hydroxy<br>progesterone | 3 $\alpha$ HP             | 5 $\alpha$ P              | 20 $\alpha$ HP            | 5 $\alpha$ P/3 $\alpha$ HP | E2                        | Progesterone/<br>E2       |
|--------------------------------------------|---------------------------|--------------------------------------|---------------------------|--------------------------------------|---------------------------|---------------------------|---------------------------|----------------------------|---------------------------|---------------------------|
|                                            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)  | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) |
| <b>Percent MBD-V</b>                       | 3729 (2958-4701)          | 3872 (3002-4993)                     | 8448 (4418-16153)         | 1689 (1293-2207)                     | 91 (64-130)               | 1704 (1162-2501)          | 2784 (1590-4874)          | 19 (13-28)                 | 226 (146-350)             | 46 (19-107)               |
| T1                                         | 3705 (2977-4612)          | 3844 (3022-4889)                     | 10057 (5449-18561)        | 1852 (1439-2385)                     | 64 (46-90)                | 1505 (1047-2162)          | 3280 (1932-5569)          | 23 (16-34)                 | 207 (138-311)             | 41 (19-92)                |
| T2                                         | 4557 (3558-5838)          | 4059 (3093-5328)                     | 11765 (5883-23527)        | 1881 (1414-2503)                     | 84 (57-123)               | 2026 (1345-3052)          | 3535 (1943-6434)          | 24 (16-37)                 | 280 (188-418)             | 46 (21-101)               |
| T3                                         | 0.31                      | 0.83                                 | 0.53                      | 0.62                                 | 0.75                      | 0.61                      | 0.60                      | 0.44                       | 0.47                      | 0.97                      |
| P-trend                                    | (0.12, 0.41)              | (-0.002, 0.98)                       | (0.11, 0.47)              | (0.05, 0.71)                         | (0.02, 0.91)              | (0.14, 0.34)              | (0.12, 0.42)              | (0.2, 0.17)                | (0.05, 0.77)              | (0.01, 0.97)              |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Percent MBD-A</b>                       | 3424 (2823-4154)          | 3736 (2992-4666)                     | 9576 (5593-16398)         | 1735 (1383-2178)                     | 95 (70-130)               | 1550 (1104-2174)          | 3180 (2025-4993)          | 16 (12-23)                 | 202 (140-291)             | 50 (25-102)               |
| T1                                         | 3674 (3025-4463)          | 3605 (2882-4509)                     | 5964 (3470-10251)         | 1532 (1219-1925)                     | 60 (44-81)                | 1578 (1122-2220)          | 1864 (1183-2936)          | 26 (19-38)                 | 221 (155-315)             | 29 (14-57)                |
| T2                                         | 5275 (4226-6585)          | 4639 (3594-5988)                     | 19867 (10711-36848)       | 2318 (1786-3008)                     | 91 (64-130)               | 2238 (1517-3302)          | 6173 (3677-10364)         | 25 (17-37)                 | 309 (212-449)             | 64 (31-132)               |
| T3                                         | 0.01                      | 0.26                                 | 0.16                      | 0.16                                 | 0.68                      | 0.19                      | 0.15                      | 0.10                       | 0.13                      | 0.68                      |
| P-trend                                    | (0.32, 0.03)              | (0.19, 0.19)                         | (0.21, 0.14)              | (0.22, 0.13)                         | (-0.01, 0.97)             | (0.21, 0.14)              | (0.21, 0.14)              | (0.31, 0.03)               | (0.18, 0.28)              | (0.07, 0.65)              |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Absolute MBD-V</b>                      | 3679 (2961-4572)          | 4498 (3569-5669)                     | 7099 (3935-12809)         | 1574 (1232-2009)                     | 80 (57-112)               | 1396 (982-1983)           | 2391 (1442-3965)          | 18 (12-25)                 | 215 (153-303)             | 33 (17-62)                |
| T1                                         | 4134 (3340-5117)          | 3602 (2870-4521)                     | 10117 (5666-18062)        | 1947 (1532-2475)                     | 75 (54-104)               | 2040 (1445-2881)          | 2962 (1802-4869)          | 27 (19-39)                 | 269 (189-382)             | 39 (20-74)                |
| T2                                         | 4117 (3234-5242)          | 3718 (2875-4809)                     | 14192 (7364-27351)        | 1911 (1456-2508)                     | 85 (59-124)               | 1814 (1227-2681)          | 4709 (2683-8263)          | 21 (14-32)                 | 238 (150-376)             | 94 (40-220)               |
| T3                                         | 0.48                      | 0.25                                 | 0.13                      | 0.27                                 | 0.83                      | 0.29                      | 0.10                      | 0.41                       | 0.62                      | 0.08                      |
| P-trend                                    | (0.01, 0.95)              | (-0.21, 0.14)                        | (0.14, 0.33)              | (0.2, 0.17)                          | (0.06, 0.68)              | (0.11, 0.43)              | (0.18, 0.21)              | (0.04, 0.76)               | (0.13, 0.41)              | (0.19, 0.23)              |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Absolute MBD-A</b>                      | 3217 (2628-3939)          | 3866 (3075-4860)                     | 7229 (4046-12915)         | 1664 (1304-2123)                     | 79 (57-109)               | 1454 (1031-2051)          | 2427 (1469-4009)          | 18 (13-26)                 | 186 (132-263)             | 46 (23-90)                |
| T1                                         | 4527 (3718-5512)          | 4370 (3498-5459)                     | 9852 (5603-17322)         | 1827 (1441-2315)                     | 93 (68-128)               | 1638 (1172-2288)          | 3165 (1942-5156)          | 18 (13-25)                 | 265 (187-377)             | 32 (16-64)                |
