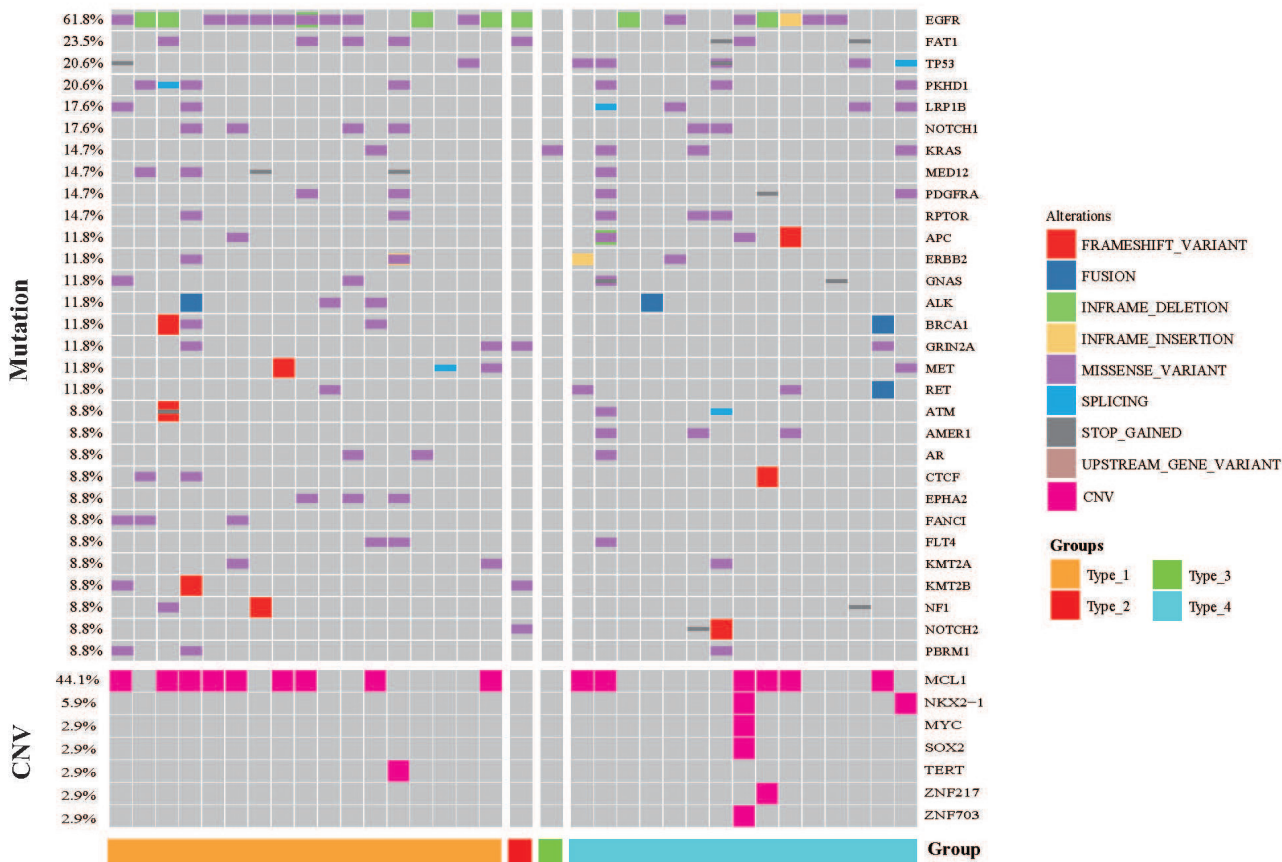**Figure S1** The frequency comparison of differentially mutated genes between different imaging features in LCCA. LCCA, lung cancer associated with cystic airspaces.

