

## Article

### Feasibility and early results of accelerated radiotherapy for head and neck carcinoma in the elderly

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#### Abstract

Accelerated radiotherapy (RT) represents a promising method with which to improve the treatment outcome in patients with head and neck carcinoma. However, its applicability to elderly patients has not been well established. This study assessed treatment toxicities, patient compliance, and oncologic results in patients age  $\geq 70$  years who were treated with an accelerated concomitant boost RT schedule.

## Reference

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# Feasibility and Early Results of Accelerated Radiotherapy for Head and Neck Carcinoma in the Elderly

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**BACKGROUND.** Accelerated radiotherapy (RT) represents a promising method with which to improve the treatment outcome in patients with head and neck carcinoma. However, its applicability to elderly patients has not been well established. This study assessed treatment toxicities, patient compliance, and oncologic results in patients age  $\geq 70$  years who were treated with an accelerated concomitant boost RT schedule.

**METHODS.** Between 1991 and 1997, 39 patients aged  $\geq 70$  years (mean,  $75 \pm 6$  years) presenting with carcinomas of the oral cavity, pharynx, or larynx were treated radically with a modified concomitant boost RT schedule (planned dose of 69.9 grays [Gy] over 38 days). Based on American Joint Committee on Cancer staging, there were 14 patients with Stage I–II disease and 25 patients with Stage III–IV disease. Eighty-one patients age  $< 70$  years who were treated with the same RT schedule served as a comparative group. The median follow-up for the surviving patients was 19 months (range, 3–65 months) and 23 months (range, 2–76 months), respectively, for the elderly and younger patient groups.

**RESULTS.** The planned RT schedule was completed in all cases. Three patients (8%) in the elderly group and none in the younger group had an unplanned treatment interruption because of acute toxicity or lack of compliance ( $P = 0.03$ ). The median tumor dose (69.9 Gy; range, 67–73 Gy) and the median overall treatment time (41 days; range, 36–60 days) were identical in both groups. According to the Radiation Therapy Oncology Group grading system, Grade 3–4 acute reactions were observed in 66% of elderly patients and in 71% of younger patients. Ten elderly patients (26%) and 19 younger patients (23%) required a nasogastric tube or a percutaneous gastrostomy for feeding, with a median weight loss of 4.1 kg and 4.4 kg, respectively, in the 2 groups. Grade 3–4 late complications were observed in 3% of the elderly patients and 10% of the younger patients ( $P = 0.43$ ). Both elderly and younger patients had similar results with regard to 3-year actuarial overall survival (68% vs. 62%;  $P = 0.48$ ) and locoregional control (73% vs. 68%;  $P = 0.31$ ).

**CONCLUSIONS.** The current study suggests that an accelerated concomitant boost RT schedule is feasible in elderly patients who are physically healthy enough to undergo curative treatment. The acute and late toxicities appear to be similar to those observed in younger patients, and treatment outcomes appear to be comparable. *Cancer* 2000;88:648–52. © 2000 American Cancer Society.

**KEYWORDS:** elderly patients, head and neck carcinoma, accelerated radiotherapy, toxicities.

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Nearly 60% of all cancers currently are diagnosed in patients age  $\geq 65$  years.<sup>1</sup> The rapid increase in cancer diagnosis in the elderly population is certain to lead to a marked rise in new cancer cases in Western countries.<sup>2</sup> Consequently, the problem of cancer manage-

ment in the elderly will gain in importance. Indeed, underestimation of the life expectancy of elderly patients and the perception that radical treatment will be poorly tolerated often lead to the prescription of less adequate therapy.<sup>3,4</sup>

For patients presenting with head and neck carcinoma, accelerated radiotherapy (RT) may lead to an improvement in the treatment outcome.<sup>5,6</sup> However, these new RT schedules may be associated with significant acute<sup>5-7</sup> and late side effects,<sup>5</sup> and to our knowledge their applicability to all patient subgroups, particularly elderly patients, is not well established. Prospective studies testing accelerated RT schedules rarely have included elderly patients, and no specific data regarding the tolerability and outcome of such treatment have been published for this particular subgroup.<sup>6</sup> Taking into account these considerations, we undertook a retrospective study to assess treatment toxicities, patient compliance, and oncologic results in patients age  $\geq 70$  years who were treated with an accelerated concomitant boost RT schedule at Geneva University Hospital. Younger patients treated with the same RT schedule served as a comparative group.