| T2                                         | 4383 (3487-5510)          | 3482 (2689-4510)                     | 15021 (7796-28941)        | 1956 (1485-2576)                     | 66 (45-95)                | 2315 (1569-3415)          | 4446 (2521-7840)          | 35 (24-52)                 | 293 (197-436)             | 65 (30-142)               |
| T3                                         | 0.05                      | 0.63                                 | 0.12                      | 0.40                                 | 0.55                      | 0.10                      | 0.13                      | 0.03                       | 0.09                      | 0.57                      |
| P-trend                                    | (0.21, 0.15)              | (-0.05, 0.75)                        | (0.19, 0.19)              | (0.14, 0.33)                         | (-0.04, 0.78)             | (0.22, 0.13)              | (0.18, 0.21)              | (0.27, 0.06)               | (0.22, 0.18)              | (0.11, 0.49)              |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>TDLU Involution Measures</b>            |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>TDLU count/100 mm<sup>2</sup></b>       | 3436 (2729-4325)          | 3524 (2740-4532)                     | 10856 (5686-20727)        | 1804 (1380-2360)                     | 95 (67-136)               | 1547 (1054-2272)          | 3682 (2130-6365)          | 16 (11-24)                 | 190 (128-283)             | 52 (24-116)               |
| T1                                         | 4065 (3311-4990)          | 3933 (3144-4921)                     | 11189 (6289-19909)        | 1834 (1444-2329)                     | 80 (58-110)               | 1988 (1412-2799)          | 3855 (2367-6277)          | 25 (17-35)                 | 311 (225-431)             | 35 (18-67)                |
| T2                                         | 4400 (3553-5449)          | 4300 (3404-5432)                     | 8100 (4441-14771)         | 1764 (1375-2263)                     | 67 (48-93)                | 1652 (1156-2361)          | 2253 (1355-3746)          | 25 (17-36)                 | 211 (147-304)             | 52 (25-109)               |
| T3                                         | 0.14                      | 0.27                                 | 0.51                      | 0.90                                 | 0.16                      | 0.85                      | 0.19                      | 0.15                       | 0.81                      | 0.96                      |
| P-trend                                    | (0.16, 0.26)              | (0.17, 0.23)                         | (-0.16, 0.27)             | (-0.08, 0.56)                        | (-0.15, 0.28)             | (-0.04, 0.8)              | (-0.22, 0.13)             | (0.18, 0.22)               | (0.04, 0.81)              | (-0.05, 0.74)             |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Median TDLU span, <math>\mu</math>m</b> | 4649 (3775-5727)          | 4362 (3354-5672)                     | 12301 (7271-20810)        | 2023 (1644-2489)                     | 79 (58-107)               | 1797 (1250-2583)          | 3846 (2400-6164)          | 23 (16-33)                 | 329 (222-488)             | 37 (18-74)                |
| T1                                         | 3609 (2908-4480)          | 3723 (2835-4889)                     | 6816 (3952-11756)         | 1529 (1233-1895)                     | 70 (51-96)                | 1848 (1268-2693)          | 2118 (1299-3453)          | 27 (18-39)                 | 212 (141-321)             | 41 (20-85)                |
| T2                                         | 4486 (3616-5567)          | 4149 (3161-5446)                     | 11198 (6498-19297)        | 1796 (1449-2226)                     | 80 (58-110)               | 1628 (1118-2371)          | 3200 (1964-5214)          | 20 (14-30)                 | 217 (141-333)             | 53 (25-114)               |
| T3                                         | 0.80                      | 0.78                                 | 0.79                      | 0.43                                 | 0.94                      | 0.71                      | 0.58                      | 0.68                       | 0.16                      | 0.49                      |
| P-trend                                    | (-0.03, 0.85)             | (-0.05, 0.75)                        | (-0.05, 0.78)             | (-0.12, 0.45)                        | (0.01, 0.97)              | (-0.09, 0.57)             | (-0.13, 0.43)             | (-0.14, 0.4)               | (-0.2, 0.27)              | (0.1, 0.58)               |
| Correlation <sup>1</sup> (rho, p-value)    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Median acini count per TDLU</b>         | 4577 (3770-5557)          | 4405 (3487-5565)                     | 12250 (7467-20097)        | 1985 (1624-2426)                     | 82 (62-110)               | 2055 (1458-2896)          | 3684 (2350-5774)          | 25 (17-36)                 | 331 (228-480)             | 38 (20-74)                |
| T1                                         | 3433 (2786-4231)          | 3111 (2419-4001)                     | 6189 (3632-10548)         | 1540 (1241-1911)                     | 66 (48-90)                | 1493 (1032-2160)          | 2013 (1240-3266)          | 23 (15-34)                 | 227 (145-354)             | 32 (15-70)                |
| T2                                         | 4833 (3834-6094)          | 5002 (3783-6613)                     | 12409 (6868-22420)        | 1793 (1411-2279)                     | 80 (56-113)               | 1698 (1127-2559)          | 3500 (2046-5988)          | 21 (14-33)                 | 188 (122-289)             | 64 (30-137)               |
| T3                                         | 0.92                      | 0.70                                 | 0.87                      | 0.45                                 | 0.82                      | 0.44                      | 0.76                      | 0.58                       | 0.06                      | 0.35                      |
| P-trend                                    | (0.0002, 0.99)            | (0.06, 0.74)                         | (-0.03, 0.87)             | (-0.13, 0.43)                        | (-0.01, 0.95)             | (-0.18, 0.27)             | (-0.09, 0.58)             | (-0.13, 0.42)              | (-0.27, 0.13)             | (0.08, 0.67)              |