**Table S1** Comparison of differentially molecular features between different imaging features in LCCA

| Gene | Category | Group | | | | P value | | | | |
|------|----------|-------|--------|--------|-------|------------------|-------------------|------------------|--------------------|-------------------|
| | | Type I | Type II | Type III | Type IV | Type I *vs.* Type II | Type I *vs.* Type III | Type I *vs.* Type IV | Type II *vs.* Type III | Type II *vs.* Type IV |
| *EGFR* | Mutation | 5 | 0 | 0 | 7 | 0.33 | 0.39 | 0.48 | >0.99 | >0.99 |
| | Wild type | 12 | 1 | 1 | 8 | | | | | |
| *FAT1* | Mutation | 1 | 0 | 0 | 2 | >0.99 | >0.99 | 0.59 | >0.99 | >0.99 |
| | Wild type | 16 | 1 | 1 | 13 | | | | | |
| *TP53* | Mutation | 2 | 0 | 0 | 5 | >0.99 | >0.99 | 0.21 | >0.99 | >0.99 |
| | Wild type | 15 | 1 | 1 | 10 | | | | | |
| *PKHD1* | Mutation | 1 | 0 | 0 | 2 | >0.99 | >0.99 | 0.59 | >0.99 | >0.99 |
| | Wild type | 16 | 1 | 1 | 13 | | | | | |
| *LRP1B* | Mutation | 2 | 0 | 0 | 3 | >0.99 | >0.99 | 0.65 | >0.99 | >0.99 |
| | Wild type | 15 | 1 | 1 | 12 | | | | | |
| *NOTCH1* | Mutation | 2 | 0 | 0 | 1 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 |
| | Wild type | 15 | 1 | 1 | 14 | | | | | |
| *KRAS* | Mutation | 2 | 0 | 1 | 2 | >0.99 | 0.17 | >0.99 | >0.99 | >0.99 |
| | Wild type | 15 | 1 | 0 | 13 | | | | | |
| *MED12* | Mutation | 2 | 0 | 0 | 1 | >0.99 | >0.99 | >0.99 | >0.99 | >0.99 |
| | Wild type | 15 | 1 | 1 | 14 | | | | | |
| *PDGFRA* | Mutation | 0 | 0 | 0 | 3 | >0.99 | >0.99 | 0.09 | >0.99 | >0.99 |
| | Wild type | 17 | 1 | 1 | 12 | | | | | |
| *MCL1* | CNV | 7 | 1 | 0 | 7 | 0.44 | >0.99 | >0.99 | >0.99 | >0.99 |
| | Wild type | 10 | 0 | 1 | 8 | | | | | |

**Table S2** Comparison of differentially mutated genes between cystic lung adenocarcinoma and common lung adenocarcinoma