## MATERIALS AND METHODS

### Patients

Between April 1991 and December 1997, 45 of the 64 patients age  $\geq 70$  years presenting with carcinomas of the oral cavity, pharynx, or larynx were treated with a concomitant boost RT schedule. The remaining 19 patients were treated with standard RT because they presented with small tumor volume (17 with glottic carcinoma, 1 with a nasopharyngeal carcinoma, and 1 with a lip carcinoma). Six patients who also received chemotherapy were excluded, leaving 39 patients eligible for the current study. The comparative group was comprised of 81 patients (of 143 referred) age  $< 70$  years who were treated during the same time period with radical RT alone using the same RT schedule. The 62 patients who were not considered for the comparison group were patients who also were treated with chemotherapy (39 patients) and patients enrolled in a Swiss cooperative group study (23 patients). All patients had a biopsy proven squamous cell (114 patients) or nasopharyngeal (6 patients) carcinoma. The characteristics of the two groups are shown in Table 1. Younger patients were found to have more advanced neck disease whereas elderly patients had more advanced primary tumors.

### Radiation Therapy

The RT schedule has been described previously.<sup>8</sup> Briefly, the planned total dose was 69.9 grays (Gy), to be delivered in 41 fractions over a period of 38 days.

**TABLE 1**  
Patient Characteristics

	Elderly patients (39)	Young patients (81)	P value
Mean age (yrs) (SD)	75 (6)	56 (7)	
Gender: male/female	34/5	63/18	
WHO performance status			
0-1	31 (79%)	66 (81%)	
2-3 <sup>a</sup>	8 (21%)	15 (19%)	
Tumor location			
Oral cavity plus oropharynx	18 (46%)	43 (53%)	0.55
Hypopharynx plus larynx	19 (49%)	32 (40%)	
Nasopharynx	2 (5%)	6 (7%)	
TN stage (UICC 1992)			
T1-2	18 (46%)	57 (70%)	0.015
T3-4	21 (54%)	24 (30%)	
N0	28 (72%)	37 (46%)	0.01
N1-3	11 (28%)	44 (54%)	
(N1/N2/N3)	(5/6/0)	(8/29/7)	
AJCC Stage			
I-II	14 (36%)	31 (38%)	
III-IV	25 (64%)	50 (62%)	

SD: standard deviations; WHO: World Health Organization; UICC: International Union Against Cancer; AJCC: American Joint Committee on Cancer.

<sup>a</sup>Included one case with unknown status in each group.

The first volume (generally the primary tumor area and both sides of the neck down to the clavicles) was to receive a dose of 50.4 Gy over 5.5 weeks given in daily fractions of 1.8 Gy, 5 times a week. The boost to the initial involved sites was comprised of 13 fractions of 1.5 Gy (total of 19.5 Gy) given as a second daily fraction beginning the last day of the second week, in a progressively accelerated fashion. The minimum interval between the 2 daily fractions was 6 hours.

The majority of the patients (82%) were treated with 2 opposed lateral fields and 1 anterior field. The other technique was comprised of 2 opposed lateral fields (8%), 2 opposed kicked out fields (9%), and 2 opposed anteroposterior fields (1%). The field arrangement for the boost was individualized according to the tumor extent and location. Six-megavolt photon beams were used in the majority of patients (95%). The cervical spinal cord was blocked at a dose of  $\leq 45$  Gy and irradiation of the posterior neck then was continued with electrons of appropriate energy. The supraclavicular lymph nodes generally received a dose of 45–50.4 Gy in 25–28 fractions. No specific technical modifications were used in the elderly patients.

### Surgery

Before RT, a planned unilateral or bilateral neck dissection was performed in 20 younger patients and 1 elderly patient, and 2 patients in the younger group

underwent an adenectomy. No patient underwent major surgery as treatment of the primary tumor. Otherwise, surgery was reserved for salvage of locoregional failures.

### Statistical Methods

The actuarial locoregional control rates as well as overall survival rates were calculated using the Kaplan–Meier method.<sup>9</sup> The Fisher exact test and the log rank test were used to assess significant differences between simple proportions and survival curves, respectively.

