


# Routine surveillance imaging after end of therapy for pediatric extracranial tumors: A retrospective analysis

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## Abstract

Frequent surveillance imaging is routine practice for pediatric patients after cancer therapy. This retrospective study evaluated the follow-up of 301 children with extracranial tumors diagnosed between 2002 and 2012, at a tertiary pediatric cancer center in Beirut, Lebanon. Recurrence occurred in 15% of patients, at a median of 12 months after end of primary therapy. Outcome was not different comparing patients with recurrence detected via imaging surveillance versus clinically. False positive findings in 55 patients led to further interventions. These results raise important questions regarding benefit of current surveillance practices as standard care, especially in countries with limited resources.

## KEYWORDS

imaging, pediatric oncology, recurrence, surveillance

## 1 | INTRODUCTION

Current guidelines for follow-up after treatment for pediatric cancer involve regular surveillance imaging. Recently, this approach has been questioned, as early detection of recurrence has not been shown to definitively affect outcome.<sup>1,2</sup> In low- or middle-resource settings, the possibly unnecessary costs of such interventions further burden the healthcare system.

We retrospectively reviewed patient medical records at the American University of Beirut Medical Center (AUBMC) to investigate whether routine imaging impacts time to detection of recurrent disease and patient overall survival.

## 2 | METHODS

Patients diagnosed with extracranial solid tumors and lymphoma between January 2002 and December 2012 who achieved complete remission were included. Clinical information was collected until December 31, 2016, including age, tumor type, recurrence, time to recurrence, method of recurrence diagnosis, patient status at most recent follow-up, duration of follow-up, and number and type of routine

imaging performed and clinic visits. Data were analyzed using the SPSS software version 22, continuous variables using Student's *t*-test, and boxplot analysis using GraphPad Prism version 6.0 Software. A *P*-value less than 0.05 was considered statistically significant. Kaplan–Meier survival curves were generated to estimate overall survival, defined as time from recurrence to time of death from any cause, or most recent follow-up. The Institutional Review Board at the AUBMC approved this study.

## 3 | RESULTS

Of 309 identified patients, eight were excluded due to deficient charts, resulting in 301 patients. Median age was 10 years (range: 9 months–17 years), with tumor type distribution shown in Table 1. At the time of analysis, 45 patients (15%) had recurrence, at a median time of 12.2 months after end of treatment (range 1–69 months) (Table 1). Of the 256 patients in remission, 122 (47%) completed 5 years of follow-up, 54 (21%) moved away earlier than 5 years (median follow-up 32 months, range 4.1–48.7 months), and 80 (31%) were still undergoing surveillance (median follow-up 23 months, range 5.1–48.7 months). Follow-up period by tumor type is shown in Table 1.

The highest rates of recurrence occurred in patients with synovial sarcoma, neuroblastoma, and bone tumors (33, 28, and 23%,

**TABLE 1** Tumor type distribution and relapse rates

Tumor type	Number (% of total)	Recurrence (% of total recurrences)	Median months to relapse (range)	Median follow-up months <sup>a</sup> (range)
Hodgkin disease	84 (28)	9 (20)	17.3 (3–49)	71 (3.9–126)
Bone sarcoma	74 (24)	17 (38)	12.2 (2–65)	40 (15–65)
Non-Hodgkin lymphoma	39 (13)	2 (4)	9.6 (5–14)	35 (0.9–76)
Wilms tumor	36 (12)	2 (4)	5.5 (1–10)	51 (9.8–72)
Rhabdomyosarcoma	29 (10)	4 (9)	5.6 (3–69)	55 (4.9–81)
Neuroblastoma	25 (8)	7 (16)	21.0 (5–60)	32 (10.8–62)
Synovial sarcoma	9 (3)	3 (7)	14.0 (2–27)	52 (29–76)
Others	5 (2)	1 (2)	9	42.5 (23–92)
Total	301 (100)	45 (100)	12.2 (1–69)	46.5 (40–71)

<sup>a</sup>For patients continuing in remission.

respectively) at a median follow-up of 14, 21, and 12 months from end of treatment, respectively. The most common diagnoses among patients with recurrence were bone sarcoma (38% of recurrences), Hodgkin disease (20%), and neuroblastoma (16%), as shown in Table 1.

