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Results and special considerations when treating elderly patients with CyberKnife®: A review of 345 cases

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Contents

Abstract

The relatively recent introduction of CyberKnife® in the field of radiotherapy has prompted the question of accessibility and usefulness of this technique for seniors. From June 2007 to June 2009, we treated 345 patients of all ages with CyberKnife as part of a single-center study. Median age was 61 years (range, 8–86 years). Ninety-eight patients were over 70 and 17 were older than 80. The treatment could not be completed with 2% (2/98) patients over 70 vs. 3.6% (9/247) among the younger (ns). Physiologic or psychologic problems in maintaining position for a long time were not more frequent among those over 70. The same was true with those over 80. Patients over 70 years old are able to tolerate CyberKnife treatment as efficiently as their younger counterparts. Elderly patients should not be restricted from access to CyberKnife radiosurgery with curative intent.

Keywords: CyberKnife; Elderly patients; Feasibility; Stereotactic radiotherapy

1. Introduction

In the western world, life expectancy, along with incidence of cancers, has been rising. This increase in cancer diagnosis

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rates appears to be strongly linked to an aging population, and presents a major demographic and medical challenge [1,2]. More than 65% of cancer deaths occur among those above 65 years of age [3]. Radiotherapy is offered to 60–70% of patients during their oncological care regardless of their age. Oncological treatment of elderly patients therefore is a common reality. Unfortunately the elderly population is under-represented in the clinical study literature, and elderly people do not appear to benefit from therapeutic advances as much as other segments of the society; as we observe mortality rates from cancer shrink in the population under 70 years old, paradoxically an increase in mortality among those older than 70 years of age is recorded, suggesting an under-treatment of this age category [4].

Radiotherapy of an older person poses several levels of consideration from a radiobiologic point of view and a technical point of view [5]. A new irradiation technique, the CyberKnife® (Accuray Incorporated, Sunnyvale, CA), enables delivery of robotic radiotherapy administered in a stereotactic, hypofractionated fashion with respiratory tracking [6]. Its utilization has already been reported in the literature for several extra- and intracranial applications at the level of phase II studies [7]. The advantages this device presents with regard specifically to the treatment of an elderly patient appear to be numerous: by reducing the number of fractions due to the hypofractionated nature of the treatment, it proportionally reduces the number of times an elderly patient has to commute to the treatment center, and the number of times he or she is handled by the medical personnel. At the same time, CyberKnife offers an equally high-precision stereotaxy without a frame, but with constant tracking of the target lesion [8]. This fact provides an easy setup and thus relieves the difficulty of remaining motionless, and represents an overall more suitable treatment. On the other hand, use of a hypofractionated method does extend the treatment time of each fraction compared with conventional radiotherapy.

Here we report our experience in the treatment of elderly patients by CyberKnife at our center. We analyzed the method's feasibility with regard to the age of the patient based on 345 treatments.

2. Patients and methods

2.1. Patients

All patients treated at the Centre Oscar Lambret of Lille by CyberKnife between June 2007 and June 2009 were studied, constituting 345 treatments. Median age was 61 years (range, 8–86 years). The distribution of the patients' ages is shown in Fig. 1. Ninety-eight patients were over 70, 17 of whom were over 80; and 247 patients were younger than 70. The treated pathologies reflected the usual more-frequent extracranial application of CyberKnife, and included primary and metastatic liver tumors (88 patients, 35 over 70), head and neck cancers in previously irradiated regions (63 patients, 13 over 70), bone and vertebral re-irradiations (52 patients, nine over 70), non-small-cell lung cancers (48 patients, 21 over 70), and all other applications. For the hepatic lesion, the common treatment planning was 40 Gy (10 Gy × 4) or 45 Gy (15 Gy × 3). For the patients treated for head and neck recurrence the mean dose was 36 Gy (6 Gy × 6) and 60 Gy (20 Gy × 3 or 15 Gy × 4 or 10 Gy × 6) for lung cancer.

2.2. Endpoints of the study

The primary endpoint of the study was the feasibility of radiotherapy treatment with CyberKnife of a population over 70 years old compared with a population of reference made up of younger patients. The secondary endpoint was identification of factors that may have influenced the feasibility of the treatment. Then, we report our experience with irradiation of hepatic metastases for elderly patients in terms of efficacy and tolerance. Finally, a more specialized study of the sub-population of patients over 80 years old was also undertaken.

