N. N. Blokhin Cancer Research Centre of Russian Academy of Medical Science, Moscow, Russia
Director – Acad. RAN, RAMS, Prof. M. I. Davidov
Results of Proton Therapy in Treatment of Oncological Diseases

Monzul G.D., Gladilina I.A.

Moscow, 2007 y.
Proton therapy in Russia
N=5814

1. Joint Institute of Nuclear Research (JINR), Dubna (since 1967)
2. Institute of Theoretical and Experimental Physics (ITEP), Moscow (since 1969)
3. Institute of Nuclear Physics (INP), St. Petersburg (since 1975)
Proton therapy in Russia

N=5814
Proton Therapy Center
Institute of Theoretical and Experimental Physics (ITEP)
Moscow

N = 3980

1. N. N. Blokhin Cancer Research Centre of Russian Academy of Medical Science, Moscow
2. Neurosurgery Research Centre, Moscow
3. Ophthalmology Research Centre, Moscow
4. Endocrinology Research Centre, Moscow
Proton therapy
Cancer Research Centre of Russian Academy of Medical Science, Moscow

<table>
<thead>
<tr>
<th>Site</th>
<th>Dubna 1967-1995</th>
<th>ITEP, Moscow 1969-2005</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung</td>
<td>23</td>
<td>15</td>
<td>38</td>
</tr>
<tr>
<td>Esophagus</td>
<td>41</td>
<td></td>
<td>41</td>
</tr>
<tr>
<td>Larynx</td>
<td>14</td>
<td></td>
<td>14</td>
</tr>
<tr>
<td>Uterine cervix</td>
<td>31</td>
<td>160</td>
<td>191</td>
</tr>
<tr>
<td>Vulva</td>
<td>-</td>
<td>40</td>
<td>40</td>
</tr>
<tr>
<td>Prostate</td>
<td>-</td>
<td>88</td>
<td>88</td>
</tr>
<tr>
<td>Prostate (with distant metastases)</td>
<td>-</td>
<td>142</td>
<td>142</td>
</tr>
<tr>
<td>Breast</td>
<td>-</td>
<td>208</td>
<td>208</td>
</tr>
<tr>
<td>Breast (with distant metastases)</td>
<td>-</td>
<td>1059</td>
<td>1059</td>
</tr>
<tr>
<td>Skin</td>
<td>-</td>
<td>56</td>
<td>56</td>
</tr>
<tr>
<td>Melanoma</td>
<td>4</td>
<td>37</td>
<td>41</td>
</tr>
<tr>
<td>Melanoma (with distant metastases)</td>
<td>-</td>
<td>51</td>
<td>51</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2</td>
<td>18</td>
<td>20</td>
</tr>
<tr>
<td>Patients with distant metastases in skin, nodules, lung, liver and other</td>
<td>8</td>
<td>332</td>
<td>340</td>
</tr>
<tr>
<td>Others</td>
<td>-</td>
<td>45</td>
<td>45</td>
</tr>
<tr>
<td>Total</td>
<td>123</td>
<td>2226</td>
<td>2374</td>
</tr>
</tbody>
</table>
Structure of tumor site
N = 2226
Cancer Research Centre of Russian Academy of Medical Science, Moscow
Treatment rooms
Institute of Theoretical and Experimental Physics (ITEP), Moscow

- 3 treatment rooms, designed for both fixed horizontal beam: 2 treatment tables and 1 treatment chair.
- Laser pointers.
- X-ray DR system
Melanoma of the skin

N = 41

Protons
130 - 180 MV
Depths 80-180 mm
10-12 Gy/fr
5-7 fraction

Total dose to tumor – 110-120 IsoGy
Total dose to surround tissues - 60-80 IsoGy
Total dose to lymph node – 100-110 IsoGy
Melanoma of the skin
N = 41
5-years complete response rate