<sup>1</sup>Adjusted for age, body mass index, and day in menstrual cycle of blood draw.

Abbreviations: GM, Geometric Mean; LCI, Lower Confidence Interval; UCI Upper Confidence Interval; T1-3, Tertiles 1-3; MBD Mammographic Breast Density; TDLU Terminal Ductal Lobular Unit, MBD-V Mammographic Breast Density-Volume, MBD-A Mammographic Breast Density-Area; E2 Unconjugated Estradiol; Bold values are P-value <0.05

**Supplemental Table S4.** Relationships of MBD and TDLU measures with circulating geometric mean concentrations of progesterone and progesterone metabolites (pmol/L) in follicular phase women with benign biopsy diagnoses.

|                                           | Pregnenolone              | 17a-hydroxy<br>pregnenolone | Progesterone              | 17a-hydroxy<br>progesterone | 3aHP                      | 5aP                       | 20aHP                     | 5aP/3aHP                  | E2                        | Progesterone/E2           |
|-------------------------------------------|---------------------------|-----------------------------|---------------------------|-----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                                           | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) |
| <b>Percent MBD-V</b>                      |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2309 (1733-3077)          | 2722 (1987-3729)            | 201 (122-334)             | 479 (347-661)               | 52 (39-67)                | 707 (488-1025)            | 173 (125-239)             | 14 (9-22)                 | 120 (62-234)              | 2 (1-4)                   |
| T2                                        | 3040 (2348-3937)          | 4126 (3107-5478)            | 718 (456-1130)            | 823 (615-1101)              | 57 (44-72)                | 887 (635-1240)            | 400 (299-535)             | 16 (10-24)                | 178 (94-336)              | 4 (2-11)                  |
| T3                                        | 3001 (2355-3826)          | 3942 (3021-5145)            | 281 (183-430)             | 627 (477-824)               | 37 (30-47)                | 682 (498-933)             | 220 (168-289)             | 18 (12-27)                | 173 (98-304)              | 2 (1-3)                   |
| P-trend                                   | 0.28                      | 0.18                        | 0.90                      | 0.49                        | 0.06                      | 0.72                      | 0.83                      | 0.40                      | 0.53                      | 0.62                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (0.16, 0.24)              | (0.2, 0.15)                 | (0.09, 0.51)              | (0.08, 0.58)                | (-0.25, 0.07)             | (-0.01, 0.95)             | (0.13, 0.34)              | (0.07, 0.59)              | (0.07, 0.64)              | (-0.05, 0.73)             |
| <b>Percent MBD-A</b>                      |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2589 (1921-3491)          | 3172 (2268-4438)            | 356 (198-641)             | 558 (394-791)               | 50 (37-67)                | 887 (604-1304)            | 258 (177-378)             | 18 (11-29)                | 111 (56-220)              | 4 (1-10)                  |
| T2                                        | 3112 (2466-3928)          | 3691 (2841-4795)            | 388 (245-613)             | 697 (531-914)               | 51 (40-64)                | 754 (559-1018)            | 256 (190-344)             | 15 (10-22)                | 176 (103-299)             | 2 (1-4)                   |
| T3                                        | 2582 (2006-3322)          | 3716 (2799-4934)            | 265 (161-435)             | 604 (450-811)               | 41 (32-52)                | 634 (458-878)             | 217 (158-299)             | 15 (10-24)                | 180 (98-330)              | 1 (1-3)                   |
| P-trend                                   | 0.82                      | 0.56                        | 0.40                      | 0.89                        | 0.28                      | 0.22                      | 0.48                      | 0.76                      | 0.40                      | 0.16                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (0.00008, 1.)             | (0.14, 0.3)                 | (0.001, 0.99)             | (-0.003, 0.98)              | (-0.12, 0.39)             | (-0.16, 0.26)             | (0.13, 0.36)              | (-0.03, 0.82)             | (0.09, 0.54)              | (-0.12, 0.42)             |
| <b>Absolute MBD-V</b>                     |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2512 (1991-3171)          | 3246 (2502-4210)            | 355 (224-563)             | 646 (492-849)               | 47 (37-59)                | 752 (555-1018)            | 236 (176-318)             | 16 (11-24)                | 126 (77-203)              | 3 (1-6)                   |
| T2                                        | 3031 (2305-3985)          | 3776 (2781-5128)            | 332 (193-571)             | 626 (454-863)               | 47 (36-62)                | 752 (526-1074)            | 244 (172-345)             | 16 (10-25)                | 152 (78-296)              | 2 (1-6)                   |
| T3                                        | 2863 (2263-3621)          | 3699 (2844-4811)            | 309 (194-492)             | 594 (451-783)               | 47 (37-59)                | 734 (540-997)             | 248 (184-335)             | 16 (11-23)                | 205 (117-359)             | 2 (1-3)                   |
| P-trend                                   | 0.46                      | 0.50                        | 0.69                      | 0.68                        | 0.99                      | 0.92                      | 0.82                      | 0.93                      | 0.21                      | 0.26                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (0.14, 0.32)              | (0.14, 0.3)                 | (0.06, 0.64)              | (-0.03, 0.84)               | (0.04, 0.76)              | (-0.12, 0.39)             | (0.26, 0.05)              | (-0.08, 0.56)             | (0.18, 0.24)              | (-0.11, 0.46)             |
| <b>Absolute MBD-A</b>                     |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2369 (1877-2990)          | 2929 (2259-3798)            | 297 (187-473)             | 585 (443-773)               | 54 (43-69)                | 728 (534-991)             | 227 (168-306)             | 13 (9-20)                 | 149 (89-249)              | 2 (1-4)                   |
| T2                                        | 3418 (2572-4541)          | 4255 (3099-5842)            | 476 (270-838)             | 710 (506-996)               | 41 (31-54)                | 833 (571-1214)            | 283 (196-409)             | 21 (13-33)                | 126 (63-251)              | 4 (2-11)                  |
| T3                                        | 2798 (2256-3471)          | 3760 (2956-4782)            | 294 (191-452)             | 606 (468-783)               | 45 (36-55)                | 712 (535-948)             | 234 (177-310)             | 16 (11-23)                | 179 (105-305)             | 1 (1-3)                   |
| P-trend                                   | 0.39                      | 0.22                        | 0.88                      | 0.92                        | 0.27                      | 0.88                      | 0.94                      | 0.59                      | 0.62                      | 0.53                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (0.13, 0.34)              | (0.22, 0.11)                | (0.09, 0.53)              | (0.03, 0.85)                | (-0.12, 0.38)             | (-0.08, 0.56)             | (0.23, 0.1)               | (0.01, 0.95)              | (0.04, 0.77)              | (-0.04, 0.82)             |
| <b>TDLU Involution Measures</b>           |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| <b>TDLU count/100 mm<sup>2</sup></b>      |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2634 (1956-3547)          | 3032 (2180-4216)            | 266 (153-462)             | 411 (297-568)               | 41 (31-55)                | 744 (504-1097)            | 223 (155-320)             | 18 (11-29)                | 72 (41-127)               | 4 (2-9)                   |
| T2                                        | 3021 (2392-3816)          | 4096 (3162-5307)            | 547 (355-844)             | 775 (601-1000)              | 52 (41-65)                | 704 (518-955)             | 316 (238-420)             | 14 (9-20)                 | 158 (95-262)              | 4 (2-8)                   |
| T3                                        | 2559 (2034-3220)          | 3357 (2603-4329)            | 234 (153-358)             | 643 (500-825)               | 46 (36-57)                | 786 (582-1061)            | 199 (150-263)             | 17 (12-25)                | 255 (156-417)             | 1 (0-2)                   |
| P-trend                                   | 0.75                      | 0.83                        | 0.43                      | 0.11                        | 0.78                      | 0.77                      | 0.40                      | 0.95                      | 0.002                     | <b>0.01</b>               |
| Correlation <sup>1</sup> ((rho, p-value)) | (-0.03, 0.82)             | (0.06, 0.66)                | (-0.1, 0.49)              | (0.14, 0.31)                | (-0.02, 0.88)             | (0.06, 0.66)              | (-0.11, 0.42)             | (0.05, 0.74)              | (0.3, 0.05)               | (-0.28, 0.07)             |
| <b>Median TDLU span, µm</b>               |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2625 (2008-3432)          | 3663 (2675-5016)            | 403 (219-744)             | 774 (542-1104)              | 51 (38-69)                | 820 (568-1185)            | 259 (176-384)             | 16 (10-25)                | 150 (68-333)              | 4 (1-13)                  |
| T2                                        | 2898 (2265-3708)          | 4212 (3155-5624)            | 443 (252-778)             | 731 (528-1014)              | 50 (38-66)                | 561 (400-787)             | 268 (187-383)             | 11 (7-17)                 | 188 (107-332)             | 2 (1-6)                   |
| T3                                        | 2636 (2049-3393)          | 3032 (2255-4075)            | 263 (148-468)             | 593 (425-829)               | 43 (32-56)                | 925 (655-1308)            | 230 (159-332)             | 22 (14-33)                | 216 (126-369)             | 1 (1-3)                   |
| P-trend                                   | 0.99                      | 0.38                        | 0.32                      | 0.30                        | 0.38                      | 0.58                      | 0.65                      | 0.33                      | 0.47                      | 0.16                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (0.12, 0.47)              | (-0.02, 0.9)                | (-0.16, 0.3)              | (-0.15, 0.36)               | (-0.13, 0.43)             | (0.18, 0.25)              | (0.08, 0.6)               | (0.24, 0.13)              | (0.04, 0.81)              | (-0.07, 0.7)              |
| <b>Median acini count per TDLU</b>        |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                        | 2331 (1764-3080)          | 3143 (2241-4407)            | 338 (176-651)             | 771 (521-1140)              | 41 (30-57)                | 669 (434-1032)            | 209 (136-321)             | 16 (9-28)                 | 138 (61-312)              | 2 (1-9)                   |
| T2                                        | 3280 (2599-4141)          | 4033 (3040-5350)            | 596 (345-1031)            | 797 (575-1106)              | 53 (40-69)                | 796 (554-1144)            | 321 (224-459)             | 15 (10-24)                | 246 (145-418)             | 3 (1-6)                   |
| T3                                        | 2588 (2028-3301)          | 3612 (2689-4854)            | 232 (131-411)             | 555 (395-782)               | 51 (39-69)                | 743 (509-1085)            | 239 (164-347)             | 14 (9-23)                 | 203 (117-351)             | 1 (0-3)                   |
| P-trend                                   | 0.84                      | 0.67                        | 0.26                      | 0.18                        | 0.41                      | 0.80                      | 0.86                      | 0.77                      | 0.65                      | 0.27                      |
| Correlation <sup>1</sup> ((rho, p-value)) | (-0.01, 0.95)             | (0.09, 0.59)                | (-0.28, 0.08)             | (-0.16, 0.33)               | (0.14, 0.38)              | (-0.06, 0.7)              | (0.04, 0.79)              | (-0.11, 0.51)             | (0.02, 0.9)               | (-0.26, 0.16)             |