Of the 45 patients with recurrence, 19 (42%) presented with clinical signs including pain ( $n = 8$ ), lymphadenopathy ( $n = 4$ ), hematuria ( $n = 1$ ), numbness ( $n = 1$ ), fever ( $n = 1$ ), mass ( $n = 3$ ), and fatigue ( $n = 1$ ). The remainder ( $n = 26$ , 48%) had recurrence diagnosed during routine imaging. When analyzed by disease subtype, similar proportions of recurrences were detected by routine imaging versus clinical symptoms for patients with bone sarcoma and Hodgkin disease (Table 2). For Wilms tumor, there was one patient with recurrence detected in each group. Patients with neuroblastoma, rhabdomyosarcoma, and synovial sarcoma seemed to have recurrences detected more often by surveillance imaging, while the two patients with recurrence of Non-Hodgkin lymphoma had symptomatic disease (Table 2). Local recurrences accounted for five of the 19 (26%) detected by symptoms, and eight of the 26 (31%) detected by surveillance. There was no association between initial tumor risk group and method of detecting recurrence (Supplementary Table S1), within the limitation of the small number of patients in each subgroup.

The median time to detection of recurrence in the imaging-diagnosed group was 9.1 months, and 14.2 months in the clinically detected group ( $P$ -value = 0.2). Analysis of early (within 2 years after end of treatment) versus later recurrences by method of detection did not reveal a significant difference (odds ratio = 0.55, CI = 0.15–2.03,  $P$ -value 0.376).

When analyzed by disease subtype, patients with Hodgkin lymphoma whose recurrence was detected by surveillance had a significantly earlier median time to recurrence (Fig. 1A). Difference was not significant in patients with bone tumors, while for the remaining groups, patient numbers were too low for a comparison.

Of the 45 patients with recurrence, 25 (56%) subsequently died of disease, accounting for 47% of those diagnosed by symptoms, and 61% of those by imaging (Table 2). There was no demonstrable difference in outcome between the two groups (Fig. 1B).

Overall, patients had a median of 11 clinic visits and 14 imaging studies, with a range of 1–27 visits and 6–24 imaging studies per

patient, over a follow-up median of 49 months (range 5–129 months). Notably, 55 patients (18%) had one or more false-positive findings during surveillance, leading to further investigations, including 69 computed tomography (CT) scans, six gallium scans, 10 biopsies, one bronchoscopy, three positron emission tomography (PET) scans, three bone scans, and six magnetic resonance imaging scans.

