

Malignant salivary gland tumours: Can fast neutron therapy results point the way to carbon ion therapy?

Clare Stannard, Frederik Vernimmen, Henri Carrara, Dan Jones, Shaheeda Fredericks, Jos Hille and Evan de Kock

Abstract:

Background and purpose: To evaluate the outcome of malignant salivary gland tumours treated with neutron therapy to assess the potential for other high linear energy transfer (LET) beams.

Materials and methods: Neutrons at iThemba LABS are produced by the reaction of 66 MeV protons on a beryllium target. A median dose 20.4 Gy, in 12 fractions in 4 weeks or 15 fractions in 5 weeks, was given to 335 patients with 176 irresectable, 104 macroscopically residual and 55 unresected tumours.

Results: Locoregional control was 60.6% at 5 years and 39.1% at 10 years and DSS was 66.8% and 53.7% at 5 and 10 years respectively.

In the univariate analysis T4, >4 cm, high grade, squamous carcinoma, unresected and irresectable tumours, and positive nodes were significantly worse for LRC. In the multivariate analysis tumours >6 cm, squamous carcinoma, irresectable tumours and nodes were significantly worse for LRC. Tumours >6 cm, high grade, squamous carcinoma and nodes were significantly worse for DSS. Neither LRC nor DSS was influenced by age, sex, site, dose, fractionation or for initial or recurrent disease.

Conclusions: Neutron therapy appears to be the treatment of choice for macroscopically incompletely excised and irresectable salivary gland tumours with improved survival rates. Further improvement may be achieved with other high LET modalities with a superior dose profile, such as carbon ions.

The increasing number of hadron therapy centres around the world and their use of carbon ion beams have resulted in a growing interest in high-linear energy transfer (LET) radiotherapy. Carbon ions combine the advantages of high-LET radiation with the superior ballistic properties of charged particles. The most commonly used high-LET therapy to date is neutron therapy. The rationale for using it for salivary gland tumours is based on Battermann's observations of growth delay of pulmonary metastases treated with neutrons relative to cobalt-60 radiation [1]. He derived a relative biological effect (RBE) of 8 for fractionated therapy to adenoid cystic carcinoma metastases compared with 3 for most normal tissues, implying a significant therapeutic gain for salivary gland tumours. The safe application of high-LET hadron therapy requires biologically driven treatment planning that has to be based on clinical data. We contribute to this

- [20] Muntner MW, Schulz-Ertner D, Hof H, et al. Inverse planned stereotactic intensity modulated radiotherapy (IMRT) in the treatment of incompletely and completely resected adenoid cystic carcinomas of the head and neck: initial clinical results and toxicity of treatment. *Radiat Oncol* 2006;1:17.
- [21] Pommier P, Liebsch NJ, Deschler DG, et al. Proton beam radiation therapy for skull base adenoid cystic carcinoma. *Arch Otolaryngol Head Neck Surg* 2006;132:1242–9.
- [22] Mizoe J, Hasegawa A, Jingu K, et al. Results of carbon ion therapy for head and neck cancer. *Radiother Oncol* 2012;103:32–7.
- [23] Schultz-Ertner D, Nikoghosyan A, Didinger B, et al. Therapy strategies for locally advanced adenoid cystic carcinomas using modern radiation therapy techniques. *Cancer* 2005;104:338–44.
- [24] Goitein M. Trials and tribulations of charged particle radiotherapy. *Radiother Oncol* 2010;95:23–31.