<sup>1</sup>Adjusted for age and body mass index..

Abbreviations: GM, Geometric Mean; LCI, Lower Confidence Interval; UCI Upper Confidence Interval; T1-3, Tertiles 1-3; MBD Mammographic Breast Density; TDLU Terminal Ductal Lobular Unit, MBD-V Mammographic Breast Density-Volume, MBD-A Mammographic Breast Density-Area; E2 Unconjugated Estradiol; Bold values are P-value <0.05

**Supplemental Table S5.** Relationships of MBD and TDLU measures with circulating geometric mean concentrations of progesterone and progesterone metabolites (pmol/L) in postmenopausal women with benign biopsy diagnoses.

|                                            | Pregnenolone              | 17a-hydroxy<br>pregnenolone | Progesterone              | 17a-hydroxy<br>progesterone | 3aHP                      | 5aP                       | 20aHP                     | 5aP/3aHP                  | E2                        | Progesterone/<br>E2       |
|--------------------------------------------|---------------------------|-----------------------------|---------------------------|-----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                                            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) |
| <b>Percent MBD-V</b>                       |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1777 (1429-2210)          | 3077 (2383-3975)            | 113 (96-132)              | 387 (307-488)               | 49 (39-60)                | 890 (664-1192)            | 108 (93-127)              | 18 (12-27)                | 10 (6-15)                 | 11 (7-17)                 |
| T2                                         | 1976 (1611-2423)          | 2701 (2126-3432)            | 123 (106-142)             | 353 (284-438)               | 48 (39-58)                | 930 (707-1223)            | 120 (104-139)             | 20 (13-28)                | 10 (6-15)                 | 12 (8-19)                 |
| T3                                         | 1558 (1244-1952)          | 2811 (2157-3663)            | 117 (100-138)             | 400 (315-509)               | 41 (33-51)                | 629 (465-851)             | 113 (96-133)              | 15 (10-23)                | 8 (5-12)                  | 15 (10-23)                |
| P-trend                                    | 0.50                      | 0.63                        | 0.73                      | 0.89                        | 0.29                      | 0.16                      | 0.70                      | 0.63                      | 0.60                      | 0.37                      |
| Correlation <sup>1</sup> (rho, p-value)    | (-0.07, 0.53)             | (0.02, 0.89)                | (0.1, 0.39)               | (0.06, 0.6)                 | (-0.13, 0.26)             | (-0.19, 0.11)             | (0.04, 0.71)              | (-0.07, 0.55)             | (-0.09, 0.48)             | (0.15, 0.22)              |
| <b>Percent MBD-A</b>                       |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1506 (1220-1859)          | 2640 (2052-3397)            | 111 (95-130)              | 356 (283-449)               | 45 (36-55)                | 880 (653-1184)            | 111 (95-130)              | 20 (13-29)                | 12 (8-18)                 | 9 (6-14)                  |
| T2                                         | 2172 (1779-2651)          | 2607 (2053-3310)            | 117 (101-136)             | 368 (295-458)               | 46 (37-56)                | 807 (609-1069)            | 114 (98-132)              | 18 (12-26)                | 9 (6-13)                  | 13 (9-20)                 |
| T3                                         | 1673 (1340-2089)          | 3396 (2602-4431)            | 125 (106-148)             | 417 (326-532)               | 46 (37-58)                | 733 (535-1003)            | 117 (99-138)              | 16 (10-24)                | 7 (5-11)                  | 17 (11-26)                |
| P-trend                                    | 0.41                      | 0.25                        | 0.36                      | 0.41                        | 0.87                      | 0.44                      | 0.67                      | 0.51                      | 0.12                      | <b>0.07</b>               |
| Correlation <sup>1</sup> (rho, p-value)    | (0.06, 0.61)              | (0.05, 0.67)                | (0.06, 0.58)              | (0.06, 0.63)                | (-0.01, 0.97)             | (-0.1, 0.38)              | (0.04, 0.76)              | (-0.08, 0.47)             | (-0.21, 0.09)             | <b>(0.28, 0.02)</b>       |
| <b>Absolute MBD-V</b>                      |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1563 (1271-1922)          | 2523 (1971-3229)            | 102 (87-118)              | 311 (249-388)               | 47 (38-58)                | 850 (638-1133)            | 108 (92-126)              | 18 (12-27)                | 6 (4-9)                   | 17 (11-26)                |
| T2                                         | 2186 (1789-2670)          | 3305 (2604-4196)            | 128 (111-148)             | 430 (347-532)               | 43 (35-52)                | 928 (703-1225)            | 114 (98-132)              | 22 (15-32)                | 10 (6-15)                 | 12 (8-18)                 |
| T3                                         | 1600 (1311-1954)          | 2792 (2200-3542)            | 124 (107-143)             | 405 (327-501)               | 47 (38-57)                | 665 (505-878)             | 119 (103-138)             | 14 (10-21)                | 12 (8-18)                 | 11 (7-16)                 |
| P-trend                                    | 0.91                      | 0.59                        | 0.08                      | 0.11                        | 0.98                      | 0.24                      | 0.36                      | 0.37                      | <b>0.03</b>               | 0.13                      |
| Correlation <sup>1</sup> (rho, p-value)    | (-0.04, 0.74)             | (0.04, 0.74)                | <b>(0.23, 0.04)</b>       | (0.22, 0.06)                | (-0.01, 0.91)             | (-0.15, 0.19)             | (0.1, 0.39)               | (-0.13, 0.25)             | <b>(0.31, 0.01)</b>       | (-0.22, 0.08)             |
| <b>Absolute MBD-A</b>                      |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1585 (1298-1935)          | 2670 (2102-3392)            | 114 (98-132)              | 387 (312-479)               | 43 (35-53)                | 901 (683-1189)            | 112 (97-130)              | 21 (14-30)                | 10 (7-15)                 | 11 (8-17)                 |
