Establishment and Validation of the Axillary Lymph Node Burden Using Cone-Beam Computerized Tomography and Ultrasound-Based Prediction Models in T1-2 Breast Cancer Patients

Shen Chen1†, Jiao Li1† , Peiqiang Cai1† Tiebao Meng1, Weimei Ma1, Jieting Chen1, Chuanmiao Xie1, Jianye Liang1, Shengting Pei1, Lizhi Liu1, Chunyan Zhou1, Ni He1\* and Yaopan Wu1\*

\* Correspondence: heni@sysucc.org.cn and [wuyp@sysucc.org.cn](mailto:wuyp@sysucc.org,cn)

† Shen Chen, Jiao Li, Peiqiang Cai contributed equally to this work.

1 Department of Medical Imaging, Sun Yat-sen University Cancer Center, Dongfeng Dong Road, Guangzhou 510060, P.R. China

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| (Supplementary) TABLE 1 | Clinicalpathological characteristics of patients in training and validation cohorts | | | | | | | | | |
| Characteristic | Training cohort (*n* = 271) |  |  | p-value |  | Validation cohort (*n* = 130) |  | p-value |
|  | N0 (n=172) | N1-2(n=48) | N≥3(n=51) |  | N0 (n=67) | N1-2 (n=30) | N≥3 (n=19) |  |
| Age, mean ± SD, years | 50.7±9.7 | 50.9±11.7 | 49.3±9.5 | 0.356 | 48 | 55.5 | 44 | 0.124 |
| Side |  |  |  | 0.256 |  |  |  | 0.387 |
| left | 94 (54.7) | 28 (58.3) | 22 (43.1) |  | 37 (55.2) | 21 (70.0) | 11 (57.9) |  |
| right | 78 (45.3) | 20 (41.7) | 29 (56.9) |  | 30 (44.8) | 9 (30.0) | 8 (42.1) |  |
| Histological type |  |  |  | 0.339 |  |  |  | 0.052 |
| pure IDC | 64 (37.2) | 12 (25.0) | 13 (25.5) |  | 39 (58.2) | 12 (40.0) | 6 (31.6) |  |
| mixed IDC | 99 (57.6) | 34 (70.8) | 36 (70.6) |  | 23 (34.3) | 17 (56.7) | 13 (68.4) |  |
| other special types of BC | 9 ( 5.2) | 2 ( 4.2) | 2 ( 3.9) |  | 5 ( 7.5) | 1 ( 3.3) | 0 ( 0.0) |  |
| Pathologic grade |  |  |  | 0.628 |  |  |  | 0.687 |
| Low | 3 ( 1.7) | 1 ( 2.1) | 1 ( 2.0) |  | 3 ( 4.5) | 0 ( 0.0) | 0 ( 0.0) |  |
| Moderate | 95 (55.2) | 28 (58.3) | 22 (43.1) |  | 32 (47.8) | 19 (63.3) | 12 (63.2) |  |
| High | 65 (37.8) | 18 (37.5) | 26 (51.0) |  | 27 (40.3) | 10 (33.3) | 7 (36.8) |  |
| absent | 9 ( 5.2) | 1 ( 2.1) | 2 ( 3.9) |  | 5 ( 7.5) | 1 ( 3.3) | 0 ( 0.0) |  |
| ER/PR |  |  |  | 0.204 |  |  |  | 0.201 |
| positive | 29(10.7) | 9(3.3) | 4(1.5) |  | 6(5.2) | 4(3.4) | 0 |  |
| negative | 143(52.8) | 39(14.4) | 47(17.3) |  | 61(52.6) | 26(22.4) | 19(16.4) |  |
| HER2 overexpression |  |  |  |  |  |  |  |  |
| with | 135 (78.5) | 37 (77.1) | 39 (76.5) | 0.945 | 58 (86.6) | 22 (73.3) | 13 (68.4) | 0.134 |
| without | 37 (21.5) | 11 (22.9) | 12 (23.5) |  | 9 (13.4) | 8 (26.7) | 6 (31.6) |  |
| Ki-67 status |  |  |  |  |  |  |  |  |
| low | 48 (27.9) | 16 (33.3) | 11 (21.6) | 0.423 | 24 (35.8) | 10 (33.3) | 6 (31.6) | 0.928 |
| high | 124 (72.1) | 32 (66.7) | 40 (78.4) |  | 43 (64.2) | 20 (66.7) | 13 (68.4) |  |