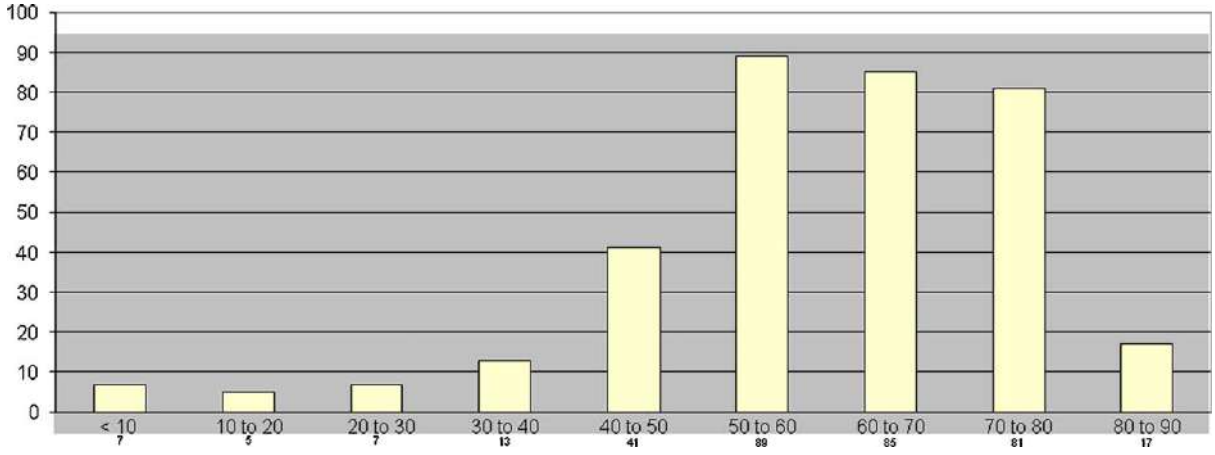

Fig. 1. Distribution of the ages of 345 patients treated by CyberKnife between June 2007 and June 2009.

2.3. Studied data

Discontinuation of the treatment or a prolonged interruption during the session was identified as major criteria with impact on the outcome of the patient. Cancelation of a session by the patient, toxicities requiring adjustments of dose or fractionation, physical problems requiring a temporary interruption (coughing, dyspnea, general malaise, unmaintainable treatment position, fatigue, pain, psychological reasons, etc.), patient setup challenges, and technical problems encountered during application of tracking techniques (Xsight® Spine, Xsight® Lung, Synchrony®, 6D Skull Tracking, or fiducial tracking) were identified as minor criteria. For each patient, duration of the sessions, total treatment time in days, number of fractions, tumor location, and the tracking technique were recorded. The ratio of the total treatment time in days to the number of fractions was calculated for each case to compare the rates of delivery. Furthermore epidemiologic data such as gender, age, OMS score, weight, height, existence of comorbidities, trend of weight loss, and number of medications taken by the patient were also collected. For patients over 80, we calculated the G8 score, which is a screening tool that allows identification of frailer patients for more profound geriatric evaluation [9–11].

2.4. Statistics

This is a retrospective, single-center study of all patients treated with CyberKnife. A comparative study by Student test, according to tumor sites and the techniques employed for each patient based on age (over or under 70, or over or under 80), along with a univariate analysis of potential causes effecting feasibility, were conducted. Proportions were compared using the chi-square test for values ≥ 5, and Fisher's exact test for those <5. All patients treated with CyberKnife signed an informed consent form authorizing the use of the collected data for scientific purposes.

