

**Supplementary Table 3. Distribution of Clinical Variables by RT dose**

| Variable                 | Level         | N (%)       |             |             | P Value |
|--------------------------|---------------|-------------|-------------|-------------|---------|
|                          |               | Total       | ≤66Gy       | >66Gy       |         |
| Age                      | Median(Range) | 44 (23,50)  | 44 (23,50)  | 43(28,50)   | 0.4849  |
| RSI_Subtype              | Sensitive     | 86 (25.1%)  | 59 (24.4%)  | 27 (27%)    | 0.8859  |
|                          | Intermediate  | 173 (50.6%) | 124 (51.2%) | 49 (49%)    |         |
|                          | Resistant     | 83 (24.3%)  | 59 (24.4%)  | 24 (24%)    |         |
|                          | Total         | 342         | 242 (70.8%) | 100 (29.2%) |         |
| Origin                   | Dutch         | 147 (43%)   | 105 (43.4%) | 42 (42%)    | 0.9088  |
|                          | French        | 195 (57%)   | 137 (56.6%) | 58 (58%)    |         |
|                          | Total         | 342         | 242 (70.8%) | 100 (29.2%) |         |
| Local_Recurrence         | No Recurrence | 224 (65.5%) | 152 (62.8%) | 72 (72%)    | 0.1014  |
|                          | Recurrence    | 118 (34.5%) | 90 (37.2%)  | 28 (28%)    |         |
|                          | Total         | 342         | 242 (70.8%) | 100 (29.2%) |         |
| T stage                  | pT1           | 215 (63.2%) | 158 (65.6%) | 57 (57.6%)  | 0.1760  |
|                          | pT2-3         | 125 (36.8%) | 83 (34.4%)  | 42 (42.4%)  |         |
|                          | Total         | 340         | 241 (70.9%) | 99 (29.1%)  |         |
| Surgical Margin          | positive      | 37 (11.2%)  | 13 (5.5%)   | 24 (26.1%)  | <.0001  |
|                          | negative      | 293 (88.8%) | 225 (94.5%) | 68 (73.9%)  |         |
|                          | Total         | 330         | 238 (72.1%) | 92 (27.9%)  |         |
| Surgical margin invasive | positive      | 21 (6.5%)   | 7 (3%)      | 14 (15.7%)  | 0.0002  |
|                          | negative      | 301 (93.5%) | 226 (97%)   | 75 (84.3%)  |         |
|                          | Total         | 322         | 233 (72.4%) | 89 (27.6%)  |         |
| Surgical margin DCIS     | positive      | 8 (4.3%)    | 1 (0.7%)    | 7 (13.2%)   | 0.0009  |
|                          | negative      | 176 (94.1%) | 131 (97.8%) | 45 (84.9%)  |         |
|                          | unknown       | 3 (1.6%)    | 2 (1.5%)    | 1 (1.9%)    |         |
|                          | Total         | 187         | 134 (71.7%) | 53 (28.3%)  |         |
| N stage                  | pN+           | 121 (36%)   | 76 (32.2%)  | 45 (45%)    | 0.0326  |
|                          | pN-           | 215 (64%)   | 160 (67.8%) | 55 (55%)    |         |