| Gene | OncoSG | | Our Study | | P value |
|------|-----------|----------|-----------|----------|---------|
| | Wild type | Mutation | Wild type | Mutation | |
| MET | 296 | 6 | 29 | 4 | 0.01 |
| GNAS | 297 | 5 | 30 | 3 | 0.04 |
| PMS2 | 300 | 2 | 31 | 2 | 0.050 |
| PTCH1 | 300 | 2 | 31 | 2 | 0.050 |
| MED12 | 295 | 7 | 30 | 3 | 0.07 |
| AMER1 | 299 | 3 | 31 | 2 | 0.08 |
| CDKN2A | 299 | 3 | 31 | 2 | 0.08 |
| NOTCH1 | 294 | 8 | 30 | 3 | 0.08 |
| PDGFRA | 293 | 9 | 30 | 3 | 0.10 |
| EPHA5 | 298 | 4 | 31 | 2 | 0.11 |
| FLT4 | 298 | 4 | 31 | 2 | 0.11 |
| TP53 | 193 | 109 | 26 | 7 | 0.12 |
| NF1 | 292 | 10 | 30 | 3 | 0.13 |
| BRCA1 | 297 | 5 | 31 | 2 | 0.14 |
| KMT2A | 297 | 5 | 31 | 2 | 0.14 |
| RET | 297 | 5 | 31 | 2 | 0.14 |
| ALK | 291 | 11 | 30 | 3 | 0.15 |
| AR | 296 | 6 | 31 | 2 | 0.18 |
| EGFR | 159 | 143 | 13 | 20 | 0.20 |
| RUNX1T1 | 295 | 7 | 31 | 2 | 0.22 |
| ATR | 294 | 8 | 31 | 2 | 0.26 |
| ROS1 | 294 | 8 | 31 | 2 | 0.26 |
| SMARCA4 | 294 | 8 | 31 | 2 | 0.26 |
| ATM | 293 | 9 | 31 | 2 | 0.30 |
| PTEN | 293 | 9 | 31 | 2 | 0.30 |
| SETBP1 | 292 | 10 | 31 | 2 | 0.34 |
| GRM3 | 299 | 3 | 32 | 1 | 0.34 |
| FAT1 | 286 | 16 | 30 | 3 | 0.42 |
| PKHD1 | 283 | 19 | 30 | 3 | 0.47 |
| KRAS | 269 | 33 | 28 | 5 | 0.56 |
| LRP1B | 267 | 35 | 28 | 5 | 0.57 |
| EPHA3 | 290 | 12 | 31 | 2 | 0.64 |
| ERBB2 | 290 | 12 | 31 | 2 | 0.64 |
| ABCB1 | 293 | 9 | 32 | 1 | >0.99 |
| APC | 283 | 19 | 31 | 2 | >0.99 |
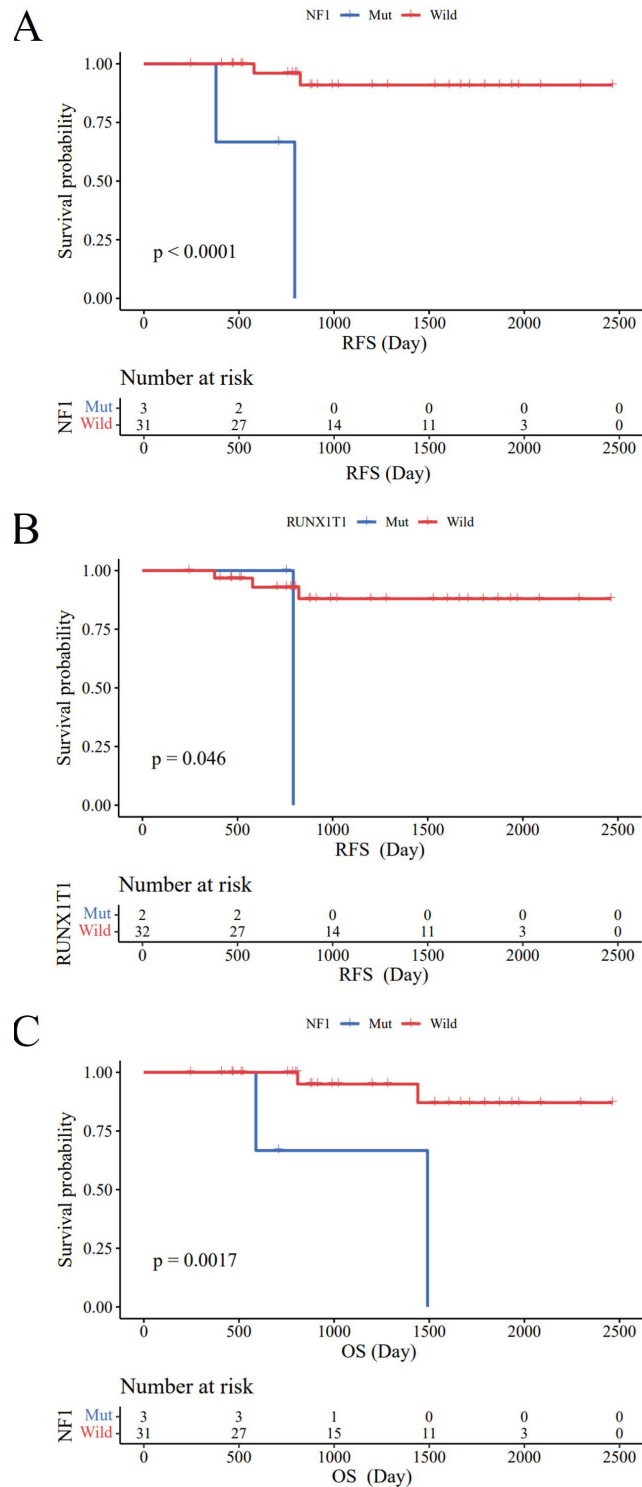
**Figure S2** (A) Relapse-free survival (RFS) of *NF1* mutations and wildtype in the cystic lung adenocarcinoma. (B) RFS of *RUNX1T1* mutations and wildtype in the cystic lung adenocarcinoma. (C) Overall survival (OS) of *NF1* mutations and wildtype in the cystic lung adenocarcinoma. Mut, mutant; wild, wild type.