| T2                                         | 2174 (1759-2686)          | 2935 (2277-3783)            | 114 (97-133)              | 326 (260-410)               | 45 (37-56)                | 830 (618-1113)            | 116 (99-136)              | 18 (12-27)                | 7 (4-11)                  | 16 (10-25)                |
| T3                                         | 1643 (1350-1999)          | 2988 (2361-3783)            | 124 (107-144)             | 422 (341-521)               | 48 (39-58)                | 703 (535-923)             | 113 (98-131)              | 15 (10-21)                | 10 (7-14)                 | 12 (8-18)                 |
| P-trend                                    | 0.82                      | 0.52                        | 0.43                      | 0.58                        | 0.49                      | 0.22                      | 0.92                      | 0.20                      | 0.88                      | 0.75                      |
| Correlation <sup>1</sup> (rho, p-value)    | (0.01, 0.96)              | (0.0009, 0.99)              | (0.05, 0.66)              | (0.05, 0.65)                | (0.06, 0.6)               | (-0.15, 0.2)              | (0.02, 0.89)              | (-0.16, 0.16)             | (-0.02, 0.88)             | (0.07, 0.56)              |
| <b>TDLU Involution Measures</b>            |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| <b>TDLU count/100 mm<sup>2</sup></b>       |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1576 (1262-1967)          | 2799 (2157-3631)            | 113 (96-133)              | 357 (282-452)               | 42 (34-52)                | 1131 (846-1512)           | 112 (97-131)              | 27 (18-40)                | 13 (9-21)                 | 8 (6-13)                  |
| T2                                         | 1728 (1393-2142)          | 3037 (2360-3908)            | 112 (96-131)              | 386 (307-486)               | 53 (43-65)                | 709 (536-939)             | 97 (83-112)               | 13 (9-20)                 | 6 (4-10)                  | 16 (10-25)                |
| T3                                         | 1944 (1598-2364)          | 2772 (2203-3488)            | 125 (109-145)             | 391 (318-482)               | 43 (36-52)                | 688 (533-889)             | 130 (113-149)             | 16 (11-23)                | 9 (6-12)                  | 15 (10-21)                |
| P-trend                                    | 0.18                      | 0.95                        | 0.34                      | 0.59                        | 0.90                      | <b>0.02</b>               | 0.18                      | 0.07                      | 0.19                      | 0.08                      |
| Correlation <sup>1</sup> (rho, p-value)    | (0.18, 0.13)              | (0.04, 0.71)                | (0.13, 0.26)              | (0.1, 0.4)                  | (0.06, 0.63)              | <b>(-0.24, 0.04)</b>      | (0.11, 0.37)              | (-0.17, 0.15)             | (-0.14, 0.27)             | (0.22, 0.08)              |
| <b>Median TDLU span, <math>\mu</math>m</b> |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1894 (1511-2374)          | 3173 (2439-4128)            | 127 (107-150)             | 431 (341-544)               | 44 (35-55)                | 919 (711-1186)            | 123 (104-146)             | 21 (15-30)                | 7 (4-11)                  | 18 (12-29)                |
| T2                                         | 1847 (1475-2312)          | 2529 (1947-3285)            | 109 (92-130)              | 312 (248-394)               | 51 (41-64)                | 667 (517-861)             | 113 (95-133)              | 13 (9-18)                 | 7 (5-11)                  | 15 (10-24)                |
| T3                                         | 1894 (1490-2406)          | 3006 (2275-3974)            | 125 (104-150)             | 426 (333-546)               | 45 (35-57)                | 556 (424-729)             | 108 (90-129)              | 12 (9-18)                 | 10 (6-17)                 | 12 (7-20)                 |
| P-trend                                    | 0.99                      | 0.75                        | 0.89                      | 0.89                        | 0.83                      | <b>0.01</b>               | 0.29                      | <b>0.04</b>               | 0.36                      | 0.25                      |
| Correlation <sup>1</sup> (rho, p-value)    | (-0.06, 0.66)             | (-0.15, 0.28)               | (-0.04, 0.79)             | (-0.06, 0.65)               | (0.03, 0.84)              | <b>(-0.36, 0.01)</b>      | (-0.11, 0.44)             | <b>(-0.31, 0.03)</b>      | (0.1, 0.49)               | (-0.15, 0.32)             |
| <b>Median acini count per TDLU</b>         |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                         | 1900 (1526-2364)          | 3289 (2548-4246)            | 127 (108-151)             | 412 (325-521)               | 47 (38-59)                | 690 (533-892)             | 125 (106-147)             | 15 (10-21)                | 7 (5-12)                  | 17 (11-27)                |
| T2                                         | 1982 (1550-2534)          | 2810 (2109-3743)            | 115 (95-139)              | 388 (298-506)               | 50 (39-63)                | 867 (649-1158)            | 108 (90-130)              | 17 (12-26)                | 5 (3-9)                   | 20 (12-33)                |
| T3                                         | 1761 (1396-2221)          | 2558 (1951-3353)            | 116 (97-139)              | 352 (274-452)               | 43 (34-54)                | 592 (451-778)             | 110 (92-130)              | 14 (10-20)                | 11 (7-17)                 | 11 (7-18)                 |
| P-trend                                    | 0.65                      | 0.18                        | 0.46                      | 0.37                        | 0.55                      | 0.47                      | 0.27                      | 0.86                      | 0.33                      | 0.22                      |
| Correlation <sup>1</sup> (rho, p-value)    | (-0.09, 0.52)             | <b>(-0.31, 0.03)</b>        | (-0.1, 0.49)              | (-0.16, 0.24)               | (-0.06, 0.66)             | (-0.11, 0.41)             | (-0.16, 0.26)             | (-0.02, 0.88)             | (0.14, 0.35)              | (-0.19, 0.19)             |

<sup>1</sup>Adjusted for age, body mass index, and day in menstrual cycle of blood draw.