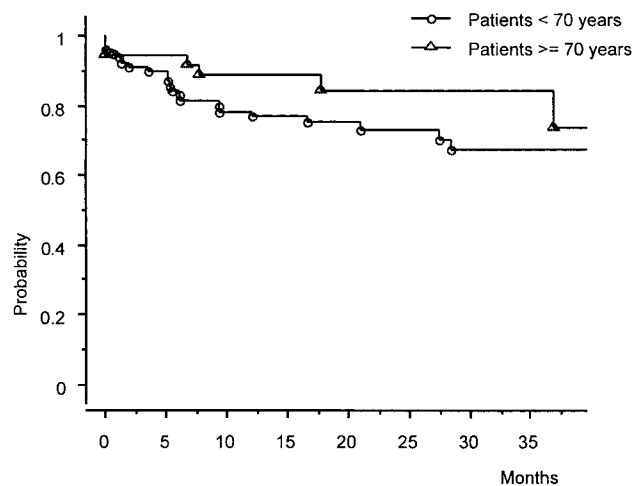
## RESULTS

### Treatment Compliance and Toxicity

The planned RT schedule was completed in all cases. Because of acute toxicity or lack of compliance, 3 patients (7%) in the elderly group had an unplanned RT interruption (split duration of 2–9 days), whereas none of the younger patients had such an interruption ( $P = 0.03$ ). The median tumor dose was 69.9 Gy in both groups (range, 67–73 Gy) and the median overall treatment time was 41 days in both groups (range, 36–60 days).

According to the Radiation Therapy Oncology Group (RTOG) grading system,<sup>10</sup> all acute reactions were  $\geq$  Grade 2. The majority were Grade 3 reactions (64% in elderly patients vs. 71% in the younger patients), with only 1 patient in the elderly group presenting with Grade 4 acute toxicity. The main acute toxicities were mucosal ( $\geq$  Grade 2 in 90% of the elderly patients vs. 98% of the younger patients) and dysphagia ( $\geq$  Grade 2 in 82% of the elderly patients vs. 93% of the younger patients). Ten patients in the elderly group (26%) and 19 patients in the younger group (23%) required a nasogastric tube or a percutaneous gastrostomy for feeding. Seven elderly patients (18%) were hospitalized for feeding, hydration, and other supportive care, whereas 10 of the younger patients (12%) were hospitalized for the same purposes ( $P = 0.41$ ). The median duration of hospitalization was identical in the two groups (12 days). During RT, the median weight loss was 4.1 kg (range, 0–10 kg) and 4.4 kg (range, -3–14 kg) in the elderly and younger patient groups, respectively.

Thirty-four elderly patients and 72 younger patients were evaluable for long term complications (patients with a minimum follow-up of 3 months and with available data). The majority of complications were RTOG Grade 2 (56% and 51% in the elderly and younger patient groups, respectively). Grade 3–4 complications were observed in 3% and 10% in the elderly and younger patient groups, respectively ( $P = 0.43$ ). Three patients died without evidence of disease dur-



**FIGURE 1.** Actuarial locoregional control for both groups of patients.

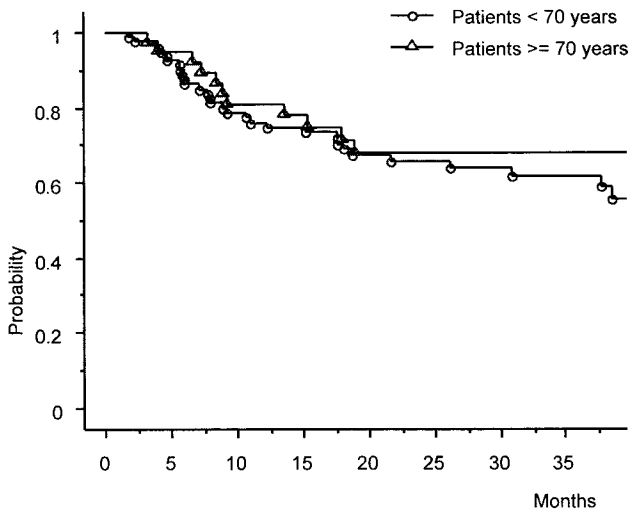
ing the 3 months after RT (1 patient in the elderly group died of septicemia and 2 patients in the younger group died of pneumonia and cachexia, respectively) and were considered treatment-related deaths.

### Clinical Outcome

At last follow-up, 25 patients in the elderly group and 46 in the younger group were still alive, and 1 patient in each group had been lost to follow-up (at 0 months and 4 months, respectively). In those patients who died, head and neck carcinoma was considered the cause of death in 5 of 13 patients in the elderly patient group and 23 of 34 patients in the younger patient group. The median follow-up for the surviving patients was 19 months (range, 3–65 months) and was 23 months (range, 2–76 months) for the elderly and younger patient groups, respectively. For the elderly and younger patient groups the 3-year actuarial outcomes were similar, with regard to both locoregional control (73% and 68%, respectively;  $P = 0.31$ ) (Fig. 1) and overall survival (68% and 62%, respectively;  $P = 0.48$ ) (Fig. 2).