- T1-3N0M0: 70%
- T1-3N1-3M0: 50%
Primary nodal breast cancer
N = 183

T1-2N0M0 (N=21) 11.0%
T1-3N0-3M0 (N=162) 89.0%
Breast cancer
stage $T_{1-2}N_0M_0$ (N = 21)

ALONE LOCAL PROTON THERAPY

Local irradiation of the tumor

Protons
130 MV (60 mm)
160 MV (80 mm)
1-3 fields
5-7 Gy/fr
5-4 fraction
Total dose – 80-90 isoGy
# Breast cancer

**stage T\textsubscript{1-3}N\textsubscript{0-3}M\textsubscript{0} (N = 162)**

**Photon + Proton therapy**

**Photon**
- Mammary gland: 2 photon fields
- Regional lymph nodes: 1 electron field
  - 4 Gy /fr
  - 2 fr /week
  - 6-7 fractions

**Protons 130 MV**
- Local irradiation of the tumor
  - Local irradiation of the lymph nodes
    - 5-7 Gy /fr
    - 3 fr /week
    - 4-5 fractions

**Total tumor doses (Ph + Pr) - 110 - 120 IsoGy**

**PROTON "HYPOPHYSECTOMY"**
- 200 MV PROTONS, 25-50 Fields,
  - 3-4 Gy per field, 1-2 fractions,
  - 100-130 Gy in the convergent center
Breast cancer
stage $T_{1-3}N_{0-3}M_0$ ($N = 162$)

The role of the first component – Improvement in the tumor control rate.

The role of the second component – Normalization of hormonal activity
Breast cancer
stage $T_{1-3}N_{0-3}M_0$ (N = 162)
Clinical results

- Complete response rates
  - Proton therapy - 98.7%
  - Conventional radiotherapy - 81.8% ($p < 0.05$).
Breast cancer
stage $T_{1-3}N_{0-3}M_0$ (N = 162)
Overall survival rates
Breast cancer
stage $T_{1-3}N_{0-3}M_0$
Five-year overall survival

- Proton therapy (83.3%)
- Convencional RT (45.5%)
Breast cancer
stage $T_{1-2}N_0M_0$
Five-year overall survival

Overall survival %

Proton RT
Conv. RT
Cosmetic outcome
(Joint Center for Radiation Therapy, Boston)

- after proton therapy
  - an excellent result - 98.4%
  - a good result – 1.6%
  - a fair result - 0%
  - a poor result - 0%

  vs.

- after conventional RT
  - an excellent result – 10.1%
  - a good result – 64.2%
  - a fair result - 25.7%
  - a poor result - 0%

Follow up – 24 years
<table>
<thead>
<tr>
<th>Late complications</th>
<th>Follow up – 15 years</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RTOG grade ≥ 2 late complications</strong></td>
<td></td>
</tr>
<tr>
<td>CR - 55%</td>
<td></td>
</tr>
<tr>
<td>PT - 2.7%</td>
<td></td>
</tr>
<tr>
<td><strong>RTOG grade I late complications</strong></td>
<td></td>
</tr>
<tr>
<td>CR - 42%</td>
<td></td>
</tr>
<tr>
<td>PT - 29%</td>
<td></td>
</tr>
<tr>
<td><strong>RTOG grade 1-2 late complications (pneumonitis)</strong></td>
<td></td>
</tr>
<tr>
<td>CR - 53.3%</td>
<td></td>
</tr>
<tr>
<td>PT - 1.8%</td>
<td></td>
</tr>
</tbody>
</table>
Breast cancer
stage $T_{1-2}N_0M_0$ (N = 25)

protons after breast conserving surgery
130 -180 MV
depths 80-180 mm
5-7 Gy/fr
4-6 fraction

Total dose to tumor bed – 60-80 IsoGy
Recurrence rates - 5,6%

The 5- year overall survival - 92%
Cosmetic results at 5 years were good and excellent in 96%
Breast cancer

