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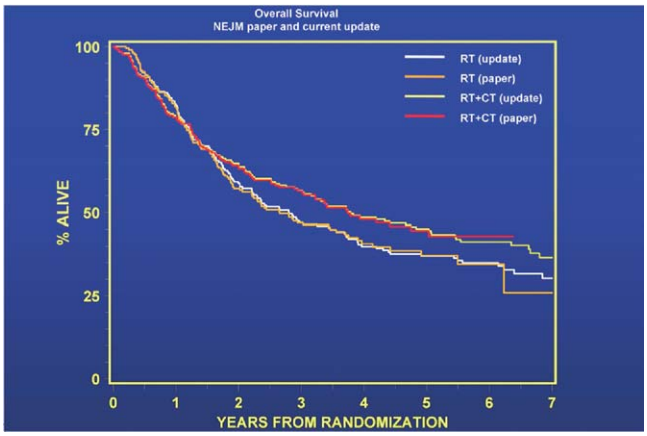

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26 A Randomized Trial of Hyperfractionation Versus Standard Fractionation In T2 Squamous Cell Carcinoma of The Vocal Cord

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Purpose/Objective(s): To compare the efficacy of hyperfractionation versus standard fractionation for the treatment of T2N0 carcinoma of the vocal cord.

Materials/Methods: Between April 1996 and July 2003, 250 patients were stratified by substage (T2a vs T2b) and randomly assigned to receive either hyperfractionation (HFX) to 79.2 Gy in 66 fractions of 1.2 Gy given twice a day, or standard fractionation (SFX) to 70 Gy in 35 fractions given once a day. The trial was designed to detect a 55% reduction in the yearly hazard rate for local failure with 80% statistical power. 238 patients were analyzable for outcomes. The median follow-up for all surviving patients was 4.2 years (range: 0.6 - 9.4). 95% were male, 83% had KPS 90-100, and 63% were T2a.

Results: The five-year local control (LC) rate was modestly higher for HFX (79%) vs SFX (70%), which translates to a 35% reduction in the hazard rate, but this difference was not statistically significant (p=0.11). Five-year disease-free survival (DFS) was 51 vs 37 % (p=0.07). Five-year overall survival was 73 vs 62% (p=0.19). HFX had modestly higher rates of acute skin, mucosal, and laryngeal toxicity. High-grade late effects were uncommon in both groups.

Conclusions: Local control was modestly higher with HFX compared to standard fractionation for T2 carcinoma of the vocal cord, but the difference did not reach statistical significance. With only 58 local failures, the statistical power of detecting the observed 35% hazard reduction is only 36%. There was a trend for better disease free survival with HFX. Results are consistent with other studies showing a modest benefit for altered fractionation in cancers of the H&N.

Five-year rates

	SFX	HFX	p-Value
Endpoint	% (95% CI)	% (95% CI)	
Local Control	70 (62, 79)	79 (71, 87)	0.11
Disease-Free Survival	37 (27, 46)	51 (41, 61)	0.07
Overall Survival	62 (52, 72)	73 (64, 82)	0.19

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27 Five-year Update on a Randomized Factorial Study on Concurrent and Adjuvant Chemotherapy for Advanced Nasopharyngeal Carcinoma

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Purpose/Objective(s): To update the results of a randomized factorial trial studying the role of concurrent chemoradiation (CRT) and adjuvant chemotherapy (AC) for advanced nasopharygngeal carcinoma (NPC).

Materials/Methods: Ho's stage T3 or N2 /N3 or > 4cm neck node, M0 disease were eligible. Patients were first randomized to receive CRT or radiotherapy (RT) alone and then further randomized to receive AC or no AC after CRT/RT. CRT involved UFT (uracil and tegafur in 4:1 molar ratio) 200mg, 3 times a day, during RT. AC consisted of alternating PF (cisplatin 100mg/m^2 D1 and 5FU 1g/m^2 D1-3) and VBM (vincristine 2mg, bleomycin 30mg and methotrexate 150mg/m^2, all on D1) for 6 cycles, after CRT/RT. There were 4 treatment arms: 1. RT, 2. CRT, 3. RT + AC, 4. CRT + AC. To analyze the efficacy of CRT, arms 1 and 3 were compared with arms 2 and 4 (i.e. RT vs. CRT). To analyze the efficacy of AC, arms 1 and 2 were compared with arms 3 and 4 (i.e. no AC vs. AC). Analysis was performed according to intention to treat. Persistent disease or recurrence in nasopharynx (NP) or neck nodes and distant metastases were considered disease failure. Death after recurrence was considered due to NPC.

