Dose to the masseter muscle and risk of trismus after chemoradiation for advanced head & neck cancer

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Purpose / objective:
Head and neck cancer patients treated with chemoradiation are at risk for developing trismus (reduced mouth opening). Trismus is often a persisting side-effect and difficult to manage. It impairs eating, speech and oral hygiene, affecting quality of life. Although several studies identified the masseter muscle (MM) as one of the main organs at risk, currently this structure is rarely considered during treatment planning. Prospective studies for chemoradiation are lacking. The aim of our study was to quantify the relationship between radiation dose to the MM and development of radiation-induced trismus in an IMRT-VMAT population.

Materials and Methods:
The 93 patients in this study participated in a prospective preventive exercise program to preserve oral functioning between 2006-2013. All received concomitant high-dose chemotherapy during VMAT- or IMRT-radiotherapy (70 Gy in 35 fractions). Tumor locations were mainly oropharynx (37%) and hypopharynx (33%). Maximum interincisor mouth opening was measured before and approximately 10 weeks after the end of treatment. Bilateral delineations of the MM were available from 2 retrospective studies. Patients were excluded if trismus was present at baseline, or if gross tumor infiltration of the MM was present on CT evaluation. Evaluated outcomes were trismus (mouth opening ≤ 35 mm) and decrease in mouth opening. Logistic regression (using maximum likelihood) was performed.

Results:
At the first evaluation, 6-12 weeks post-treatment, fourteen patients had developed radiation-induced trismus (15%). On average, mouth opening decreased with 4.1 mm, or 8.2 % relative to baseline. Mean dose to the ipsilateral MM was a stronger predictor for trismus than mean dose to the contralateral MM, as indicated by the lowest -2 log likelihood (**Table 1**). **Figure 1A** shows the correlation between the ipsilateral mean masseter dose and the relative decrease in mouth opening, with trismus cases indicated in red. No trismus cases were observed in 33 patients (35%) with a mean dose to the ipsilateral MM < 20 Gy. The risk of trismus in the other 60 patients (65%) increased with higher mean doses to the ipsilateral MM. **Figure 1B** shows the fitted NTCP curve as a function of the mean dose, with a TD50 of 55 Gy. The actual incidence (with 1 SE) of trismus cases within 5 dose bins is indicated as well, showing a good correspondence with the NTCP fit with a relatively large uncertainty in the dose area > 50 Gy. Patients with tumors located in the oropharynx were at highest risk.

Conclusions:

The risk of trismus can be established with the mean dose to the ipsilateral masseter muscle. The majority of head and neck cancer patients could benefit from dose reduction to the masseter muscles to prevent trismus, especially patients with a mean dose to the ipsilateral masseter > 20 Gy. Further development of a NTCP model could identify dose objectives to guide treatment planning.

Table 1. Results of univariate logistic regression analysis.

Dose parameter	-2 LLH	RR per 10 units	p value
Ipsilateral Masseter			
Volume > 20 Gy (%)	66.5	1.5	0.004
Volume > 40 Gy (%)	69.8	1.4	0.004
Mean dose (Gy)	65.3	2.3	0.001
Contralateral Masseter			
Volume > 20 Gy (%)	66.5	1.4	0.002
Volume > 40 Gy (%)	70.6	1.5	0.007
Mean dose (Gy)	68.2	2.2	0.003

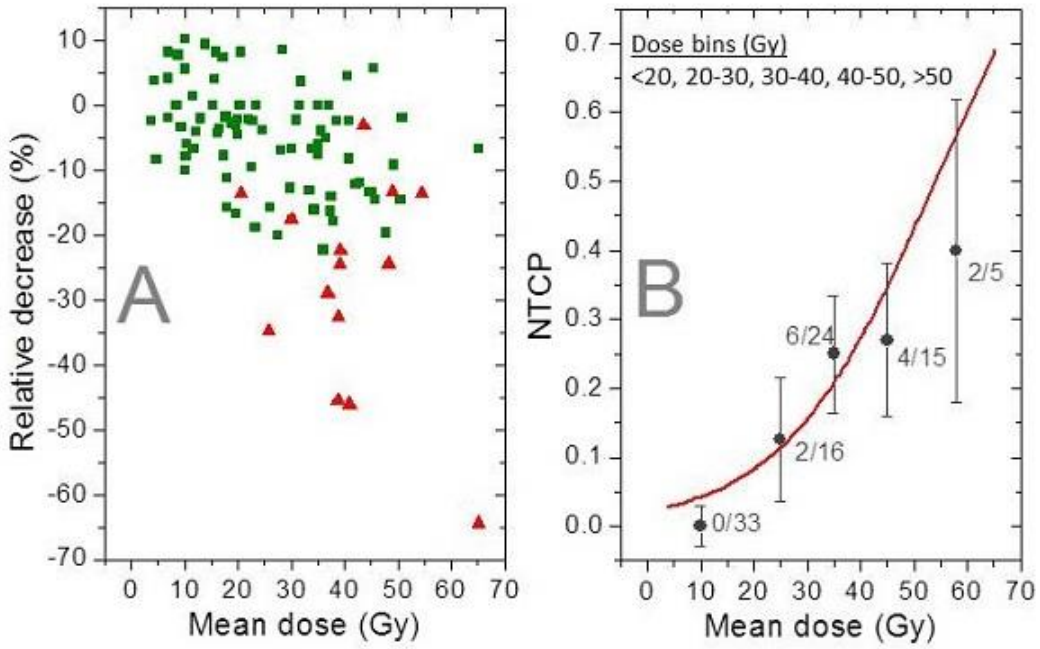

Figure 1. % decrease in mouth opening (A), NTCP for trismus & actual incidence with 1SE (B), both as function of mean dose to the ipsilateral masseter muscle.