## DISCUSSION

The increasing life span in Western countries confronts the clinical oncologist with the therapeutic dilemma of providing adequate cancer management in geriatric patients. Progress in the management of comorbidities in the elderly has allowed curative treatment to be considered more frequently,<sup>11</sup> and recent reports have stressed that advanced chronologic age is not in itself a criterion for excluding patients from standard treatment with either RT, chemotherapy, or surgery.<sup>12–15</sup> Moreover, in many types of cancer age is not an independent negative prognostic factor.<sup>15–18</sup>



**FIGURE 2.** Actuarial overall survival for both groups of patients.

Because elderly patients often are excluded from prospective trials, to our knowledge reliable information regarding the feasibility and results of new aggressive therapeutic approaches in this subpopulation are dramatically lacking.

For patients with head and neck carcinoma, accelerated RT holds promise as a way of potentially improving treatment outcome. However, the applicability of such potentially more toxic RT schedules to elderly patients is not well documented. In a review of clinical trials using various RT schedules in the treatment of head and neck carcinoma, Pignon et al.<sup>19</sup> assessed acute and late toxicity according to age in 1307 patients, 12% of whom were age  $\geq 70$  years. No differences in the occurrence of objective acute mucosal reactions were noted in the different age groups. However, no specific evaluation was performed in patients treated with accelerated RT. In the CHART trial,<sup>6</sup> patients age  $> 70$  years were included, but to our knowledge no data have been published regarding the tolerability of this accelerated schedule in elderly patients. To our knowledge the current study is the first to address this particular question.

Taking into account the retrospective design of the current study, our elderly patients may represent a selected population, as suggested by the low number of patients with a performance index  $> 2$  (two patients). However, the proportion of elderly subjects among all patients treated with this RT schedule (24%) appears higher than that reported in other series (range, 12–16%).<sup>14,19</sup> Moreover, according to the Geneva Tumor Registry, patients age  $\geq 70$  years represent 21% of all patients with carcinomas of the oral cavity, pharynx, or larynx. Thus, these data suggest that in Geneva, elderly patients selected for acceler-

ated RT may have selection criteria similar to younger patients, and consequently the results obtained may be considered as representative.

Although objective acute toxicities appeared to be similar to those observed in younger patients treated with the same RT schedule, in elderly patients there were significantly more RT interruptions due to toxicity or lack of compliance. This fact may reflect diminished tolerance of acute toxicity in geriatric patients, as was noted by Pignon et al. using a subjective scoring system.<sup>19</sup> However, this finding was not confirmed in a small series of 14 elderly patients (age 70 years) treated conventionally for oropharyngeal carcinoma.<sup>14</sup> Moreover, Chin et al.<sup>14</sup> reported no difference in the rate of hospitalization for supportive care during RT, but elderly patients tended to have longer durations of hospitalization. In the current series, although the rate of hospitalization was slightly higher in the elderly patient group, the median duration was similar. Otherwise, the planned RT schedule was completed in all patients in the current study, and the median delivered tumor dose and overall treatment times were similar in both groups. In addition, there were no significant differences in the need for artificial feeding or weight loss during RT between the two patient groups.

With respect to late complications, there were no significant differences in the rates of Grade 2 or Grade 3–4 complications between younger and elderly patients. The same finding has been reported for patients presenting with head and neck carcinoma<sup>19</sup> or tumors at other locations.<sup>15</sup> However, a longer follow-up period is needed to confirm this finding. Although the oncologic results were not the main endpoint in the current study, considering the differences in patient characteristics (Table 1), it is interesting to note that there were no apparent differences between the 2 groups of patients in terms of 3-year actuarial locoregional control (73% in the elderly patient group vs. 68% in the younger patient group) or overall survival (68% in the elderly patient group vs. 62% in the younger patient group). This finding is consistent with other reports concerning patients treated with RT<sup>14,19</sup> or surgery.<sup>17,20,21</sup>

The results of the current study confirm previously established beliefs that radical RT can be performed successfully in elderly patients with head and neck carcinoma and suggest that even relatively aggressive accelerated RT schedules are feasible in geriatric patients who are physically healthy enough to receive such treatment. However, recent data suggest that treatment effectiveness can be improved further by the concomitant delivery of RT and chemotherapy. Indeed, despite the greater toxicity, our current ap-

proach is to combine accelerated concomitant boost RT and chemotherapy in younger patients with advanced disease. Although such strategies may become a standard treatment option in younger patients with advanced head and neck carcinoma, their feasibility in elderly patients remains unknown and must be evaluated carefully in prospective trials.

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