The fast neutron therapy programme for patients in South Africa should come to an end

To the Editor: Neutron therapy for tumours was introduced globally and in South Africa to evaluate the possible improvement of results obtained with conventional photon radiotherapy.[1,2] This was based on the radiobiological finding that neutron irradiation is more effective in killing all cells, including poorly oxygenated tumour cells which are relatively resistant to conventional photon radiation.

Neutron therapy, however, also causes an increase in late normal tissue toxicity, in part because cells are not able to repair any sub-lethal radiation damage sustained during irradiation. These late effects are a decrease in functional parenchymal cells, increased fibrosis and a reduced vascular supply and can occur in all irradiated tissue, for example skin, soft tissues, bowel and brain. This late toxicity is progressive with time as the damaged cells produce cytokines which promote fibrosis.

Clinical studies of neutron therapy in the 1950s showed an increase in severe late toxicity. Clinical studies during the 1980s and 1990s, based on a better understanding of the radiobiology and using more refined techniques, unfortunately again showed an increase in late normal tissue toxicity.

There was an overwhelming consensus in the radiation oncology community that it was time to focus on other methods to improve results.[1,2] Neutron therapy sites were shut down in England, Europe, Canada and the USA, except for two USA-based sites. However, neutron therapy continues to be offered in South Africa, despite the referral of decreasing numbers of patients.

Those who favour this continuation of the neutron therapy programme in South Africa argue that it is useful in some specific sites, specifically salivary gland tumours and sarcomas. However, this is not supported by the evidence from phase III studies. Among patients with inoperable salivary gland tumours, a phase III randomised trial of only 32 patients compared neutron therapy with photon therapy.[3] The study showed an increase in local control, but no increase in survival and also increased complications with neutron therapy. For patients with sarcomas, a phase III trial of postoperative radiation was halted after 14 patients were accrued because of severe late normal tissue toxicity in patients treated with neutron therapy.[4]

Neutron therapy advocates also argue for its use in patients with advanced cancer on the premise that the patients will die before they have the opportunity to develop complications. This is an extremely expensive form of palliative therapy that could also be done through other means and is not the forward-looking perspective associated with clinical research.

Considerable progress towards improving the local control of tumours been made with other approaches. Photon radiation may be given concurrently with systemic chemotherapy or biological therapies and this is now established practice in many diseases, e.g. cancer of the cervix, lung and rectum. This does not cause an increase in late toxicity, although it may be associated with an increase in acute toxicity, which can be actively managed and also minimised through careful planning of radiation administration. Proton particle therapy is also effective and safe and may be particularly useful in paediatric patients.

The strong negative view of the radiation oncology research community towards neutron therapy is reflected in the almost complete absence of any publications in peer-reviewed journals on neutron therapy since 2000.

The proven toxicity of neutron therapy and the availability of other treatment approaches, indicates that the continuation of neutron therapy in South Africa is not justified in terms of patient care or clinical research, as well as our need to be fiscally responsible.

Raymond P Abratt
Radiation Oncology
Groote Schuur Hospital and University of Cape Town
Observatory
Cape Town
Raymond.Abratt@uct.ac.za

1. Jones B, Dale RG, Carabe-Fernandez A. Charged particle therapy for cancer: the inheritance of the Cavendish scientists? Journal of Applied Radiation and Isotopes 2009;67:371-377.
2. Goitein M. Trials and tribulations in charged particle radiotherapy. Radiother Oncol 2010;95:23-31.
3. Laramore GE, Krall JM, Griffin TW, et al. Neutron versus photon irradiation for unresectable salivary gland tumors: final report of an RTOG-MRC randomized clinical trial. Int J Radiat Oncol Biol Phys1993;27(2):235-240.
4. Glaholm J, Harmer C. Soft-tissue sarcoma: neutrons versus photons for post-operative irradiation. Br J Radiol 1988;729:829-834.