We prefer 2 ports, but usually 2-4 ports are used.

Proton beam does not stop in lung tissue.

Take into account for the difference between CT couch with treatment couch.
Treatment Planning 7 (DVH)

- V20 never exceed 20%
Collimator & Bolus

- Smearing of bolus is necessary to ensure dose to the target

Smearing diameter = 15 mm
Dose-Fractionation

- **Protons**
  - 80 GyE / 20 fr / 4 w (Japanese standard)
  - ➔ 60-66 GyE / 10 fr / 2 w (similar with Loma Linda U MC)

- **Carbons (NIRS)**
  - 72 GyE / 9 fr / 3 w
  - ➔ 52.8 GyE / 4 fr / 1 w for stage IA,
    60 GyE / 4 fr / 1 w for stage IB
  - ➔ Single fraction (dose-escalating study)

Note: this dose-fractionation should be applied for peripheral type cancer
Fig. 1. Response-dose curve for NSCLC patient survival at 30 months constructed using the parameters reported by Martel et al. (16): D-50 = 84.5 Gy and slope \( \gamma = 1.5 \). The LQ parameters assumed for NSCLC tumors are \( \alpha/\beta = 10 \) Gy, \( \alpha = 0.35 \) ln/Gy, \( Tk = 28 \) days, and \( Tp = 3 \) days (See text). The difference between the BEDs calculated with and without proliferation (3rd and 4th lines of x axis legend) illustrates the loss of tumor effect due to repopulation.
### Biological Effective Dose > 100 Gy

<table>
<thead>
<tr>
<th></th>
<th>/ fraction</th>
<th>Total</th>
<th>BED</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Loma Linda</strong></td>
<td>5.1 Gy</td>
<td>51 Gy</td>
<td>77.0 Gy</td>
</tr>
<tr>
<td></td>
<td>6.0 Gy</td>
<td>60 Gy</td>
<td>96.0 Gy</td>
</tr>
<tr>
<td><strong>NCC, Kashiwa</strong></td>
<td>4.0 Gy</td>
<td>80 Gy</td>
<td>112.0 Gy</td>
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<tr>
<td></td>
<td>6.6 Gy</td>
<td>66 Gy</td>
<td>109.6 Gy</td>
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<tr>
<td><strong>SRT (Japan)</strong></td>
<td>12 Gy</td>
<td>48 Gy</td>
<td>105.6 Gy</td>
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<tr>
<td></td>
<td>10 Gy</td>
<td>50 Gy</td>
<td>100.0 Gy</td>
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<tr>
<td><strong>3D-CRT (RTOG)</strong></td>
<td></td>
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<tr>
<td>93-11</td>
<td>2.15 Gy</td>
<td>83.8 Gy</td>
<td>101.8 Gy</td>
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<tr>
<td></td>
<td>2.15 Gy</td>
<td>90.3 Gy</td>
<td>109.7 Gy</td>
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<tr>
<td>0117</td>
<td>2.4 Gy</td>
<td>84 Gy</td>
<td>104.2 Gy</td>
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<tr>
<td></td>
<td>2.65 Gy</td>
<td>79.5 Gy</td>
<td>100.6 Gy</td>
</tr>
</tbody>
</table>

PTCOG46 Educational Workshop. T. Ogino. NCC. Kashiwa
Irradiation

- Passive scattering with respiratory-gating is safe, reliable, and easy way

Bar Ridge Filter

Propeller Range Modulator

Japan

US & Europe
Respiratory-Gated Irradiation

- End exhalation phase is used
- Irradiation duration might be 2-3 times longer
- All ports should be irradiated in each fraction
Proton Therapy for NSCLC

- **Tsukuba U.** (Shioyama Y, IJROBP 2003;56:7-)
  - Stage I-III NSCLC 51 pts
  - 76-93 GyE (Median 76 GyE)/20-27 fr.
  - 5y OAS stage I-II 41%, stage IA 62.5% (Median FU 79 m)

- **Loma Linda U. MC** (Bush DA, Chest 2004;126:1198-)
  - Stage I NSCLC 68 pts
  - 51, 60 GyE/10 fr./2 w
  - 3y LC 74%, 3y OAS 72% (Median FU 30 m)

- **NCC, Kashiwa** (Nihei K, IJROBP 2006;65:107-)
  - Stage I NSCLC 37 pts (T1/T2 : 17/20)
  - 70-94 GyE (Median 80 GyE)/20 fr./4-5 w
  - 2y LC 80%, 2y OAS 84% (Median FU 24 m)
Carbon-ion Therapy for NSCLC