## 4 | DISCUSSION

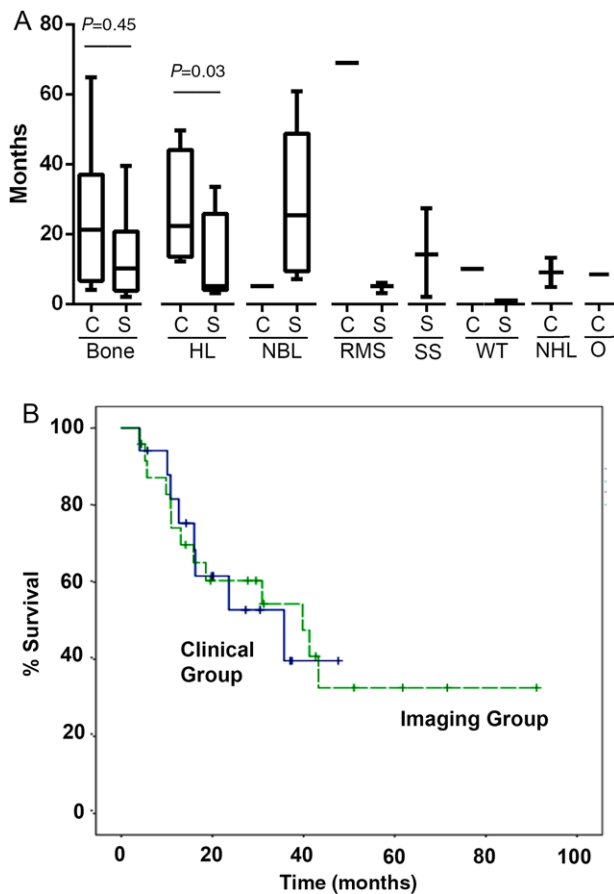
Our results add to the increasing literature raising the issue of risk versus perceived benefit of frequent imaging among survivors of childhood tumors. In our cohort of patients, those diagnosed clinically fared similar to those diagnosed by surveillance. For Hodgkin lymphoma, several studies have shown that surveillance with CT or PET/CT has minimum influence on overall patient survival once complete remission for 12–18 months has been sustained.<sup>2,3</sup> Hence, a current recommendation is to tailor surveillance imaging to patients with high risk of recurrence and high likelihood of benefit.<sup>4</sup> For non-Hodgkin lymphoma, one study showed that while three of 44 patients developed recurrence, none was diagnosed by CT or PET scans.<sup>5</sup> Two studies focusing on children with sarcoma and rhabdomyosarcoma, respectively, showed that regular imaging studies neither facilitated earlier detection of recurrence nor improved overall survival.<sup>6,7</sup> In Wilms tumor, routine surveillance CT scans of the pelvis were shown to be unnecessary, recommending substitution with abdominal ultrasound,<sup>8,9</sup> and in patients with Neuroblastoma, CT scans seem to minimally contribute to detection of recurrences.<sup>10</sup>

Our results highlight the fact that frequent surveillance imaging carries, in addition to the increased clinic visits, costs and radiation exposure, a high burden of false positive findings and their consequences. These included additional imaging, invasive procedures, and more frequent follow-up, all of which carry a high emotional and financial cost, as well as radiation exposure and risks of procedure-related complications.

Notably, for patients with neuroblastoma, rhabdomyosarcoma, and synovial sarcoma, the majority of recurrences were detected by imaging; however, the outcome in all cases was poor. For other tumors,

**TABLE 2** Patient outcome by mode of relapse detection and diagnosis group

Tumor type	Symptomatic		Routine imaging	
	Total	Died of disease (%)	Total	Died of disease (%)
Bone sarcoma	9	5 (56)	8	5 (62)
Hodgkin lymphoma	4	1 (25)	5	0
Neuroblastoma	1	1 (100)	6	5 (83)
Rhabdomyosarcoma	1	0	3	3 (100)
Synovial sarcoma	0	NA	3	2 (67)
Wilms tumor	1	0	1	1 (100)
Non-Hodgkin lymphoma	2	2 (100)	0	NA
Others	1	0	0	NA
Total	19	9 (47)	26	16 (61)

**FIGURE 1** Outcome analysis of patients with recurrence detected by clinical symptoms versus surveillance imaging. (A) Boxplot analysis of time to detection of relapse (number of months after end of treatment), detected by clinical symptoms (C) or by surveillance screening (S), shown by tumor type; P-values are shown for the groups where comparisons are possible. (B) Kaplan-Meier survival estimates by diagnosis method, as indicated

survival seemed similar in both detection groups, even though in Hodgkin lymphoma earlier recurrences were noted in the surveillance group. Thus, it would seem that, for tumors associated with poor outcome after recurrence, earlier detection by imaging is unlikely to

improve survival, while tumor types with available effective therapies likely do well irrespective of method of detection. The challenge is to identify whether specific patient subgroups would still benefit from surveillance and its optimal frequency.

Our study is limited by the small number of patients and by its retrospective nature. Well-designed randomized prospective studies are needed to evaluate a possible role for surveillance imaging in specific patient subgroups, which could have been missed in our study. Future studies should optimally be designed taking into account the known patterns of recurrence for each tumor type and initial risk status, and the expected associated salvage rates for locally recurrent and metastatic disease.

#### CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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## SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

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