Abbreviations: GM, Geometric Mean; LCI, Lower Confidence Interval; UCI Upper Confidence Interval; T1-3, Tertiles 1-3; MBD Mammographic Breast Density; TDLU Terminal Ductal Lobular Unit, MBD-V Mammographic Breast Density-Volume, MBD-A Mammographic Breast Density-Area; E2 Unconjugated Estradiol; Bold values are P-value <0.05

**Supplemental Table S6.** Relationships of MBD and TDLU measures with circulating geometric mean concentrations of progesterone and progesterone metabolites (pmol/L) in luteal phase women who reported regular menstrual cycle lengths (N=47).

|                                                          |    | Pregnenolone              | 17a-hydroxy<br>pregnenolone | Progesterone              | 17a-hydroxy<br>progesterone | 3aHP                      | 5aP                       | 20aHP                     | 5aP/3aHP                  | E2                        | Progesterone/E<br>2       |
|----------------------------------------------------------|----|---------------------------|-----------------------------|---------------------------|-----------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|---------------------------|
|                                                          | N  | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)   | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) |
| <b>MBD Measures</b>                                      |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| <b>Percent MBD-V</b>                                     |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 15 | 3901 (3073-4952)          | 4271 (3236-5638)            | 9816 (5295-18199)         | 1690 (1256-2274)            | 83 (57-122)               | 1637 (1107-2419)          | 2876 (1636-5058)          | 20 (13-30)                | 247 (145-420)             | 40 (14-113)               |
| T2                                                       | 16 | 3632 (2959-4457)          | 3415 (2691-4334)            | 10177 (5991-17288)        | 1842 (1428-2377)            | 64 (46-90)                | 1852 (1324-2589)          | 3007 (1852-4880)          | 29 (20-41)                | 241 (158-370)             | 38 (17-87)                |
| T3                                                       | 16 | 4757 (3746-6041)          | 3929 (2975-5188)            | 19934 (10743-36988)       | 2278 (1692-3067)            | 110 (75-162)              | 2797 (1892-4136)          | 5891 (3348-10367)         | 25 (17-38)                | 336 (215-523)             | 64 (27-150)               |
| P-trend <sup>2</sup>                                     |    | 0.28                      | 0.75                        | 0.14                      | 0.20                        | 0.33                      | 0.08                      | 0.11                      | 0.47                      | 0.36                      | 0.47                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.14, 0.41)              | (-0.12, 0.45)               | (0.32, 0.05)              | (0.20, 0.22)                | (0.19, 0.25)              | (0.36, 0.02)              | (0.35, 0.03)              | (0.25, 0.13)              | (0.13, 0.50)              | (0.13, 0.48)              |
| <b>Percent MBD-A</b>                                     |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 15 | 3503 (2904-4226)          | 3767 (2935-4835)            | 11667 (7031-19359)        | 1926 (1503-2467)            | 91 (64-128)               | 1646 (1163-2329)          | 3345 (2174-5146)          | 18 (13-26)                | 226 (146-348)             | 55 (23-132)               |
| T2                                                       | 16 | 3479 (2906-4164)          | 3521 (2772-4472)            | 7214 (4440-11721)         | 1508 (1189-1913)            | 62 (45-87)                | 1852 (1328-2583)          | 2006 (1327-3032)          | 30 (21-42)                | 223 (149-334)             | 28 (13-63)                |
| T3                                                       | 16 | 5613 (4599-6852)          | 4342 (3331-5661)            | 24618 (14375-42159)       | 2494 (1916-3245)            | 104 (72-150)              | 2781 (1923-4022)          | 7989 (5055-12628)         | 27 (18-39)                | 389 (261-581)             | 64 (29-142)               |
| P-trend <sup>2</sup>                                     |    | 0.004                     | 0.49                        | 0.11                      | 0.26                        | 0.70                      | 0.06                      | 0.04                      | 0.14                      | 0.09                      | 0.80                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.39, 0.01)              | (0.09, 0.58)                | (0.31, 0.06)              | (0.21, 0.20)                | (0.12, 0.46)              | (0.34, 0.03)              | (0.41, 0.01)              | (0.34, 0.03)              | (0.26, 0.17)              | (0.08, 0.67)              |
| <b>Absolute MBD-V</b>                                    |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 15 | 3884 (3135-4812)          | 4174 (3276-5318)            | 9187 (5351-15772)         | 1779 (1369-2310)            | 73 (52-104)               | 1662 (1176-2349)          | 2768 (1685-4549)          | 23 (16-33)                | 266 (183-387)             | 33 (17-67)                |
| T2                                                       | 16 | 4079 (3213-5179)          | 3496 (2670-4579)            | 11774 (6450-21493)        | 2052 (1534-2746)            | 84 (57-124)               | 2222 (1512-3266)          | 3386 (1948-5888)          | 26 (18-39)                | 345 (213-559)             | 36 (15-88)                |
| T3                                                       | 16 | 4196 (3205-5493)          | 3866 (2851-5243)            | 18444 (9347-36392)        | 1924 (1385-2674)            | 94 (60-146)               | 2280 (1476-3522)          | 5436 (2911-10153)         | 24 (15-38)                | 222 (131-376)             | 104 (39-276)              |
| P-trend <sup>2</sup>                                     |    | 0.65                      | 0.54                        | 0.14                      | 0.60                        | 0.38                      | 0.21                      | 0.13                      | 0.72                      | 0.83                      | 0.11                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.003, 0.98)             | (-0.11, 0.49)               | (0.19, 0.25)              | (0.12, 0.46)                | (0.27, 0.09)              | (0.19, 0.25)              | (0.18, 0.28)              | (-0.05, 0.77)             | (-0.07, 0.70)             | (0.22, 0.25)              |
| <b>Absolute MBD-A</b>                                    |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 15 | 3354 (2711-4148)          | 3630 (2821-4672)            | 9254 (5263-16271)         | 1671 (1279-2184)            | 71 (49-102)               | 1534 (1078-2182)          | 2565 (1541-4271)          | 22 (15-31)                | 202 (131-312)             | 48 (21-111)               |
| T2                                                       | 16 | 4605 (3781-5607)          | 4331 (3428-5471)            | 11864 (7032-20016)        | 2235 (1744-2863)            | 94 (67-131)               | 2119 (1528-2938)          | 3573 (2228-5731)          | 23 (16-32)                | 356 (240-529)             | 28 (13-59)                |
| T3                                                       | 16 | 4229 (3380-5291)          | 3501 (2683-4566)            | 18410 (10155-33375)       | 1816 (1370-2408)            | 84 (57-124)               | 2610 (1800-3786)          | 5657 (3305-9680)          | 31 (21-46)                | 272 (181-408)             | 79 (36-173)               |
| P-trend <sup>2</sup>                                     |    | 0.16                      | 0.86                        | 0.11                      | 0.68                        | 0.53                      | 0.05                      | 0.04                      | 0.20                      | 0.40                      | 0.37                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.19, 0.25)              | (-0.05, 0.75)               | (0.27, 0.10)              | (0.08, 0.62)                | (0.16, 0.33)              | (0.33, 0.04)              | (0.36, 0.02)              | (0.20, 0.23)              | (0.04, 0.85)              | (0.23, 0.22)              |
| <b>TDLU Involution Measures</b>                          |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| <b>TDLU count/100 mm<sup>2</sup></b>                     |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 15 | 3949 (3150-4950)          | 4024 (3109-5209)            | 11604 (6487-20759)        | 1966 (1495-2585)            | 82 (56-119)               | 1719 (1189-2484)          | 3399 (2004-5764)          | 21 (14-31)                | 263 (171-404)             | 45 (19-107)               |
| T2                                                       | 16 | 4187 (3363-5212)          | 3709 (2888-4763)            | 15104 (8598-26535)        | 2077 (1593-2708)            | 80 (56-115)               | 2184 (1529-3122)          | 4826 (2893-8050)          | 27 (19-39)                | 359 (248-521)             | 39 (18-83)                |
| T3                                                       | 16 | 3998 (3196-5002)          | 3801 (2943-4909)            | 10829 (6086-19270)        | 1711 (1304-2244)            | 87 (60-126)               | 2193 (1522-3159)          | 2961 (1754-4998)          | 25 (17-37)                | 201 (131-309)             | 61 (25-147)               |
| P-trend <sup>2</sup>                                     |    | 0.94                      | 0.77                        | 0.86                      | 0.49                        | 0.82                      | 0.38                      | 0.71                      | 0.52                      | 0.43                      | 0.63                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (-0.07, 0.65)             | (-0.04, 0.80)               | (-0.01, 0.94)             | (-0.15, 0.35)               | (0.07, 0.67)              | (0.14, 0.38)              | (-0.05, 0.77)             | (0.05, 0.77)              | (-0.18, 0.34)             | (0.16, 0.40)              |
| <b>Median TDLU span, μ</b>                               |    |                           |                             |                           |                             |                           |                           |                           |                           |                           |                           |
| T1                                                       | 12 | 3958 (3124-5015)          | 3355 (2588-4350)            | 11150 (5954-20883)        | 1831 (1389-2414)            | 80 (55-117)               | 1689 (1141-2499)          | 3312 (1847-5937)          | 21 (14-32)                | 362 (217-603)             | 30 (11-79)                |
| T2                                                       | 12 | 4628 (3612-5930)          | 4416 (3364-5795)            | 17527 (9085-33815)        | 2255 (1689-3012)            | 97 (65-143)               | 3320 (2202-5004)          | 4638 (2517-8548)          | 34 (22-53)                | 285 (166-488)             | 66 (24-185)               |
| T3                                                       | 12 | 4044 (3188-5129)          | 3784 (2915-4911)            | 10049 (5351-18872)        | 1885 (1428-2488)            | 74 (51-109)               | 1675 (1130-2483)          | 2959 (1646-5318)          | 22 (15-34)                | 236 (146-383)             | 46 (18-117)               |
| P-trend <sup>2</sup>                                     |    | 0.90                      | 0.53                        | 0.83                      | 0.88                        | 0.79                      | 0.99                      | 0.80                      | 0.82                      | 0.24                      | 0.55                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.03, 0.88)              | (0.15, 0.45)                | (-0.04, 0.84)             | (-0.00005, 1.00)            | (-0.05, 0.79)             | (-0.04, 0.84)             | (-0.07, 0.72)             | (-0.06, 0.77)             | (-0.21, 0.32)             | (0.04, 0.85)              |

