

Prof Abratt rightly notes the effective and safe use of proton (low LET) therapy but that is not a relevant argument against FNT. Different particles are needed for optimal treatment of different tumours.

iThemba LABS offers high LET radiation to South Africa and its neighbours at a fraction of the cost of carbon ion facilities. It has the infrastructure and knowledge to deliver this therapy safely, and its neutron therapy facility is regularly used for patients from Europe. Prof Abratt calls for fiscal responsibility – it would be fiscally irresponsible not to use South Africa's high LET facility and to send patients overseas for such therapy.

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Neutron radiotherapy: Abratt reply

To the Editor: The clinical fast neutron therapy programme in South Africa (SA) should be discontinued because:

- (i) Many experimental and clinical studies show an increase in serious late normal tissue complications with neutron therapy,^{1,2} which can be reduced in part by using the technology described in the letters by Laramore³ and Sauerwein *et al.*⁴ Nevertheless, its ability to deliver irradiation to tumours and spare normal tissue is inferior to that of other contemporary radiation modalities. More importantly, these complications arise from the interaction of neutrons with normal tissue, and are progressive with time. A patient's perspective of the debilitating morbidity after modern neutron therapy for adenoid cystic carcinoma of the parotid has been described.⁵
- (ii) Continuation of the neutron therapy programme cannot be supported based on the results of Phase III studies. The authors of the aforementioned letters refer repeatedly to the 1993 study of 32 patients with salivary gland tumours,⁶ but its data do not support the use of neutron therapy. In the study, neutron therapy was administered to 13 patients, resulting in severe toxicity in 9 patients and life-threatening toxicity in 2 patients. This toxicity was much higher than in the photon therapy arm. The trial was discontinued due to decreased referrals.
- (iii) Due to the disappointing outcome of patients treated with fast neutron therapy, all such facilities – except for 2 in the USA – have been discontinued in England, Europe, Canada and the USA.
- (iv) There are few peer-reviewed publications in the PubMed database on clinical studies of fast neutron therapy over the last 10 years.

Although the subject is the neutron therapy programme in SA, none of the 13 co-authors of the letter by Sauerwein *et al.* practice as a radiation oncologist in SA. They present no additional data to justify the continuation of this clinical fast neutron therapy programme. The radiobiological research programme is a separate matter.

Prof Laramore argues for further patient recruitment, continued resource allocation and for the neutron therapy programme to serve as a resource for Africa. The call for increased recruitment is unrealistic as the strong trend is of decreasing referrals to the programme. The average radiation oncology department in SA sees 150 - 300 new patients per month, whereas patient accrual to the neutron therapy programme is reportedly 1 - 2 patients per month in the last year.

Advocating the maintenance of resources for the programme is counter to our need for fiscal responsibility within our resource-constrained environment. Moreover, the failure of neutron therapy to meet its goals is not due to a lack of resources, but rather the biological nature of the therapy.

The neutron therapy programme, as a resource for Africa, has no basis; its shortcomings are as relevant to patients from Africa as they are elsewhere and are compounded by the distance of the site for patients. African studies give no weight to neutron therapy in cancer control programmes, but rather value conventional cancer prevention strategies and therapies.⁷

There have been exciting new developments in the technologies of other radiation modalities including proton particle therapy, and in the concurrent use of radiation with biological therapy and chemotherapy. The latter requires high precision radiation administration by contemporary radiation techniques with other modalities. Phase III studies with large numbers of patients document the safety and efficacy of these approaches for most of the common solid tumours, e.g. cancer of the cervix, lung, rectum, oesophagus,

1. Abratt RP. The fast neutron therapy programme for patients in South Africa should come to an end. *S Afr Med J* 2012;102(2):58.
2. 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 Phys* 1993;27(2):235-240.
3. Gueulette J, Slabbert JP, Bischoff P, Denis JM, Wambersie A, Jones D. Fast neutrons: Inexpensive and reliable tool to investigate high LET particle radiobiology. *Radiation Measurements* 2010; 45: 1414-1416. [http://dx.doi.org/10.1016/j.radmeas.2010.05.019]
4. Wambersie A, Jones DTL, Gueulette J, Gahbauer R, DeLuca PM. What can we learn from the neutron clinical experience for improving ion-beam techniques and high-LET patient selection? *Radiation Measurements* 2010; 45: 1374-1380. [http://dx.doi.org/10.1016/j.radmeas.2010.04.013]

brain and oral cavity. This has led to their widespread use in evidence-based patient management. Radiation oncologists in SA, as elsewhere, will seek to participate in clinical research based on these and other novel approaches.