**Table S3** Univariate Cox regression analysis of mutated genes for relapse -free survival and overall survival (Cox proportional hazards regression model) in cystic lung adenocarcinoma

| Gene | RFS | | OS | |
|---|---|---|---|---|
| | HR (95% CI for HR) | Logrank_Pval | HR (95% CI for HR) | Logrank_Pval |
| NF1 | 28(2.47–317) | <0.001 | 12.2(1.67–88.5) | 0.002 |
| RUNX1T1 | 7.92(0.71–88.4) | 0.046 | 4.48(0.461–43.5) | 0.16 |
| MED12 | 4.83(0.675–34.5) | 0.08 | 4.25(0.595–30.3) | 0.12 |
| EPHA2 | 3.37(0.349–32.5) | 0.27 | 3.02(0.307–29.8) | 0.32 |
| PMS2 | 3.37(0.349–32.5) | 0.27 | 3.02(0.307–29.8) | 0.32 |
| POLE | 3.02(0.313–29.1) | 0.32 | 2.95(0.302–28.8) | 0.33 |
| KMT2A | 3.02(0.313–29.1) | 0.32 | 2.95(0.302–28.8) | 0.33 |
| PGR | 3.02(0.313–29.1) | 0.32 | 4.9(0.441–54.3) | 0.15 |
| KRAS | 4.15e-09(0–Inf) | 0.37 | 3.82e-09(0–Inf) | 0.31 |
| FLT4 | 2.68(0.277–25.9) | 0.38 | 2.73(0.279–26.6) | 0.37 |
| GRIN2A | 2.55(0.262–24.7) | 0.40 | 1.87(0.194–18) | 0.58 |
| MET | 2.55(0.262–24.7) | 0.40 | 1.87(0.194–18) | 0.58 |
| GNAS | 4.45e-09(0–Inf) | 0.44 | 4.35e-09(0–Inf) | 0.41 |
| APC | 4.45e-09(0–Inf) | 0.44 | 3.88e-09(0–Inf) | 0.34 |
| CTCF | 1.22e-08(0–Inf) | 0.45 | 1.27e-08(0–Inf) | 0.50 |
| FANCI | 1.22e-08(0–Inf) | 0.45 | 1.27e-08(0–Inf) | 0.50 |
| KMT2B | 1.22e-08(0–Inf) | 0.45 | 4.35e-09(0–Inf) | 0.41 |
| NOTCH2 | 1.22e-08(0–Inf) | 0.45 | 4.35e-09(0–Inf) | 0.41 |
| PBRM1 | 1.22e-08(0–Inf) | 0.45 | 1.27e-08(0–Inf) | 0.50 |
| ERBB2 | 2.2(0.228–21.3) | 0.48 | 2.43(0.248–23.7) | 0.43 |
| ATM | 1.29e-08(0–Inf) | 0.51 | 1.31e-08(0–Inf) | 0.53 |
| AMER1 | 1.31e-08(0–Inf) | 0.53 | 4.44e-09(0–Inf) | 0.45 |
| PIK3CA | 1.31e-08(0–Inf) | 0.53 | 4.44e-09(0–Inf) | 0.45 |
| BRCA1 | 1.31e-08(0–Inf) | 0.54 | 1.32e-08(0–Inf) | 0.56 |
| AR | 1.32e-08(0–Inf) | 0.55 | 4.44e-09(0–Inf) | 0.45 |
| CREBBP | 1.32e-08(0–Inf) | 0.55 | 4.44e-09(0–Inf) | 0.45 |
| PTEN | 1.33e-08(0–Inf) | 0.56 | 3.74e-08(0–Inf) | 0.72 |
| PDGFRA | 1.91(0.199–18.4) | 0.57 | 2.23(0.229–21.8) | 0.48 |
| ABCB1 | 1.35e-08(0–Inf) | 0.58 | 3.74e-08(0–Inf) | 0.72 |
| RET | 1.37e-08(0–Inf) | 0.62 | 3.86e-08(0–Inf) | 0.77 |
| LRP1B | 1.55(0.161–15) | 0.70 | 1.24(0.128–12) | 0.85 |
| SMARCA4_SV | 3.92e-08(0–Inf) | 0.79 | 1.06e-07(0–Inf) | 0.85 |
| RPTOR | 1.28(0.132–12.5) | 0.83 | 1.04(0.106–10.1) | 0.98 |
| PKHD1 | 1.05(0.109–10.2) | 0.96 | 1.17(0.121–11.4) | 0.89 |
| NOTCH1 | 1.01(0.103–9.87) | >0.99 | 0.758(0.0774–7.42) | 0.81 |
| TP53 | 0.99(0.103–9.55) | >0.99 | 1.23(0.125–12.1) | 0.86 |

RFS, relapse-free survival; OS, overall survival; HR, hazard ratio; CI, confidence interval; Logrank_Pval: Log-rank test P value.