Neutron Therapy Programs at Medical Radiological Research Center RAMS, Obninsk, Russia

A new technology for the treatment of advanced, radioresistant forms of malignant tumors was developed in the Medical Radiological Research Center (MRRC), Obninsk, Russia. It is based on the use of fast neutrons extracted from a nuclear reactor core. From 1985 to 2002, more than 500 patients with tumours localized at larynx, nasopharynx, breast and other sites underwent treatment at the therapeutic channel of the BR-10 reactor at the Institute for Physics and Power Engineering (IPPE).
Technical facilities for radiological studies with neutrons and neutron capture therapy in Obninsk

| Institute of Physics and Power Engineering | Reactor BR-10  
E<sub>av</sub> = 0.85 MeV | Clinical trials with neutron teletherapy at the fast neutron beam (1985-2002) |
|-------------------------------------------|---------------------------------|-----------------------------------------------------------------|
|                                           | Pulsed nuclear reactor BARS-6  
E<sub>av</sub> = 1.44 MeV | Radiobiological and dosimetry studies with pulsed neutron, γ- and γ-neutron radiation with ultra-high dose rates |
|                                           | Accelerator KG-2,5  
E = 0.4 - 16 MeV | Modernization for radiobiological and clinical purposes |
| Institute of Chemical Physics             | Reactor WWRc  
E<sub>av</sub> = 1.1 MeV | Designing of a new therapeutic unit; radiobiological and dosimetry studies |
| Medical Radiological Research Center, VNIIA | Portable neutron generator  
E = 14.5 MeV | Radiobiological and dosimetry studies; assessment of prospects for clinical application |
SCHEME OF MEDICAL FACILITY AT THE BR-10 REACTOR

SSD: 10 m

Doserate 0.18 Gy/min,

\( D_\gamma / D_{tot} = 0.05 \) at surface

Field size: 4x4 ... 10x10 cm²
Results for head and neck tumours (1)

I. Gulidov, A. Sysoev, Yu. Mardynsky, S. Ulyanenko,
S. Kapchigashev, V. Kononov, B. Fursov

133 patients with squamous cell carcinoma
(90% locally advanced or recurrent tumours)

Treatment scheme of laryngeal carcinoma

1. neutron dose 2.0 - 5.6 Gy
2. photon dose 32 - 40 Gy (total, n+γ)
3. Evaluation of local reactions and tumour regression:

   Complete or partial tumour response ➞ Photon dose up to 52-60 Gy

   No tumour response ➞ Radical surgery

Primary or recurrent tumours of oral cavity or oropharynx
1st stage: neutron dose 3-4 Gy (3-4 fractions in 7 days)
2nd stage: photon dose 56-60 Gy (n+γ)
Evaluation 1 month after end of radiation therapy
5 year local control

- **Breast carcinoma (complex treatment)**: 93.7%, P < 0.005
- **Larynx (radiation therapy)**: 67.8%, P < 0.05
- **Larynx (combined therapy)**: 62.7%, P < 0.05
- **Larynx (complex treatment)**: 72.7%, P < 0.05
- **Oral cavity and oropharynx (radiation therapy)**: 51.3%, P < 0.05
- **Sarcoma of bone (complex treatment)**: 73%, P > 0.05

**Legend:**
- Red: Gamma-neutron therapy
- Blue: Gamma-therapy
Results for head and neck tumours (2)

(Gulidov et al.)

Serious late local radiation complications (Grade III): 6-11 %
(perichondritis, osteoradionecrosis, ulcer of mucosa)

Tumour control
No response after 1st stage: 27 % (laryngeal CA)

Five-year actuarial local control
1. Primary laryngeal CA
   - After radical course of n-γ-therapy: 63 %
   - 1st stage n-γ-therapy, then surgery: 73 %
2. Primary CA of oral cavity and oral pharynx: 51 %

Recurrences of CA of oral cavity and oral pharynx: 57 %
One-year actuarial overall disease-specific survival: 82 %)
## Occurrence of Local Reactions in Patients with Laryngeal Cancer

### Character of Local Reaction

<table>
<thead>
<tr>
<th>Character of Local Reaction</th>
<th>Occurrence of Local Reaction</th>
<th>Level of Probability</th>
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<tbody>
<tr>
<td>- no reaction</td>
<td>Gamma-neutron therapy (%)</td>
<td>Gamma therapy (%)</td>
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<tr>
<td>- exsudative mucositis</td>
<td>8,5</td>
<td>15,2</td>
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<tr>
<td>- spotted mucositis</td>
<td>57,6</td>
<td>68,3</td>
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<td>- panniculus mucositis</td>
<td>22,0</td>
<td>11,0</td>
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<td>- skin erythema and dry desquamation</td>
<td>11,9</td>
<td>5,5</td>
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<tr>
<td>- moist desquamation</td>
<td>52,5</td>
<td>20,0</td>
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<tr>
<td>- late oedema of laryngeal mucosa</td>
<td>11,9</td>
<td>1,4</td>
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<tr>
<td>- perichondritis</td>
<td>41,9</td>
<td>16,4</td>
</tr>
<tr>
<td></td>
<td>7,0</td>
<td>2,7</td>
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Salivary gland tumor

Before treatment

30 days after treatment
The reactor neutrons were demonstrated to have a therapeutic effectiveness 15-25% higher than that of conventional treatment methods.

Reactor neutron technology does not replace or exclude other approaches to cancer treatment such as surgery, chemotherapy, gamma, proton and electron irradiation, but it supplements them with a new and powerful weapon against tumours that can not be effectively treated by conventional methods.
Future Aspects

Now MRRC scientists and specialists are developing a more complicated technology - neutron capture therapy (boost). Its use provides localized radiation of only the malignant cells. The medical room creation at the WWRc reactor, the KG-2.5 accelerator application for BNCT, the development of new medical compact neutron generators are main directions for the project of neutron and neutron capture therapy.
Accelerator KG-2,5 at IPPE

Phantom study for BNCT and NT
Design of the medical block for gamma-neutron and BNC Therapy

1. Treatment room
2. Technological unit
3. Emergency shutter
4. Filter
5. Collimator
6, 7. Rolling doors
8. Centring laser
9. TV camera
10. Neutron beam catcher
Start of Phase I of clinical trials at pulse neutron generator ING-031 of VNIIA (MRRC RAMS, Obninsk)
Neutron therapeutic source “MARS”

- Intraclinically localized
- Reactor size: 3.5 x 2 x 3.5 m
- Resource - 20 years
- Two medical channels (NT and BNCT)
- Start-stop work regime
- Thermal power - 10 kW
- Fuel - UO$_2$, enrichment – 17%, load – 34 kg
- Size of active zone - 12×48.1×45 cm