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1. Jones B, Dale RG and Carabe-Fernandez A. Charged particle therapy for cancer: The inheritance of the Cavendish scientists? *Appl Radiat Isot* 2009;67: 371-377.
2. Goitein M. Trials and tribulations in charged particle radiotherapy. *Radiother Oncol* 2010;95:23-31.
3. Laramore GE. Neutron radiotherapy in South Africa: A different perspective. *S Afr Med J* 2012;102(5):269.
4. Sauerwein WAG, Engenhart-Cabillic R, Forman JD, et al. *S Afr Med J* 2012;102(5):269-270.
5. Ebert R. *Life Itself: A Memoir*. New York: Grand Central Publishing (Hachette Book Group), 2011.
6. 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 Phys* 1993;27(2):235-240.
7. Sitas F, Parkin DM, Chirenje M, Stein L, Abratt RP, Wabinga H. Cancer in indigenous Africans. Part II. Epidemiology and control. *Lancet Oncol* 2008;9:786-795.

Neutron radiotherapy: Society comments

To the Editor: The radiation oncology community in South Africa can no longer support the continuation of neutron therapy. The lack of new phase III data to support this treatment modality and the fact that patients numbers never really materialised resulted in very inefficient utilisation of available resources that could have been better spent. Progress in clinical and radiation oncology during the past 20 years with new technologies readily available in this country resulted in even fewer reasons to continue this programme. The logistics involved in trying to utilise this as a national resource – which would be the same if one were to try and argue for this to be used as a resource for the continent of Africa – would result in even less benefit to society as a whole.

South Africa can no longer afford to fund such programmes given the many competing priorities in oncology and health in general. To do so would border on being socially irresponsible.

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Neutron radiotherapy: Abratt supported

To the Editor: We write, with some unease, given that much of this matter is internal to the medical affairs of South Africa (SA), to lend support to the stance of Prof Abratt,^{1,2} regarding closure of the neutron facility in SA.

We recognise clearly the limitations of participating in this debate when we are not South African and do not practise medicine in the African continent. That said, there are points of illogic in the criticisms of Prof Abratt's stand that must be challenged.

Firstly, the rhetoric supporting the purported importance of recent research on neutron therapy, and the charge that Prof Abratt's

view of neutron therapy is outdated, are simply unreasonable. The whole issue of the utility of neutron therapy remains highly controversial internationally after more than 25 years of research and clinical practice. The issues remain unchanged: lack of proven benefit, narrow spectrum of clinical indications, offset by excessive toxicity demonstrated in the majority of published studies. While we recognise the difficulty of completing randomised clinical trials in this setting, it is important to note the absence of high-quality data to support this expensive technology.

Despite the claims of the proponents of such research on the topic of neutron therapy, we note a paucity of well-structured published research on the role of this treatment modality. It appears that the majority of use of available equipment has been for routine clinical practice, despite the absence of significant, recent published data to support such therapy; one might have hoped that investigational equipment might have been used to produce new data.

Perhaps of more importance, in a continent that is challenged by a shortage of costly medical resources, it seems importune to make a case for maintenance of an expensive, controversial, unproven therapy with so few indications, and to criticise an earnest and honest attempt to bring reason to the debate. We support Prof Abratt's view, based on logic, fiscal pragmatism, and recognise his presence as a leader in academic radiation oncology with several decades of carefully structured published data.

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1. Abratt RP. The fast neutron therapy programme for patients in South Africa should come to an end. *S Afr Med J* 2012;102(2):58.
2. Abratt RP. Neutron radiotherapy in South Africa: Abratt replies. *S Afr Med J* 2012;102(5):270-271.

Traumatic rhabdomyolysis (crush syndrome) in the rural setting

To the Editor: I read with interest the article entitled "Traumatic rhabdomyolysis (crush syndrome) in the rural setting."¹ Crush syndrome from sjambok injury is a uniquely southern African experience.² It is unfortunately commonplace, making treatment guidelines essential to prevent the progression of acute kidney injury (AKI) and subsequent need for renal replacement therapy. The advent of the RIFLE and AKIN criteria in the description and risk stratification of AKI provides a framework from which strategies to prevent ongoing injury can be implemented.³ Their use has become commonplace in critical care and should be implemented in the emergency department.

Careful monitoring of fluid balance is essential, and a paper discussing the ATN and RENAL trial results shows that avoiding a positive fluid balance improves renal recovery times.⁴ Therefore I urge caution in trying to force a diuresis with resuscitation fluids if patients present with anuria/oliguria and do not respond to initial fluid therapy as they can be pushed into fluid overload with subsequent need for ventilatory support.

Alkalinisation of the urine with bicarbonate has been challenged as the standard of care. Evidence for this practice is weak; in 2 083 trauma ICU admissions, Velmahos' group failed to show improvement in outcomes despite urinary alkalinisation.⁵