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Should all mucosal H&N cancer patients be treated in large volume centres, or can some be appropriately triaged to local centres for treatment.

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In this edition, Drs Masoud Rahbari et al present their results of treating oropharyngeal cancer in an integrated regional Australian cancer centre¹. In this small retrospective study they describe the outcomes of 61 patients treated with curative intent over 5 years (average of 12 patients per year) with IMRT and various systemic therapies. It is not stated how many patients were excluded from the analysis on the basis of receiving non-curative treatment.

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Their cancer outcome results were excellent, readily comparable to published international series^{2, 3}. At this early stage (median follow-up only 22 months) the 2 year loco-regional relapse free survival (LRRFS) was 98% and overall survival (OS) 90%. In this cohort of patients, almost 70% were p16 (denoting human papilloma virus, HPV) positive and 80% were ex or non-smokers (pack year smoking history unknown). The majority had Stage IVa disease, essentially on the basis of nodal classification; very few had T4 or N3 disease. Hence we can assume that largely these patients fall into the low risk group category, described by Ang et al as having a 3 year OS in the order of 90%².

Cancer outcomes are important, but treatment completion and toxicity are also important. There is some concern that in this particular low risk patient group, 2 patients didn't complete their prescribed radiotherapy, but this may just be an aberration of small numbers. Of more concern is the relative high rate (13%) of PEG tube dependence at more than 6 months post treatment. The study by Matchay et al⁴ reporting late toxicity following chemoradiation is oft quoted, particularly the late grade 3 (PEG dependent) rate of 29%. However this data is from the pre-IMRT treatment era. Current rates of grade 3 dysphagia 6 or more months following chemoradiation using IMRT are 2 or less percent^{5, 6}. Hence the 13% rate described in this study is relatively high for IMRT treated head and neck cancer (HNC) patients.

Patients with p16/HPV oropharyngeal cancer are currently the focus of much clinical research. The general thrust of this research is investigating treatment deintensification, with the aim of reducing late toxicities in this younger group of patients who have excellent life expectancy due to the high curability of their primary disease and the lack of mortality from smoking related co-morbidities or second cancers. It was not mentioned if any of the patients treated in this integrated regional centre were entered in clinical trials. There is an Australia wide randomised trial on this very topic (www.trog.com.au/TROG-1201-HPV). Patients having access to participation in clinical trials is one of the key ways to improve cancer treatments and patient outcomes. Currently this aspect of patient care resides mainly in the province of large HNC cancer centres.

Whilst the authors are to be commended on auditing their results, I think they draw a long bow if suggesting from their results for this selected good prognosis group of

HNC patients, that all HNC patients can be optimally treated in small regional centres. The authors state that “not all rural or regional centres are low volume centres” and “IMRT in rural or regional centres can produce comparable outcomes to large tertiary centres”. These statements need to be further explored in relation to HNC specifically.

What is actually meant by the term “low or high volume” HNC centres? The authors correctly denote that both large prospective studies showing major survival benefit in HNC patients in large HNC centres used surrogate markers for denoting the size of the HNC centres involved^{7,8}. So how do we define a high volume HNC centre? When assessing appropriate workloads for our HNC service, I asked the centres who enrolled > 20 patients in the TROG 02.02 study (those centres with the best OS outcomes across a range of HNC subsites) to provide the numbers of HNC patients treated annually at their centre. The minimum was 150 patients per centre, ranging to over 600 patients per centre. Based on all the data, the Victorian Department of Health accepted the (conservative) recommendation from the Victorian Optimal Care Pathway for HNC patients committee (including rural centre representatives) that it is preferable for HNC patients to be treated in a centre treating a minimum of 100 mucosal HNC cases per year (www.cancer.org.au/OCP). The high prevalence of cancers such as prostate, breast, and bowel means that oncologists in small regional centres have the opportunity to develop expertise in the treatment of these cancers. However the numbers just don't stack up for HNC. The number of patients with HNC is about a sixth that of the top 3, so it is difficult for individual rural centres not to be low volume centres for HNC. While some of the problems associated with low volume can be overcome by videoconference-based MDMs with major tertiary centres (as is the practice at the authors' centres), the limitation that cannot be cost-effectively overcome is provision of the extensive paramedical support services required by most patients with advanced HNC.