| Bundle invasion |  |  |  | 0.010 |  |  |  | 0.181 |
| absent | 150 (87.2) | 36 (75.0) | 36 (70.6) |  | 56 (83.6) | 21 (70.0) | 17 (89.5) |  |
| present | 22 (12.8) | 12 (25.0) | 15 (29.4) |  | 11 (16.4) | 9 (30.0) | 2 (10.5) |  |
| Vascular invasion |  |  |  | <0.001 |  |  |  | <0.001 |
| absent | 149 (86.6) | 18 (37.5) | 15 (29.4) |  | 56 (83.6) | 18 (60.0) | 5 (26.3) |  |
| present | 23 (13.4) | 30 (62.5) | 36 (70.6) |  | 11 (16.4) | 12 (40.0) | 14 (73.7) |  |
|  |  |  |  |  |  |  |  |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| (Supplementary) TABLE 2 |Semantic features of primary tumor on CBBCT in training cohort | | | | |
|  | N0 (n=172) | N1-2 (n=48) | N≥3 (n=51) | p-value |
| Maximum diameter (mm) | 20(14.6, 26.0) | 24.8(18.8, 30.0) | 27(21.3, 35.6) | <0.001 |
| △CT(HU) | 85.2±32.8 | 90.1±37.8 | 94.0±44.3 | 0.478 |
| Lesion number |  |  |  | 0.003 |
| one lesion | 117 (68.0) | 36 (75.0) | 23 (45.1) |  |
| More than one lesion | 55 (32.0) | 12 (25.0) | 28 (54.9) |  |
| Lesion types |  |  |  | 0.080 |
| masses only | 81 (47.1) | 13 (27.1) | 20 (39.2) |  |
| masses with calcification | 89 (51.7) | 35 (72.9) | 31 (60.8) |  |
| calcification only | 2 ( 1.2) | 0 ( 0.0) | 0 ( 0.0) |  |
| Density |  |  |  | 0.792 |
| low | 16(6.0) | 2(0.7) | 3(1.1) |  |
| isodensity | 84(30.0) | 22(8.1) | 27(10.0) |  |
| high | 57(21.0) | 20(7.4) | 15(5.5) |  |
| miss | 15(5.5) | 4(1.5) | 6(2.2) |  |
| Shape |  |  |  | 0.037 |
| round | 23 (13.4) | 4 ( 8.3) | 0 ( 0.0) |  |
| oval | 25 (14.5) | 7 (14.6) | 10 (19.6) |  |
| irrugular | 109 (63.4) | 33 (68.8) | 35 (68.6) |  |
| miss | 15 ( 8.7) | 4 ( 8.3) | 6 (11.8) |  |
| Margin |  |  |  | 0.277 |
| smooth | 25 (14.5) | 7 (14.6) | 3 ( 5.9) |  |
| lobular | 102 (59.3) | 26 (54.2) | 31 (60.8) |  |
| spiculated | 17 ( 9.9) | 10 (20.8) | 8 (15.7) |  |
| miss | 28 (16.3) | 5 (10.4) | 9 (17.6) |  |
| Distance to nipple (mm) | 36(22.8, 54) | 29.6(19, 36.2) | 37(12.5, 42.6) | 0.005 |
| Pattern of enhancement |  |  |  | 0.755 |
| mass-like enhancement | 147 (85.5) | 43 (89.6) | 42 (82.4) |  |
| non-mass enhancement | 15 ( 8.7) | 4 ( 8.3) | 6 (11.8) |  |
| mass-like alongside non-mass enhancement | 10 ( 5.8) | 1 ( 2.1) | 3 ( 5.9) |  |
| Calcification morphology |  |  |  | 0.036 |
| typically benign type | 30 (33.0) | 14 (40.0) | 3 ( 9.4) |  |
| coarse heterogeneous | 16 (17.6) | 4 (11.4) | 3 ( 9.4) |  |
| fine pleomorphic | 28 (30.8) | 12 (34.3) | 15 (46.9) |  |
| [amorphous](https://radiopaedia.org/articles/amorphous-calcification-within-breast?lang=us" \o "https://radiopaedia.org/articles/amorphous-calcification-within-breast?lang=us) | 17 (18.7) | 5 (14.3) | 11 (34.4) |  |