- **NIRS, Carbon ion** (Miyamoto T, IJROBP 2007;67:750-)
  - Stage I NSCLC  51 pts  (T1/T2 : 30/21)
  - 72 GyE/9 fr./3 w
  - 5y LC 95%,  5y OAS 50%  (Median FU 59 m)
<table>
<thead>
<tr>
<th>Author/Year</th>
<th>Treatment</th>
<th>Detail of Tx.</th>
<th>N</th>
<th>T1/T2</th>
<th>3y OS</th>
<th>5y OS</th>
<th>3y LC</th>
<th>5y LC</th>
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</thead>
<tbody>
<tr>
<td>Mountain/1997</td>
<td>Surgery</td>
<td>Surgery</td>
<td>1876</td>
<td>T1(687) T2(1189)</td>
<td>T1:71% T2:46%</td>
<td>T1:61% T2:38%</td>
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<tr>
<td>Rens/2000</td>
<td>Surgery</td>
<td>Surgery</td>
<td>1201</td>
<td>T1(404) T2(797)</td>
<td>T1:76% T2:59%</td>
<td>T1:63% T2:46%</td>
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<tr>
<td>Krol/1996</td>
<td>X</td>
<td>60Gy/20fr-65Gy/26fr</td>
<td>108</td>
<td>T1(51) T2(57)</td>
<td>31%</td>
<td>15%</td>
<td>71%</td>
<td>66%</td>
</tr>
<tr>
<td>Morita/1997</td>
<td>X</td>
<td>64.7Gy(55-74) 2-3Gy/fr</td>
<td>149</td>
<td>T1(60) T2(89)</td>
<td>34%</td>
<td>22%</td>
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<tr>
<td>Uematsu/2001</td>
<td>X-SRT</td>
<td>50-60Gy/5-10fr/1-2w</td>
<td>50</td>
<td>T1(24) T2(26)</td>
<td>66%</td>
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<td>94%</td>
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<tr>
<td>Bradley/2003</td>
<td>X-SRT</td>
<td>70Gy(60-84)/1.8-2Gy/fr</td>
<td>56</td>
<td>T1(31) T2(25)</td>
<td>34%</td>
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<td>63%</td>
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<tr>
<td>Shioyama/2003</td>
<td>Proton</td>
<td>76Gy(49-93) 3Gy(2-6)/fr</td>
<td>51</td>
<td>Stage(28)</td>
<td></td>
<td></td>
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<tr>
<td>Bush/2004</td>
<td>Proton</td>
<td>51Gy/10fr 60 Gy/10fr</td>
<td>68</td>
<td>T1(29) T2(39)</td>
<td>72%</td>
<td></td>
<td>74%</td>
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<tr>
<td>Ogino/2007</td>
<td>Proton</td>
<td>70-94Gy/20fr</td>
<td>61</td>
<td>T1(33) T2(28)</td>
<td>87%</td>
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<td>90%</td>
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<td>Miyamoto/2003</td>
<td>Carbon</td>
<td>59.4-95.4Gy/18fr 68.4-79.2Gy/9fr</td>
<td>81</td>
<td>T1(41) T2(40)</td>
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</tbody>
</table>
Acute Adverse Events

- Grade 2 or greater toxicities (mostly Grade 2)
  - Pneumonitis: < 5%
  - Dermatitis: < 5%
  - Esophagitis: = 0%
Late Adverse Events

- Grade 2 or greater toxicities
  - Pneumonitis, pleural effusion: 0-8%
  - Chest pain: <5%
  - Rib fracture: 5% (NCC experience)
    - Aged female patients
    - Tumor close to the chest wall
Protocols for Locally Advanced NSCLC

- NCC, Kashiwa: Phase I/II
  - Stage IIIA/IIIB
  - Concurrent Chemo + Proton
    - Chemo: CDDP (80mg/m\(^2\), d1)+VNR (20mg/m\(^2\), d1,8), q4w
    - Proton: 66-70-74 GyE, 2 GyE/fr

- MDACC: Phase II
  - Stage IIIA/IIIB
  - Concurrent Chemo + Proton
    - Chemo:TAX(50mg/m\(^2\))+CBDCA(AUC 2mg/min/ml), weekly
    - Proton: 74 GyE, 2 GyE/fr
Final Outlook

- PBT is a promising treatment modality for stage I NSCLC
- The loco-regional progression-free and overall survival rates may be comparable to those of surgery in stage I patients
- To evaluate the efficacy of PBT, a prospective study is mandatory