On their other point - IMRT has been a wonderful technological advance in radiation oncology. As the ANROTAT study showed, IMRT demonstrated better safety, efficacy and cost effectiveness when compared to conventional conformal radiotherapy in the treatment of diseases such as nasopharyngeal cancer (<http://www.trog.com.au/ANROTAT>). However it is well recognised that the conformality of dose generated by IMRT can be a double edged sword, particularly

in HNC. Technology is only a tool; good outcomes are very dependent on the HN radiation oncologist having the ability to accurately assess, clinically and radiologically, the extent of disease and to volume that disease and the OARs accurately. If these volumes aren't correct then IMRT cannot deliver good results. The role of radiotherapy quality assurance (RT QA) in improving HNC survival outcomes was very clear in the Peters study. Subsequently, all randomised HNC trials have incorporated some degree of RT QA. What is not known is if there is a lower degree of RT QA, i.e. less than review of every patient's RT plan that could deliver similar results. The authors are to be commended on having a RT QA programme, more details in the Masoud Rahbari manuscript regarding the intensity and type of RT QA applied at their centres would have been of great interest.

Clearly, all clinicians want the best possible outcomes for their patients. Thus it is crucial that we all engage in the discussion of how optimal outcomes can be achieved for relative rare cancers such as HNC. This is particularly relevant in Australia with its small population, large geographical area and traditional reluctance for patients to travel to large centres for their medical care. Interestingly, this is not seen as an issue for other rare cancers such as paediatrics or sarcoma. I am not sure why there is not equal buy in to this management strategy by HNC clinicians and HNC patients.

I think a more constructive conclusion for this manuscript would have been that this data adds to the discussion of "Should all mucosal H&N cancer patients be treated in large volume centres, or can some be appropriately triaged to local centres for treatment".

Maybe the authors are correct, that we can select out good prognosis patients (and very poor prognosis patients), for whom the expertise of high volume HNC centres will provide relatively little additional benefit, allowing these patients to be appropriately treated locally. The challenge here is where to make the cut-off for referral. I believe that this is best achieved by review of all new patients seen at low volume centres in collaboration with a high volume HNC centre, the latter contributing via MDM teleconferencing to recommendations for triaging and to distant review of radiotherapy plans for patients assigned to receive treatment at the volume centre.

This is a crucial topic for discussion requiring active participation by all stakeholders involved in HNC. Publishing results from low volume HNC centres makes an important contribution to this discussion, but a wider forum needs to be convened to formulate an Australian wide HNC policy and/ or project to optimally resolve this important issue.

REFERENCES:

1. Masoud Rahbari R, Winkley L, Hill J, et al. Definitive intensity modulated radiotherapy concurrent with systemic therapy for oropharyngeal squamous cell carcinoma: outcomes from an integrated regional Australian cancer centre. J Med Imaging Radiat Oncol
2. Ang KK, Harris J, Wheeler R, et al. Human papillomavirus and survival of patients with oropharyngeal cancer. N Engl J Med 2010;363:24-35
3. Rischin D, Young RJ, Fisher R, et al. Prognostic significance of p16 INK4A and human papilloma virus in patients with oropharyngeal cancer treated on TROG 02.02 phase III trial. J Clin Oncol 2010;28:4142-8
4. Machtay M, Moughan J, Trotti A, et al. Factors Associated With Severe Late Toxicity After Concurrent Chemoradiation for Locally Advanced Head and Neck Cancer: An RTOG Analysis. J Clin Oncol 2008;26:3582-9
5. Feng FY, Kim HM, Lyden TH, Haxer MJ, et al. Intensity-Modulated Chemoradiotherapy Aiming to Reduce Dysphagia in Patients With Oropharyngeal Cancer: Clinical and Functional Results. J Clin Oncol 2010;28:2732-8
6. Nuyts S, Lambrecht M, Duprez F, et al. Reduction of the dose to the elective neck in head and neck squamous cell carcinoma, a randomized clinical trial using

intensity modulated radiotherapy (IMRT). Dosimetrical analysis and effect on acute toxicity. *Radiother Oncol* 2013;109(2):323-9

7. Peters LJ, O'Sullivan B, Giralt J, et al. Critical impact of radiotherapy protocol compliance and quality in the treatment of advanced head and neck cancer: Results from the TROG 02.02. *J Clin Oncol* 2010;28:2996-3001

8. Wuthrick EJ, Zhang Q, Machtay M, et al. Institutional clinical trial accrual volume and survival of patients with head and neck cancer. *J Clin Oncol* 2014;33:156-164.

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