3. Results

3.1. Feasibility

Between June 2007 and June 2009, we were able to conduct 345 CyberKnife treatments at the Centre Oscar Lambret of Lille, France. Mean time of a treatment session was 69.5 min (range, 17–199 min); it was 76.2 min for patients over 70 (at 95% CI, 69.6–82.9 min) vs. 66.8 min (at 95% CI, 62.5–71 min) for those under 70 years ($p = 0.019$). Within the elderly population, the mean session time was 83.4 min in patients over 80 (CI = 95%, 64.7–102.1 min) compared to 68.7 min (CI = 95%, 65–72.4 min) for those under 80 (p = ns). A study of the treatment time as a function of tumor location was done, and the results are shown in Fig. 2. For head and neck applications, mean treatment time was 47 min for all patients (CI = 95%, 44–50 min), 46.4 min for those over 70, and 47.2 min for those under 70 (p = ns). For hepatic applications, mean treatment time was 105.9 min (CI = 95%, 100–111.8 min), 105 min for those over 70 compared with 106 min for those under 70 (p = ns). Regarding lung tumors, mean treatment time was 63.8 min (CI = 95%, 54.3–73.4 min), 68.4 and 60.3 min for those over and under 70, respectively (p = ns). Mean treatment time for bony locations was 68.9 min (CI = 95%, 62.2–75.6 min), 60.3 for those over the age of 70 compared to 70.6 min for those younger than 70 (p = ns). Treatment times as a function of location and patient age are summarized in Table 1.

Table 1
Treatment time per session as a function of the location treated and age of patient.

	Treatment time in minutes (CI = 95%)		p
	Less than 70 years	More than 70 years	
All locations combined	66.8 (62.5–71)	76.2 (69.5–82.9)	0.019
Cancer UADT	47.2 (43.8–50.6)	46.4 (38.8–53.9)	0.821
Hepatic irradiation	106.2 (98.8–114.3)	105 (95.4–114.6)	0.807
Bronchial cancer	60.3 (45.7–74.9)	68.4 (56.1–80.6)	0.405
Bone irradiation	70.6 (63.3–78)	60.3 (40.4–80.3)	0.256

CI: confidence interval.

The length of a CyberKnife session can also depend on the tracking technique used in the treatment (see Fig. 3). For 6D Skull Tracking, mean treatment time was 42.4 min (CI = 95%, 38.9–45.9 min); 47.9 and 40.8 min for those over and under 70, respectively (p = ns). For Xsight Spine system, mean treatment time for all patients was 55.4 min (CI = 95%, 52–58.8 min), 54.3 min for those over 70 compared to 55.7 min for the younger patients (p = ns). Synchrony tracking allowed a mean treatment time per patient of 104.9 min (CI = 95%, 98.7–111 min), 107 min and 103.5 min for those over and under 70, respectively (p = ns). Xsight Lung tracking resulted in a mean treatment time of 80.4 min (CI = 95%, 66.6–94.1 min), 77.6 and 83.2 min for those over and under 70, respectively (p = ns). Finally, using the fiducial tracking system, mean treatment time was 70.9 min (CI = 95%, 60.4–81.5 min), 60.9 min for those over 70 vs. 75 min for the younger patients (p = ns) (see Table 2).

Median CyberKnife treatment was delivered over nine days (range, 1–77 days). Median number of fractions was four (1–31 fractions). Average fraction was delivered every 2.4 days (CI = 95%, 2.21–2.58 days). This interval was 2.37 and 2.46 days for those over and under 70, respectively (p = ns). Tumor location as a function of age did not carry any significance, either, nor did the treatment length or the fractionation scheme.

3.2. Major and minor criteria with potential impact on feasibility

Eleven major criteria were recorded during the 345 CyberKnife treatments. Treatment was not completed in 2% (2/98) of the cases in patients over 70 years old vs. 3.6% (9/247) among younger patients (p = ns). Both major events involved octogenarians. The first patient demonstrated dis-