Conclusion

High local control rates
Prolongation of survival
Improved quality of life
Minimized late complication rates
Contributing to reduction of patients psychological distress
Produced excellent cosmetic results
Work and family rehabilitations
Prostate cancer
Staging of patients (N=261)
Prostate cancer
Staging of patients (N=261)
Prostate cancer
Characteristics of patients
(N=261)
Prostate cancer stage $T_{2-4}N_{0-3}M_0$ (N=261)

RT (pelvis)
50Gy
in 25 fractions

Proton beam (N=88)
(local)
27Gy
in 9 fractions

Conformal RT (N=105)
(local)
21Gy
in 7 fractions

Convention RT (N=68)
(local)
16Gy
in 8 fractions

G.V. Makarova, G.D. Monzul, I.A. Gladilina, T.G. Ratner,
Prostate cancer
stage $T_{2-4}N_{0-3}M_0$ (N = 88)

Original fixation - peritoneal wedge
Photon irradiation pelvis TD 50 Gy
Proton local irradiation:
1 peritoneal field,
wide beam,
energy 180 MV,
3Gy/fr,
3 fr/week,
9 fr,
TD 27 Gy.
Total tumor doses 82 IsoGy
(proposed by G.V. Makarova et al)
Prostate cancer
stage $T_{3-4}N_{0-3}M_0$ (N=261)
Complete response rate

- Conv. (N=68): 91%
- Photon conf. (N=105): 82%
- Photon+proton (N=88): 54%
Prostate cancer
stage $T_{3-4}N_{0-3}M_0$ (N=261)
Local Recurrence

- Photon+proton (N=88)
- Photon conf. (N=105)
- Conv. (N=68)
Prostate cancer
stage $T_{2-4}N_{0-3}M_0$ (N=261)
Overall survival rates
Prostate cancer
stage $T_2N_{0-3}M_0$ ($N=72$)
Overall survival rates
Prostate cancer
stage $T_{3-4}N_{0-3}M_0$ (N=189)
Overall survival rates
Prostate cancer
stage T_{2-4}N_0M_0 (N = 225)
Overall survival rates
Prostate cancer
Gleason score > 6 (N = 121)
Overall survival rates
Prostate cancer
stage T_{2-4}N_{0-3}M_0 (N=261)
Late complications (RTOG grade = 2)

- Conv. (N=68)
- Photon conf. (N=105)
- Photon+proton (N=88)

- 8% complications
- 8% complications
- 28% complications
Prostate cancer

Conclusion

Increased local control rates

Increased overall survival rates

Low complication rates
Generalize Cancer

Breast cancer N=1056
Prostate cancer N=142

Combine method

Zonal irradiation bones
4 Gy x 6

Proton irradiation hypophysis
25-40 narrow fields
4-5 Gy per field
2-3 Fr.
total dose 300 Gy
Breast cancer
1056 patients with bone metastases
Overall survival rates
Prostate cancer
142 patients with bone metastases
Overall survival rates

<table>
<thead>
<tr>
<th>Years</th>
<th>Overall Survival Rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>0-5</td>
<td>39.4%</td>
</tr>
<tr>
<td>5-10</td>
<td>21.1%</td>
</tr>
<tr>
<td>10-15</td>
<td>18.3%</td>
</tr>
<tr>
<td>15-20</td>
<td>12%</td>
</tr>
<tr>
<td>20-25</td>
<td>9%</td>
</tr>
<tr>
<td>25-30</td>
<td>5%</td>
</tr>
<tr>
<td>30-35</td>
<td>4%</td>
</tr>
<tr>
<td>35-40</td>
<td>2%</td>
</tr>
</tbody>
</table>
Generalize cancer
Clinical results

All patients tolerated the treatment quite well

Pain was relieved in 93.9% of patients after 2 weeks of completing therapy till their last follow up

Long-term stabilization of diseases in 79.3% of patients

This method has not only improved the quality life, but also increased patient's span of life