<sup>1</sup>Adjusted for age, body mass index, and day in menstrual cycle of blood draw.

<sup>2</sup> P-values were not statistically significant at Bonferroni threshold.

Abbreviations: GM, Geometric Mean; LCI, Lower Confidence Interval; UCI Upper Confidence Interval; T1-3, Tertiles 1-3; MBD Mammographic Breast Density; TDLU Terminal Ductal Lobular Unit, MBD-V Mammographic Breast Density-Volume, MBD-A Mammographic Breast Density-Area; E2 Unconjugated Estradiol.

**Supplemental Table 7.** Relationships of MBD and TDLU measures with circulating geometric mean concentrations of progesterone and progesterone metabolites (pmol/L) in follicular phase women who reported regular menstrual cycle lengths (N=59).

|                                                          |    | Pregnenolone              | 17 $\alpha$ -hydroxy<br>pregnenolone | Progesterone              | 17 $\alpha$ -hydroxy<br>progesterone | 3 $\alpha$ HP             | 5 $\alpha$ P              | 20 $\alpha$ HP            | 5 $\alpha$ P/3 $\alpha$ HP | E2                        | Progesterone/E2           |
|----------------------------------------------------------|----|---------------------------|--------------------------------------|---------------------------|--------------------------------------|---------------------------|---------------------------|---------------------------|----------------------------|---------------------------|---------------------------|
|                                                          | N  | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)            | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI)  | GM <sup>1</sup> (LCI-UCI) | GM <sup>1</sup> (LCI-UCI) |
| <b>MBD Measures</b>                                      |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>Percent MBD-V</b>                                     |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 19 | 2336 (1472-3707)          | 2690 (1619-4471)                     | 629 (280-1413)            | 639 (395-1034)                       | 74 (51-107)               | 893 (512-1558)            | 414 (240-714)             | 12 (6-24)                  | 167 (63-443)              | 5 (1-20)                  |
| T2                                                       | 20 | 2930 (2123-4043)          | 4167 (2924-5937)                     | 477 (271-839)             | 790 (566-1105)                       | 46 (36-60)                | 790 (536-1164)            | 270 (184-394)             | 17 (11-28)                 | 219 (106-454)             | 3 (1-9)                   |
| T3                                                       | 20 | 2688 (1935-3734)          | 3672 (2558-5271)                     | 226 (127-402)             | 551 (391-775)                        | 33 (25-43)                | 708 (477-1053)            | 199 (135-293)             | 21 (13-35)                 | 181 (97-335)              | 1 (1-3)                   |
| P-trend <sup>2</sup>                                     |    | 0.79                      | 0.55                                 | 0.04                      | 0.40                                 | 0.00                      | 0.52                      | 0.05                      | 0.22                       | 0.96                      | 0.16                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.05, 0.79)              | (0.11, 0.53)                         | (-0.21, 0.22)             | (-0.14, 0.44)                        | (-0.47, 0.01)             | (-0.05, 0.77)             | (-0.15, 0.41)             | (0.22, 0.21)               | (-0.07, 0.73)             | (-0.21, 0.29)             |
| <b>Percent MBD-A</b>                                     |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 19 | 2346 (1592-3457)          | 2710 (1745-4209)                     | 613 (296-1271)            | 707 (459-1089)                       | 69 (49-96)                | 727 (446-1184)            | 399 (247-645)             | 11 (6-19)                  | 155 (64-375)              | 6 (1-22)                  |
| T2                                                       | 20 | 3336 (2466-4513)          | 4183 (2968-5894)                     | 398 (226-702)             | 680 (486-953)                        | 43 (33-56)                | 777 (531-1137)            | 249 (171-362)             | 18 (11-29)                 | 235 (128-433)             | 2 (1-4)                   |
| T3                                                       | 20 | 2355 (1700-3262)          | 3725 (2573-5393)                     | 258 (140-477)             | 592 (412-851)                        | 36 (27-47)                | 829 (550-1250)            | 210 (140-315)             | 23 (14-38)                 | 165 (81-336)              | 2 (1-5)                   |
| P-trend <sup>2</sup>                                     |    | 0.83                      | 0.39                                 | 0.09                      | 0.53                                 | 0.01                      | 0.70                      | 0.07                      | 0.07                       | 0.97                      | 0.28                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (-0.05, 0.76)             | (0.24, 0.18)                         | (-0.18, 0.31)             | (-0.13, 0.46)                        | (-0.36, 0.04)             | (0.11, 0.53)              | (-0.14, 0.42)             | (0.34, 0.05)               | (-0.03, 0.89)             | (-0.11, 0.58)             |
| <b>Absolute MBD-V</b>                                    |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 19 | 2379 (1734-3265)          | 2989 (2105-4244)                     | 493 (273-888)             | 743 (530-1042)                       | 51 (38-68)                | 672 (46-983)              | 319 (216-472)             | 13 (8-21)                  | 177 (98-321)              | 3 (1-8)                   |
| T2                                                       | 20 | 2898 (2018-4160)          | 4018 (2691-6000)                     | 370 (189-725)             | 620 (421-913)                        | 45 (32-63)                | 848 (549-1310)            | 253 (162-396)             | 19 (11-32)                 | 272 (135-546)             | 1 (0-4)                   |
| T3                                                       | 20 | 2879 (2035-4073)          | 3945 (2686-5794)                     | 298 (156-568)             | 594 (410-860)                        | 41 (30-56)                | 861 (568-1307)            | 227 (148-348)             | 21 (13-36)                 | 137 (66-284)              | 2 (1-7)                   |