| Calcification distribution |  |  |  | 0.007 |
| [grouped](https://radiopaedia.org/articles/grouped-calcifications?lang=us" \o "https://radiopaedia.org/articles/grouped-calcifications?lang=us) | 46 (50.5) | 19 (54.3) | 25 (78.1) |  |
| regional | 9 ( 9.9) | 0 ( 0.0) | 0 ( 0.0) |  |
| linear or segmental | 8 ( 8.8) | 1 ( 2.9) | 1 ( 3.1) |  |
| diffuse | 28 (30.8) | 15 (42.9) | 6 (18.8) |  |
| Relationship between vessels and masses |  |  |  | 0.130 |
| assess to tumor | 98 (57.0) | 27 (56.2) | 21 (41.2) |  |
| no access to tumor | 74 (43.0) | 21 (43.8) | 30 (58.8) |  |
| Thickened or sunken skin |  |  |  | 0.001 |
| absent | 155 (90.1) | 35 (72.9) | 37 (72.5) |  |
| present | 17 ( 9.9) | 13 (27.1) | 14 (27.5) |  |
| Subcutaneous fat space |  |  |  | <0.001 |
| clear | 91 (52.9) | 19 (39.6) | 8 (15.7) |  |
| misty | 81 (47.1) | 29 (60.4) | 43 (84.3) |  |
| Invasion of pectoralis major |  |  |  | 0.001 |
| absent | 155(57.2) | 35(12.9) | 37(13.6) |  |
| present | 17(6.3) | 13(4.8) | 14(5.2) |  |
| Mammary gland types |  |  |  | 0.305 |
| Almost entirely fat | 2 ( 1.2) | 0 ( 0.0) | 0 ( 0.0) |  |
| Scattered fibroglandular tissue | 26 (15.1) | 12 (25.0) | 13 (25.5) |  |
| Heterogeneous fibroglandular tissue | 120 (69.8) | 32 (66.7) | 29 (56.9) |  |
| Extreme fibroglandular tissue | 24 (14.0) | 4 ( 8.3) | 9 (17.6) |  |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| (Supplementary) TABLE 3 |Axillary lymph node's morphology on Ultrasound in training cohort | | | |  |
|  | N0 (n=172) | N1-2 (n=48) | N≥3 (n=51) | p-value |
| number of LN |  |  |  | <0.001 |
| none | 62 (36.0) | 13 (27.1) | 3 ( 5.9) |  |
| solitary | 5 ( 2.9) | 1 ( 2.1) | 2 ( 3.9) |  |
| more than one LN | 105 (61.0) | 34 (70.8) | 46 (90.2) |  |
| maximum LN length(mm) | 11.00 (0.00, 16.00) | 12.50 (0.00, 17.00) | 13.00 (10.00, 20.00) | 0.006 |
| maximum LN axis (mm) | 5.00 (0.00, 7.00) | 6.00 (0.00, 8.00) | 8.00 (6.00, 10.00) | <0.001 |
| Lymph node's shape |  |  |  | <0.001 |
| oval | 171（63.1） | 48（17.7) | 44(16.2) |  |
| round | 1(0.4) | 0 | 7(2.6) |  |
| absent | 62 | 13 | 3 |  |
| Blood flow type |  |  |  | 0.003 |
| undetected | 128 (74.4) | 28 (58.3) | 29 (56.9) |  |
| portal type | 38 (22.1) | 13 (27.1) | 14 (27.5) |  |
| peripheral type | 0 ( 0.0) | 1 ( 2.1) | 3 ( 5.9) |  |
| mixed peripheral type | 6 ( 3.5) | 6 (12.5) | 5 ( 9.8) |  |
| Boundary between cortex and medulla |  |  |  | <0.001 |
| distinct | 161 (93.6) | 38 (79.2) | 20 (39.2) |  |
| indistinct | 11 ( 6.4) | 10 (20.8) | 31 (60.8) |  |
| Lymph gland hilum type |  |  |  | <0.001 |
| exist | 149(55.0) | 32(11.9) | 16(5.9) |  |
| disappear | 10(3.7) | 11(4.0) | 29(10.7) |  |
| eccentric | 13(4.8) | 5(1.8) | 6(2.2) |  |