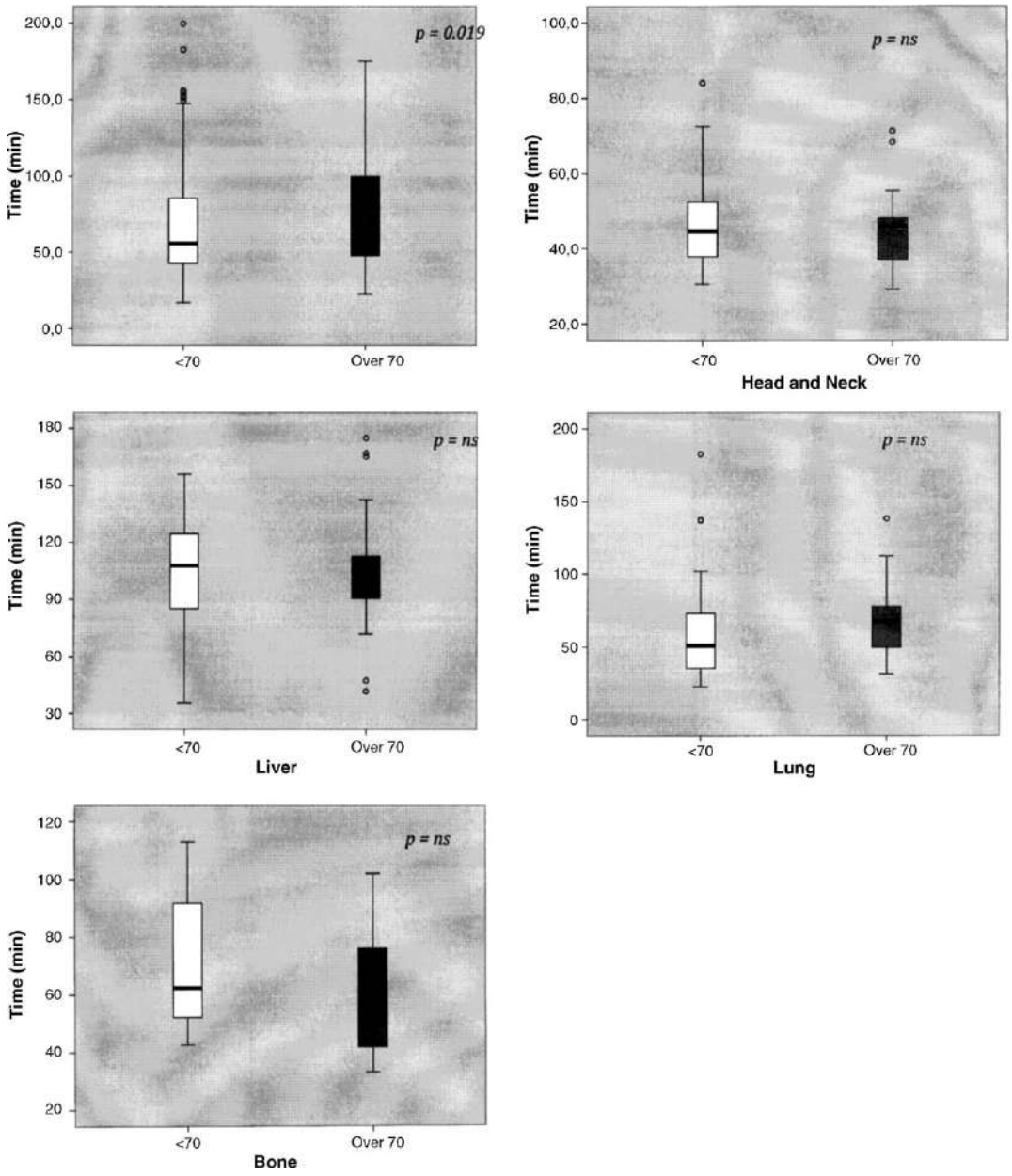

Fig. 2. Representation of treatment time as a function of age and tumor location.

Table 2
Treatment time per session as a function of the technique utilized and age of patient.

	Treatment time in minutes (CI = 95%)		*p*
	Less than 70 years	More than 70 years	
All techniques combined	66.8 (62.5–71)	76.2 (69.5–82.9)	0.019
Skull	40.8 (37.4–44.2)	47.9 (37.1–58.6)	0.092
Xsight Spine	55.7 (51.7–59.6)	54.3 (47.8–60.7)	0.745
Synchrony	103.5 (95–112)	107 (98–116)	0.59
Xsight Lung	83.2 (58.8–107.5)	77.6 (61.1–94)	0.68
Fiducials	75 (61.4–88.7)	60.9 (43.3–78.4)	0.214

CI: confidence interval.