|                       |                    |             |             |             |        |
|-----------------------|--------------------|-------------|-------------|-------------|--------|
|                       | Total              | 336         | 236 (70.2%) | 100 (29.8%) |        |
| RT boost              |                    | 248         |             |             |        |
|                       | boost              | (72.5%)     | 148 (61.2%) | 100 (100%)  | <.0001 |
|                       | no boost           | 94 (27.5%)  | 94 (38.8%)  | 0 (0%)      |        |
|                       | Total              | 342         | 242 (70.8%) | 100 (29.2%) |        |
| Chemotherapy (CT)     |                    | 132         |             |             |        |
|                       | CT                 | (38.7%)     | 83 (34.4%)  | 49 (49%)    | 0.0142 |
|                       | no CT              | 209 (61.3%) | 158 (65.6%) | 51 (51%)    |        |
|                       | Total              | 341         | 241 (70.7%) | 100 (29.3%) |        |
| Hormonal therapy (HT) |                    | 31 (9.1%)   |             |             |        |
|                       | HT                 |             | 18 (7.5%)   | 13 (13%)    | 0.1481 |
|                       | no HT              | 310 (90.9%) | 223 (92.5%) | 87 (87%)    |        |
|                       | Total              | 341         | 241 (70.7%) | 100 (29.3%) |        |
| Histology shape       |                    | 16 (4.9%)   |             |             |        |
|                       | multinodular       |             | 9 (3.9%)    | 7 (7.7%)    | 0.2439 |
|                       | sharply demarcated | 85 (26.2%)  | 65 (27.9%)  | 20 (22%)    |        |
|                       | stellate           | 223 (68.8%) | 159 (68.2%) | 64 (70.3%)  |        |
|                       | Total              | 324         | 233 (71.9%) | 91 (28.1%)  |        |
| Histology type        |                    | 291         |             |             |        |
|                       | ductal             | (85.1%)     | 203 (83.9%) | 88 (88%)    | 0.5557 |
|                       | lobular            | 26 (7.6%)   | 19 (7.9%)   | 7 (7%)      |        |
|                       | other type         | 25 (7.3%)   | 20 (8.3%)   | 5 (5%)      |        |
|                       | Total              | 342         | 242 (70.8%) | 100 (29.2%) |        |
| Histology grade       |                    | 55          |             |             |        |
|                       | I                  | (16.3%)     | 40 (16.7%)  | 15 (15.3%)  | 0.8956 |
|                       | II                 | 147 (43.5%) | 105 (43.8%) | 42 (42.9%)  |        |
|                       | III                | 136 (40.2%) | 95 (39.6%)  | 41 (41.8%)  |        |
|                       | Total              | 338         | 240 (71%)   | 98 (29%)    |        |
| Tubule formation      |                    | 9 (2.6%)    |             |             |        |
|                       | NA                 |             | 6 (2.5%)    | 3 (3%)      | 0.8611 |
|                       | tubule50-90%       | 79 (23.1%)  | 58 (24%)    | 21 (21%)    |        |
|                       | tubule<10%         | 234 (68.4%) | 163 (67.4%) | 71 (71%)    |        |
|                       | tubule>90%         | 20 (5.8%)   | 15 (6.2%)   | 5 (5%)      |        |
|                       | Total              | 342         | 242 (70.8%) | 100 (29.2%) |        |
| polymorphism          |                    | 15 (4.5%)   |             |             |        |
|                       | polymorph1         |             | 13 (5.5%)   | 2 (2.1%)    | 0.1895 |
|                       | polymorph2         | 131 (39.5%) | 87 (37%)    | 44 (45.4%)  |        |