| P-trend <sup>2</sup>                                     |    | 0.41                      | 0.28                                 | 0.26                      | 0.37                                 | 0.32                      | 0.38                      | 0.25                      | 0.19                       | 0.70                      | 0.57                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.18, 0.32)              | (0.27, 0.12)                         | (-0.18, 0.31)             | (-0.19, 0.27)                        | (-0.18, 0.31)             | (0.16, 0.37)              | (-0.04, 0.84)             | (0.25, 0.15)               | (-0.06, 0.78)             | (-0.04, 0.86)             |
| <b>Absolute MBD-A</b>                                    |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 19 | 2623 (1930-3563)          | 2985 (2132-4178)                     | 469 (264-833)             | 657 (473-914)                        | 54 (41-71)                | 752 (519-1088)            | 323 (222-471)             | 14 (9-22)                  | 195 (106-360)             | 3 (1-8)                   |
| T2                                                       | 20 | 2294 (1450-3629)          | 3582 (2165-5926)                     | 352 (149-831)             | 744 (454-1220)                       | 42 (28-63)                | 672 (387-1169)            | 218 (124-384)             | 16 (8-32)                  | 270 (112-653)             | 1 (0-5)                   |
| T3                                                       | 20 | 2955 (2179-4008)          | 4267 (3054-5962)                     | 328 (185-581)             | 614 (442-852)                        | 40 (31-53)                | 870 (602-1256)            | 241 (166-351)             | 21 (14-34)                 | 149 (79-279)              | 2 (1-7)                   |
| P-trend <sup>2</sup>                                     |    | 0.59                      | 0.15                                 | 0.39                      | 0.77                                 | 0.16                      | 0.58                      | 0.29                      | 0.20                       | 0.54                      | 0.82                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.13, 0.45)              | (0.35, 0.05)                         | (-0.13, 0.48)             | (-0.09, 0.63)                        | (-0.20, 0.25)             | (0.14, 0.44)              | (-0.10, 0.56)             | (0.24, 0.18)               | (-0.07, 0.73)             | (-0.01, 0.96)             |
| <b>TDLU Involution Measures</b>                          |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| <b>TDLU count/100 mm<sup>2</sup></b>                     |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 20 | 2776 (1841-4186)          | 3770 (2379-5975)                     | 288 (143-581)             | 517 (339-787)                        | 42 (29-62)                | 826 (504-1355)            | 239 (148-387)             | 20 (10-36)                 | 154 (71-335)              | 2 (1-6)                   |
| T2                                                       | 19 | 2763 (1989-3837)          | 3464 (2397-5006)                     | 689 (393-1208)            | 812 (580-1137)                       | 49 (36-66)                | 755 (508-1121)            | 369 (251-542)             | 15 (9-25)                  | 122 (65-229)              | 8 (3-18)                  |
| T3                                                       | 20 | 2550 (1832-3551)          | 3535 (2439-5123)                     | 274 (156-483)             | 635 (452-892)                        | 45 (34-62)                | 774 (520-1153)            | 213 (144-314)             | 17 (10-28)                 | 322 (169-614)             | 1 (0-2)                   |
| P-trend <sup>2</sup>                                     |    | 0.74                      | 0.86                                 | 0.65                      | 0.66                                 | 0.86                      | 0.87                      | 0.53                      | 0.81                       | 0.16                      | 0.24                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (-0.17, 0.35)             | (-0.10, 0.57)                        | (-0.04, 0.81)             | (0.03, 0.86)                         | (0.03, 0.89)              | (0.01, 0.95)              | (-0.08, 0.65)             | (-0.03, 0.87)              | (0.22, 0.28)              | (-0.22, 0.29)             |
| <b>Median TDLU span, <math>\mu</math></b>                |    |                           |                                      |                           |                                      |                           |                           |                           |                            |                           |                           |
| T1                                                       | 13 | 2501 (1741-3593)          | 3100 (1995-4817)                     | 655 (282-1523)            | 755 (481-1184)                       | 55 (37-83)                | 780 (483-1262)            | 355 (198-638)             | 14 (7-27)                  | 239 (78-729)              | 6 (1-30)                  |
| T2                                                       | 13 | 2976 (2101-4215)          | 4482 (2935-6845)                     | 501 (223-1126)            | 951 (617-1465)                       | 50 (34-74)                | 665 (419-1054)            | 232 (132-407)             | 13 (7-24)                  | 187 (81-430)              | 3 (1-10)                  |
| T3                                                       | 13 | 2747 (1937-3894)          | 2983 (1951-4560)                     | 257 (114-579)             | 580 (376-895)                        | 40 (27-59)                | 1079 (679-1714)           | 231 (131-406)             | 27 (14-50)                 | 235 (101-546)             | 1 (0-3)                   |
| P-trend <sup>2</sup>                                     |    | 0.75                      | 0.84                                 | 0.13                      | 0.39                                 | 0.27                      | 0.33                      | 0.34                      | 0.16                       | 0.94                      | 0.10                      |
| Correlation <sup>1</sup><br>(rho, p-value <sup>2</sup> ) |    | (0.08, 0.73)              | (-0.02, 0.92)                        | (-0.28, 0.19)             | (-0.15, 0.48)                        | (-0.25, 0.23)             | (0.21, 0.32)              | (-0.04, 0.84)             | (0.31, 0.14)               | (0.004, 0.99)             | (-0.31, 0.20)             |

<sup>1</sup>Adjusted for age and body mass index.

<sup>2</sup>P-values were not statistically significant at Bonferroni threshold.

Abbreviations: GM, Geometric Mean; LCI, Lower Confidence Interval; UCI Upper Confidence Interval; T1-3, Tertiles 1-3; MBD Mammographic Breast Density; TDLU Terminal Ductal Lobular Unit, MBD-V Mammographic Breast Density-Volume, MBD-A Mammographic Breast Density-Area; E2 Unconjugated Estradiol.