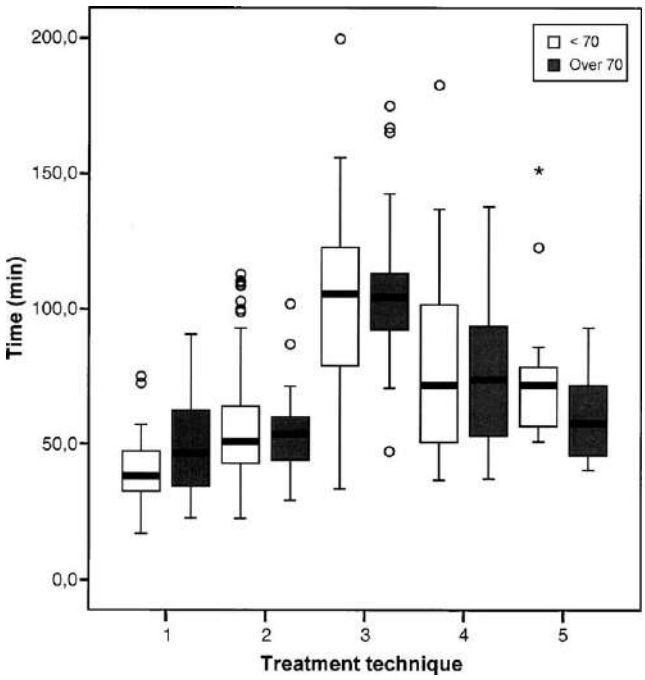

Fig. 3. Treatment time as a function of treatment technique by CyberKnife and age of patients (1 = Skull, 2 = Xsight Spine, 3 = Synchrony, 4 = Xsight Lung, 5 = Fiducials).

ease progression precluding the continuation of the treatment, and the second discontinued the sessions because of difficulty in maintaining the treatment position. Nine of the major events involved patients less than 70 years old. Four patients took a temporary break due to toxicity or an intercurrent acute event, one patient did not present for his sessions, and the rest permanently stopped due to disease progression or technical difficulties due to the device. Permanent or temporary interruption of the treatment did not correlate with age ($p = 0.09$).

Any physical difficulties related to the nature of the treatment were recorded. Sixteen of the 98 over-70 patients experienced a physical difficulty, whereas among younger patients, 29 difficulties were noted. Therefore there was no correlation between difficulties encountered during treatment and age ($p = 0.27$). Technical difficulties in image registration during treatment setup did correlate with the existence of physical difficulties of the patient ($p < 0.001$).

Difficulties in setting up the patient on the treatment couch were not connected to the age: over-70 patients encountered the same degree of difficulty climbing on the couch as did younger participants ($p = 0.2$).

3.3. Irradiation of hepatic metastases: efficacy and tolerance

Forty-three patients in our series were treated for liver metastases, 17 of whom were over 70. The patients harbored 66 hepatic targets, which were treated with CyberKnife at a dose of 40–45 Gy. Thirty-five complete responses were achieved without significant difference between the two age groups (13 in those over 70 and 22 in younger patients, $p = 0.68$). Similarly five lesions and two lesions in those under and over 70 progressed, respectively, without significance (p = ns). The number of grade 1–2 toxicities during the first three months involved seven patients over 70 compared with four younger patients ($p = 0.64$).

3.4. The treated population over the age of 80

The G8 score (from 8 to 14 points) was calculated retrospectively for all patients over 80 (Table 3). Of the 17 patients, six had a score that was $\leq$14 points. Thirteen presented with more than two co-morbidities at the time of CyberKnife treatment. Two major criteria events were observed in this population in the form of setup difficulties. No other setup difficulties were encountered in the general over-70 patient population ($p = 0.2$). Acute tolerance to treatment was described as excellent by 9 and as good by 7. One patient had to be hospitalized for a pulmonary embolism. The only acute toxicities found in this population were those of Grade 1: a type of asthenia (two patients), nausea/vomiting (one patient), and pain (one patient).

4. Discussion

We retrospectively reviewed the 345 stereotactic radiosurgery treatments performed at the Oscar Lambret Centre since June 2007. Over 28% of the patients were over the age of 70, constituting 98 of the treatments. Initially no significant difference based on treatment or fractionation was noted between the population over 70 and that under 70. The overall study of treatment time however did demonstrate a difference between the two groups ($p = 0.019$), which did not carry over to the analysis of subcategories such as the treatment location or the tracking technique (Figs. 2 and 3, and Tables 1 and 2). As far as the major and minor criteria were concerned (defined earlier), the comparative study of the two groups did not demonstrate a significant difference; the treatment was equally likely to be interrupted by members of the either age groups, both temporarily or indefinitely. Difficulties with patient setup or those experienced by the patient during the treatment were also not different in the two populations. This absence of difference in treatment feasibility with CyberKnife in patients over 70 was also the case clinically in terms of tumor control and toxicity. In fact in our series of hepatic metastases (unpublished data), 39.5% of patients were over the age of 70, and no significant difference was found in terms of complete response, target progression, or toxicity in that group, either.