Results: From May 1995 to October 2001, 222 patients were recruited. 3 patients were excluded from analysis because of major protocol violation. Median follow up time of 219 patients in analysis was 65 months. The median age was 45. Median dose to NP and neck were 68Gy and 66Gy, respectively. There were 55, 53, 54, 57 patients in arm 1, 2, 3, 4 respectively. The 5-year loco-regional control rate and distant metastases-free survival of arm 1, 2, 3, 4 were 64.2%, 74.8%, 78.7%, 81.1% and 74.2%, 85.8%, 67%, 82.4% respectively. The 5-year failure-free and disease-specific survivals of the 4 arms were and 54%, 69%, 54.6%, 66.4% and 77.1%, 79.8%, 67.7%, 81.4% respectively. CRT significantly improved the distant metastases-free and failure-free survival (p=0.02 and 0.038 respectively). The difference in disease specific survivals was not statistically significant (p=0.075). The use of AC failed to improve survival on all measures. Multivariate analysis showed only CRT as significant prognostic factor for failure-free survival. Age, T stage, N stage and CRT were significant prognostic factors for disease-specific survival. The use of AC was not significant for failure-free or disease-specific survival.

Conclusions: CRT significantly reduced distant metastases and improved failure-free survival for patients with advanced NPC. There is an improvement of disease-specific survival after adjusting for age and stage of disease. AC failed to improve survival. The positive effect of CRT was confirmed on long term follow-up.

Survival analysis comparing CRT vs RT and no AC vs AC

Treatment	No. of Patients	5-Year Loco-Regional Control Rate	5-Year Distant Metastases-Free Survival	5-Year Failure-Free Survival	5-Year Disease Specific Survival
RT	109	71.2%	70.7%	54.3%	72.5%
CRT	110	78.2%	84.1%	67.7%	80.5%
	Log-rank test p value	0.22	0.02	0.038	0.075
No AC	108	69.4%	79.8%	61.3%	78.5%
AC	111	80%	75.1%	60.8%	74.6%
	Log-rank test p value	0.078	0.26	0.99	0.78

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28 Final Report of SQNP01 - A Phase III Randomized Trial Comparing RT With Chemo-RT for Locally Advanced Nasopharyngeal Cancer

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Purpose/Objective(s): SQNP01 was designed to confirm the findings of US Intergroup 00-99 - a study showing benefit of adding chemotherapy to radiotherapy for Nasopharyngeal Cancer (NPC). This is the final report of the study and the 5 year results of the trial is presented.

Materials/Methods: Between September 1997 and May 2003, 221 patients were randomised to receive radiotherapy alone (n=110) or chemo-radiotherapy (n=111). Patients in both arms received 70Gy in 7 weeks using standard radiotherapy portals and techniques. Those on chemo-radiotherapy received concurrent cisplatin (25mg/m^2 Days 1-4) on weeks 1, 4 and 7 of radiotherapy and adjuvant cisplatin (20mg/m^2 Days 1-4) and 5-fluorouracil (1000mg/m^2 Days 1-4) every 4 weeks (weeks 11, 15, 19) for 3 cycles following completion of radiotherapy. All patients were analysed by intention-to-treat. Their median follow-up duration was 4.9 years (interquartile range 3.5 to 6.3 years).

Results: Distant metastasis occurred in 39 patients on radiotherapy alone and 18 on chemo-radiotherapy. Its 5-year cumulative incidence was 40% for R and 17% for C and this difference of 23% was statistically significant (95% CI 9% to 35%, p=0.0014). Altogether, there were 59 failures in R and 44 in C. These "failures" include those with persistent disease as well as death due to other causes. The 5-year DFS rates were 45% and 55% for R and C respectively. The median disease-free survival time for R and C were 4.1 and 7.1 years. The hazard ratio (HR) for DFS was 0.67 (95% CI 0.45 to 0.98, p=0.0393). Ninety one (55 R, 36 C) deaths were reported, of which 81 (50 R, 31 C) were disease-related. The 5-year survival rates were 46% and 65% for R and C respectively. The median overall survival time for R and C were 4.5 and 6.7 years. Patients who were randomized to receive C thus had a reduced risk of death with a HR of 0.58 (95% CI 0.39 to 0.88, p=0.0106).

Conclusions: The 5 year results of this trial continue to show a significant benefit of adding chemotherapy to radiotherapy in patients with locally advanced NPC. It conclusively confirms the findings of the Intergroup trial, and the result is also applicable to patients with the endemic form of NPC.

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