|                          |                     |                |             |            |        |
|--------------------------|---------------------|----------------|-------------|------------|--------|
|                          | polymorph3          | 186 (56%)      | 135 (57.4%) | 51 (52.6%) |        |
|                          | Total               | 332            | 235 (70.8%) | 97 (29.2%) |        |
| Mitotic index            | Mitotic 1           | 174 (53%)      | 125 (53.6%) | 49 (51.6%) | 0.9331 |
|                          | Mitotic 2           | 59 (18%)       | 42 (18%)    | 17 (17.9%) |        |
|                          | Mitotic 3           | 95 (29%)       | 66 (28.3%)  | 29 (30.5%) |        |
|                          | Total               | 328            | 233 (71%)   | 95 (29%)   |        |
| DCIS inside              | DCIS inside         | 93<br>(38.1%)  | 67 (38.5%)  | 26 (37.1%) | 0.8824 |
|                          | No DCIS inside      | 151<br>(61.9%) | 107 (61.5%) | 44 (62.9%) |        |
|                          | Total               | 244            | 174 (71.3%) | 70 (28.7%) |        |
| DCIS outside             | DCIS outside        | 75<br>(31.9%)  | 51 (30%)    | 24 (36.9%) | 0.3489 |
|                          | No DCIS outside     | 160<br>(68.1%) | 119 (70%)   | 41 (63.1%) |        |
|                          | Total               | 235            | 170 (72.3%) | 65 (27.7%) |        |
| DCIS                     | DCIS                | 210 (64%)      | 147 (62.8%) | 63 (67%)   | 0.5204 |
|                          | No DCIS             | 118 (36%)      | 87 (37.2%)  | 31 (33%)   |        |
|                          | Total               | 328            | 234 (71.3%) | 94 (28.7%) |        |
| DCIS Grade               | DCIS high grade     | 119<br>(57.2%) | 85 (58.2%)  | 34 (54.8%) | 0.1703 |
|                          | DCIS intermed grade | 69<br>(33.2%)  | 44 (30.1%)  | 25 (40.3%) |        |
|                          | DCIS low grade      | 20 (9.6%)      | 17 (11.6%)  | 3 (4.8%)   |        |
|                          | Total               | 208            | 146 (70.2%) | 62 (29.8%) |        |
| LCIS                     | LCIS present        | 31 (9.4%)      | 19 (8.1%)   | 12 (12.5%) | 0.2173 |
|                          | No LCIS             | 300<br>(90.6%) | 216 (91.9%) | 84 (87.5%) |        |
|                          | Total               | 331            | 235 (71%)   | 96 (29%)   |        |
| Lympho-vascular invasion | LVI present         | 11 (4.2%)      | 7 (3.5%)    | 4 (6.1%)   | 0.4750 |
|                          | No LVI              | 253<br>(95.8%) | 191 (96.5%) | 62 (93.9%) |        |
|                          | Total               | 264            | 198 (75%)   | 66 (25%)   |        |
| LVI quadrant             | 1 LVI               | 11<br>(13.8%)  | 7 (14.9%)   | 4 (12.1%)  | 0.5567 |
|                          | 2-5 LVI             | 31<br>(38.8%)  | 20 (42.6%)  | 11 (33.3%) |        |
|                          | >5 LVI              | 38<br>(47.5%)  | 20 (42.6%)  | 18 (54.5%) |        |
|                          | Total               | 80             | 47 (58.8%)  | 33 (41.3%) |        |
| p53                      | p53+                | 24             | 14 (22.6%)  | 10 (28.6%) | 0.6263 |

|                      |        |                |             |             |        |
|----------------------|--------|----------------|-------------|-------------|--------|
|                      |        | (24.7%)        |             |             |        |
|                      |        | 73             |             |             |        |
|                      | p53-   | (75.3%)        | 48 (77.4%)  | 25 (71.4%)  |        |
|                      | Total  | 97             | 62 (63.9%)  | 35 (36.1%)  |        |
| ER status            | 0      | 75<br>(21.9%)  | 61 (25.2%)  | 14 (14%)    | 0.0273 |
|                      | 1      | 267<br>(78.1%) | 181 (74.8%) | 86 (86%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |
| PR status            | 0      | 137<br>(40.1%) | 98 (40.5%)  | 39 (39%)    | 0.8064 |
|                      | 1      | 205<br>(59.9%) | 144 (59.5%) | 61 (61%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |
| Her-2-neu status     | 0      | 289<br>(84.5%) | 200 (82.6%) | 89 (89%)    | 0.1886 |
|                      | 1      | 53<br>(15.5%)  | 42 (17.4%)  | 11 (11%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |
| Proliferative index  | 0      | 173<br>(50.6%) | 122 (50.4%) | 51 (51%)    | 1.0000 |
|                      | 1      | 169<br>(49.4%) | 120 (49.6%) | 49 (49%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |
| Molecular subtype    | HER2   | 14 (4.1%)      | 12 (5%)     | 2 (2%)      | 0.1008 |
|                      | LUMA   | 145<br>(42.4%) | 101 (41.7%) | 44 (44%)    |        |
|                      | LUMB   | 86<br>(25.1%)  | 53 (21.9%)  | 33 (33%)    |        |
|                      | LUMHER | 39<br>(11.4%)  | 30 (12.4%)  | 9 (9%)      |        |
|                      | TN     | 58 (17%)       | 46 (19%)    | 12 (12%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |
| Triple Negative (TN) | Not TN | 284 (83%)      | 196 (81%)   | 88 (88%)    | 0.1533 |
|                      | TNP    | 58 (17%)       | 46 (19%)    | 12 (12%)    |        |
|                      | Total  | 342            | 242 (70.8%) | 100 (29.2%) |        |

**P Value is calculated using Chi square test using exact method with Monte Carlo estimation.**