Neutron radiotherapy in South Africa

Neutron radiotherapy: a different perspective

To the Editor: As the director of one of the longest running neutron radiotherapy programmes in the world (27+ years and 2 900 patients treated) and a member of an international team that reviewed the iThemba laboratories particle radiotherapy programme on behalf of the National Research Foundation in 2010, my view of neutron radiotherapy and the iThemba-Faure facility differs from that of Abratt.[1,2]

Fast neutron radiotherapy has not proved to be the panacea in cancer therapy as was hoped in the 1970s and 1980s. Most early clinical trials showed no advantage to fast neutron radiotherapy over standard photon radiotherapy for common tumours; therefore, interest waned. Long-term side-effects of the early studies were often more severe with fast neutrons, but this was largely attributable to primitive treatment facilities (e.g. laboratory-based, fixed horizontal beams, primitive collimation and blocking). The University of Washington and iThemba facilities have more sophisticated isocentric rotational gantries with movable floors and multi-leaf collimators which allow treatment configurations comparable with conventional photon radiotherapy. This allows for more normal tissue sparing, resulting in a lower incidence of side-effects than quoted in the older literature.

Salivary gland malignancies are one example where improved outcomes have consistently been reported.[3] As Abratt noted, the initial, multi-centre randomised trial accrued only 32 patients before it was closed for ethical reasons. At closure, there was a statistically significant improvement in local and regional control in the neutron-treated group and a trend towards improved survival. With longer follow-up time, the survival curves came together (everyone eventually dies of some cause). However, the cause of death differed with the largest factor being local/regional disease in the photon-treated group and distant metastases in the neutron-treated group. The improved local/regional control in the neutron-treated group allowed time for the manifestation of distant metastases. Since 2000, our research group has documented its research outcomes in 25 articles and invited book chapters. Recently, we showed that 80% of salivary gland tumours with inoperable, skull-base disease can be controlled with a multi-leaf collimator and a Gamma Knife boost.[4] We also use our neutron beam to treat inoperable sarcomas, anaplastic thyroid cancers, mucosal melanomas, and other 'radioresistant' tumours in selected clinical situations.

There is a continuing role for high linear energy transfer (LET) radiotherapy in treating human malignancies. The University of Washington, through the Seattle Cancer Care Alliance and ProCure, is building a proton radiotherapy centre that will be operational in 2013. However, we intend to keep our neutron radiotherapy facility operational as we feel that there are many instances where this will better serve patients. The iThemba-Faure neutron facility needs to be maintained as a resource for Africa, with improved patient recruitment for increased utilisation and sufficient resource allocation for optimal programme functioning.

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Neutron radiotherapy should continue

To the Editor: Abratt's letter[1] needs a response. We are currently – or have been directly – involved in treating patients with fast neutrons for decades; some with more than 20 years' experience in proton therapy, and others working at major hospitals with modern, high-end facilities for radiotherapy with photons and electrons.

Prof Abratt's opinion was held in the late 1980s when severe late effects of fast neutron therapy (FNT) were recognised, resulting in the early enthusiasm for this modality abating. FNT was introduced into clinical practice after careful radiobiological work, particularly by LH Gray. FNT, the first high linear energy transfer (LET) radiation used in radiotherapy, has not fulfilled the early optimistic laboratory-based expectations. Initial treatment beams had inferior physical characteristics. However, clinical FNT now has facilities with high-energy beams, individually shaped fields, isocentric beam delivery and full 3D treatment-planning systems and image guidance, and it can be applied safely at dedicated centres. However, well-trained personnel are needed who understand the particles' biological effects and complex physical behaviour.

Proven indications for FNT are limited and will benefit few patients. However, for some indications, neutron therapy remains superior to other modalities, despite advances in oncology. The early closure of the one prospective clinical trial,[2] due to the unexpected demonstration of superior results of FNT over conventional low-LET radiotherapy for salivary gland tumours, precluded more patients being recruited. Had the trial continued, it may have led to a better understanding of the effects of neutrons on survival. Nevertheless, today, FNT is the standard and established evidence-based treatment for adenoid cystic carcinoma of the salivary glands, and should be maintained for patients who will benefit from high LET FNT. This knowledge is advantageous for such a rare disease; in most other similar situations, treatment is based on opinion rather than facts from randomised trials. Other FNT indications should be regarded as research or prescribed as an individual treatment decision.

Research is another important role for neutron therapy facilities, e.g. basic physics (interactions of neutrons with biological materials), dosimetry, technological developments and radiobiology, clinical trials and treatment application.

Few highly industrialised countries have the financial and technical capacity to explore carbon ion therapy, which combines a high LET effect with an excellent dose-distribution profile. Their clinical results will take time to guide the radiotherapy community in its use and prove the superiority of delivering expensive high LET radiation.[3,4] FNT history also shows that new developments which excite great enthusiasm may not always be justified; they need careful evaluation over time before becoming irrefutably beneficial for patients. The medical community must accept this less exciting period as essential. It is easier to demonise neutrons and conclude that they should not be used than to spend a long time learning how to use them safely.