Deep Learning Predicts Lung Cancer Treatment Response from Serial Medical Imaging data

**SUPPLEMENTS**

**Figure Legends:**

***Figure S1: Patient Missed Scans.*** *Not all patients received scans within the defined time frame for follow-up. Blue rectangles indicate missed scans for each patient in Dataset A for the pretreatment and subsequent follow-ups at around 1, 3, and 6 months post radiation therapy.*

***Figure S2: Overall Survival Prediction Performance.*** *The AUC values for one year and two year overall survival are shown in blue and orange respectively. The AUCs were significant for both end points with additional follow-ups (Wilcoxon rank-sums test p < 0.05 in B, C, and D).*

***Figure S3: Performance Deep Learning Biomarkers with Increase in Number of Time-points.*** AUC values were evaluated on an independent test set from the deep learning models for one-year survival, distant metastasis, progression and locoregional recurrence (LRR)-free status. Values were significantly separated with the Wilcoxon rank-sums test (*p* < 0.05) in Dataset A, the definitive radiation therapy cohort with the input of the pre-treatment scan along with the addition of one, two or three follow-up scans at one, three and six months follow-up..

**Tables:**

***Table S1:*** Event percentages for overall survival and prognostic factors for the definitive radiation therapy training/validation and independent test set.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Training/Validation  (n = 107) | Test  (n = 72) |
| Overall survival fraction | 1 year | 0.7 | 0.66 |
| 2 year | 0.49 | 0.43 |
| Distant Metastasis free fraction | 1 year | 0.42 | 0.43 |
| 2 year | 0.27 | 0.22 |
| Progression free fraction | 1 year | 0.42 | 0.46 |
| 2 year | 0.33 | 0.24 |
| Locoregional recurrence free fraction | 1 year | 0.55 | 0.5 |
| 2 year | 0.32 | 0.27 |

***Table S2:*** Patient and treatment characteristics of Dataset A. Median (range) is reported for continuous and counts (percentage) for categorical variables for the training and testing cohorts with not significant differences found with the Wilcoxon’s Rank Sums test.

|  |  |  |  |
| --- | --- | --- | --- |
| Patient characteristics |  | Definitive Radiation Training | Definitive Radiation Testing |
| Age |  | 63 (35 – 85) | 67 (32 – 93) |
| Gender | Female | 48 (0.45) | 37 (0.51) |
|  | Male | 58 (0.55) | 36 (0.49) |
| Ethnicity | African-American | 7 (0.07) | 4 (0.05) |
|  | Asian | 3 (0.03) | --- |
|  | Caucasian | 94 (0.89) | 67 (0.92) |
|  | Other | 2 (0.02) | 2 (0.02) |
| Smoking | Never | 9 (0.08) | 9 (0.13) |
|  | Current | 41 (0.39) | 23 (0.32) |
|  | Former | 56 (0.53) | 40 (0.56) |
| Pack-years |  | 40 (1.2 – 160) | 40 (0.05 – 165) |
| Performance status | 0 | 39 (0.37) | 25 (0.34) |
|  | 1 | 56 (0.53) | 43 (0.59) |
|  | 2 | 10 (0.09) | 5 (0.07) |
|  | 3 | 1 (0.01) | --- |
| Tumor characteristics |  |  |  |
| Overall stage | IIIA | 46 (0.43) | 35 (0.49) |
|  | IIIB | 60 (0.57) | 37 (0.51) |
| Histology | Adenocarcinoma | 58 | 42 |
|  | Squamous cell carcinoma | 29 | 20 |
|  | Undifferentiated NSCLC | 16 | 8 |
|  | Other (Large Cell) | 3 | 3 |
|  |  |  |  |
| Treatment characteristics |  |  |  |
| Prescribed radiation dose (Gy) |  | 66 (45 – 70) | 66 (46 – 70) |
| Radiation dose delivered (Gy) |  | 66 (33 – 70) | 66 (6 – 70) |
| Number of radiation fractions |  | 33 (15 – 37) | 33 (27 – 38) |
| Delivered biologically effective dose (Gy) |  | 79.2 (48 – 84) | 79.2 (64.8 – 84) |
|  |  |  |  |
| Clinical outcomes |  |  |  |
| Distant metastasis (DM) | No/ Yes | 37/69 | 16/57 |
|  | Time to event (months) | 8.7 (1.9 – 90.5) | 11.1 (2.2 – 154.5) |
| Locoregional recurrence (LRR) | No/ Yes | 54/52 | 40/33 |
|  | Time to event (months) | 15.4 (1.9 – 121.5) | 12.3 (2.5 – 153.4) |
| Progression | No/ Yes | 26/80 | 16/57 |
|  | Time to event (months) | 8.4 (1.9 – 90.5) | 9.4 (2.2 – 153.4) |
| Survival | No/ Yes | 30/76 | 19/54 |
|  | Time to event (months) | 15.1 (2.8 – 98.9) | 15.0 (4.1 – 154.8) |

***Table S3:*** AUC values for the clinical model and pre-treatment only images, with regards to predictions of overall survival and prognostic factors.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
|  |  | Clinical (n = 72) | | Pretreatment (n = 72) | |
|  |  | AUC | Rank-sums | AUC | Rank-sums |
| Overall survival | 1 year | 0.477 | 0.75 | 0.606 | 0.145 |
| 2 year | 0.506 | 0.93 | 0.583 | 0.251 |
| Distant Metastasis Free | 1 year | 0.555 | 0.432 | 0.589 | 0.219 |
| 2 year | 0.547 | 0.578 | 0.585 | 0.242 |
| Progression Free | 1 year | 0.601 | 0.145 | 0.609 | 0.132 |
| 2 year | 0.556 | 0.488 | 0.618 | 0.104 |
| Locoregional Recurrence Free | 1 year | 0.458 | 0.546 | 0.632 | 0.069 |
| 2 year | 0.539 | 0.612 | 0.528 | 0.702 |

**Table S4:** AUC values for Dataset B (trimodality) using the two input model trained on Dataset A, with regards to predictions of overall survival and prognostic factors.

|  |  |  |  |
| --- | --- | --- | --- |
|  |  | Dataset B Test (n = 89) | |
|  |  | AUC | Rank-sums |
| Overall survival | 1 year | 0.601 | 0.182 |
| 2 year | 0.625 | 0.066 |
| Distant Metastasis  Free | 1 year | 0.635 | 0.031 |
| 2 year | 0.657 | 0.014 |
| Progression  Free | 1 year | 0.642 | 0.022 |
| 2 year | 0.672 | 0.008 |
| Locoregional  Recurrence Free | 1 year | 0.656 | 0.015 |
| 2 year | 0.643 | 0.023 |