Few studies in the literature reports specifically on the treatment of the elderly with CyberKnife. van der Voort van Zyp et al. reported an overall survival rate of 65% at one year and 44% at two years in octogenarians with stage 1 non-small cell lung cancer after CyberKnife [12]. The local control

Table 3
Characteristics of patients over the age of 80.

Patient	Age	Location	G8 score	Comorbidities > 2	Acute tolerance	Acute toxicity
1	86	Liver	14	Yes	Excellent	
2	81	Liver	14	No	Excellent	
3	80	Head and neck	8	Yes	Good	Pulmonary embolism
4	82	Liver	15	Yes	Good	Pain grade 1
5	86	Bone	14	Yes	Excellent	
6	81	Lung	16	No	Excellent	
7	82	Bone	15	Yes	Good	
8	81	Lung	16	No	Excellent	
9	81	Lung	14	No	Excellent	
10	82	Liver	16	Yes	Good	Nausea/asthenia grade 1
11	85	Lung	15	Yes	Good	
12	83	Lung	15	Yes	Good	
13	85	Lung	14	Yes	Excellent	
14	83	Liver	15	Yes	Good	Asthenia grade 1
15	83	Lung	16	Yes	Good	
16	81	Liver	15	Yes	Excellent	
17	80	Eye	15	Yes	Excellent	

rate was excellent (100%) and treatment-related toxicity was low. They concluded that CyberKnife offers a good treatment alternative for octogenarians in this case. Rare reports include patients over 80. Most studies are heterogeneous, concerning variable tumor locations, such as pancreatic and bronchial cancers, pelvic and prostatic tumors [5,7], and different treatment protocols.

The possibility of a patient selection bias exists in our retrospective study. It is ideal to evaluate all geriatric cancer patients using the Comprehensive Geriatric Assessment (CGA) guidelines to help eliminate such selection bias [13,14]. Such onco-geriatric evaluation criteria allow identification of the most vulnerable among elderly patients, in whom the risk/benefit ratio may vary [13]. But not all patients over 70 years require such systematic evaluation, and other screening methods have been implemented to circumvent this situation, like the VES-13 [15]. The G8 score that we employed in our study is also one of these screening methods. Retrospectively six patients over the age of 80 had a positive G8 score (35.3%), and therefore were likely to be frail. With regard to co-morbidities, 76.5% of patients over 80 had at least two co-morbidities in addition to their neoplastic disease during treatment. Co-morbidities are often factors that negatively influence the use of radiotherapy [16,17]. Nevertheless we believe being an elderly, frail person with several co-morbidities should not limit access to CyberKnife radiosurgery. On the contrary, in our opinion, the use of CyberKnife should be preferred in this type of patients, particularly because of the smaller number of sessions, thus fewer trips that the patient has to take to the treatment center, and the number of times he or she has to undergo the procedures of simulation, setup, and treatment.

Our results suggest that the novel radiation treatment modality known as CyberKnife should be fully accessible for elderly patients. Despite the relatively longer treatment sessions, the elderly patients seem to tolerate the treatment as well as their younger counterparts, and there is no discernible difference in the degree of feasibility between younger and older patients. Therefore CyberKnife should be considered a preferred treatment modality for older and particularly frailer patients.

5. Conclusion

Patients over the age of 70 did not demonstrate increased difficulty in maintaining treatment position, and the duration of their sessions did not appear longer than younger patients. Age did not influence the feasibility of irradiation, and the rate of indefinite discontinuation of treatment was not greater in the population over 70. Access to innovative therapies should not be restricted to those under an arbitrary threshold of 70 years. According to our data, CyberKnife treatment appears feasible, including in 70-year olds and over.

Conflict of interest statement

None declared.

Reviewer

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Biography

Eric Lartigau (M.D., Ph.D.) is professor of oncology from Lille 2 University and chairman of the academic radiotherapy department at Oscar Lambret Cancer Centre. He is currently the president of the French Radiotherapy Society (SFRO).